NEDERLANDSE **TRANSPLANTATIE** VERENIGING

Bootcongres 2016

Wetenschappelijke voorjaarsvergadering

Nederlandse Transplantatie Vereniging

9 en 10 maart 2016

MartiniPlaza, Groningen

georganiseerd in samenwerking met

UMC Groningen Transplantatie Centrum

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UMC Groningen Transplantatie Centrum

Namens de organisatiecommissie van het UMC Groningen Transplantatie Centrum heet ik u van harte welkom op het 28ste Bootcongres van de Nederlandse Transplantatie Vereniging in Groningen.

Wij hebben geprobeerd dit jaar een aantal bijzondere thema's in het programma te groeperen. Daarbij is gekozen voor de thema's 'healthy ageing' na orgaantransplantatie, complexe (grensverleggende) transplantaties en technologische ontwikkelingen, zoals machinepreservatie. In het kader van deze thema's zal een aantal gerenommeerde Nederlandse en buitenlandse gastsprekers een voordacht geven.

Bovendien is een bijzonder groot aantal goede abstracts ingediend. Op basis hiervan hebben we een interessant en representatief programma kunnen samenstellen. De verschillende disciplines en thema's binnen de Nederlandse transplantatiewereld van basaal onderzoek tot en met patiëntgebonden evaluatie zijn alle goed vertegenwoordigd en zullen zeker weer uitmonden in de voor het Bootcongres zo kenmerkende actieve participatie met levendige discussie en inhoudelijke kruisbestuiving. Naast de orale presentaties zullen er wederom gemodereerde postersessies zijn waarin hopelijk levendige discussies over de inhoud van de posterpresentaties zullen ontstaan.

Vanzelfsprekend is er dit jaar weer een aparte onderwijssessie. Nieuw is een sessie voor de 'Young Investigators' waarbij het programma geheel door een aantal jonge onderzoekers zelf is ingevuld (wie de jeugd heeft, heeft tenslotte de toekomst).

Het Bootcongres kan niet worden georganiseerd zonder de hulp van velen, die wij zeer erkentelijk zijn voor hun inzet. Onze speciale dank gaat uit naar het secretariaat van de NTV, dat met enthousiasme zeer veel werk op efficiënte wijze heeft verricht. Ten slotte nog een woord van dank aan onze sponsors voor de onontbeerlijke steun aan onze vereniging en dit congres.

Namens de organisatiecommissie van het UMC Groningen Transplantatie Centrum wens ik u allen een boeiend, interactief en vooral ook plezierig congres!

Robert J. Porte
Voorzitter organisatiecommissie UMC Groningen Transplantatie Centrum

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Organisatiecommissie Bootcongres 2016

Vanuit het UMC Groningen Transplantatie Centrum
Robert J. Porte
Henri G.D. Leuvenink, mede namens bestuur NTV
Marion J. Siebelink
Glenda J. Bolt
en vele anderen

Bestuursleden Nederlandse Transplantatie Vereniging
Luuk B. Hilbrands
Marlies E.J. Reinders
Dave L. Roelen
Frank J.M.F. Dor
Luc J.W. van der Laan
Marion J.C. Wessels

Vanuit het secretariaat NTV te Haarlem
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Accreditatie is toegekend door de volgende verenigingen

Nederlandse Vereniging voor Heelkunde	
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Nederlandse Vereniging van Maag-Darm-Leverartsen	10
Nederlandse Internisten Vereniging	10
Nederlandse Vereniging voor Kindergeneeskunde	12
V&VN, kwaliteitsregister algemeen	12
V&VN, kwaliteitsregister, deskundigheidsgebied Dialyse	12
V&VN, verpleegkundig specialisten register	12

Op individuele basis kan accreditatie worden aangevraagd bij:

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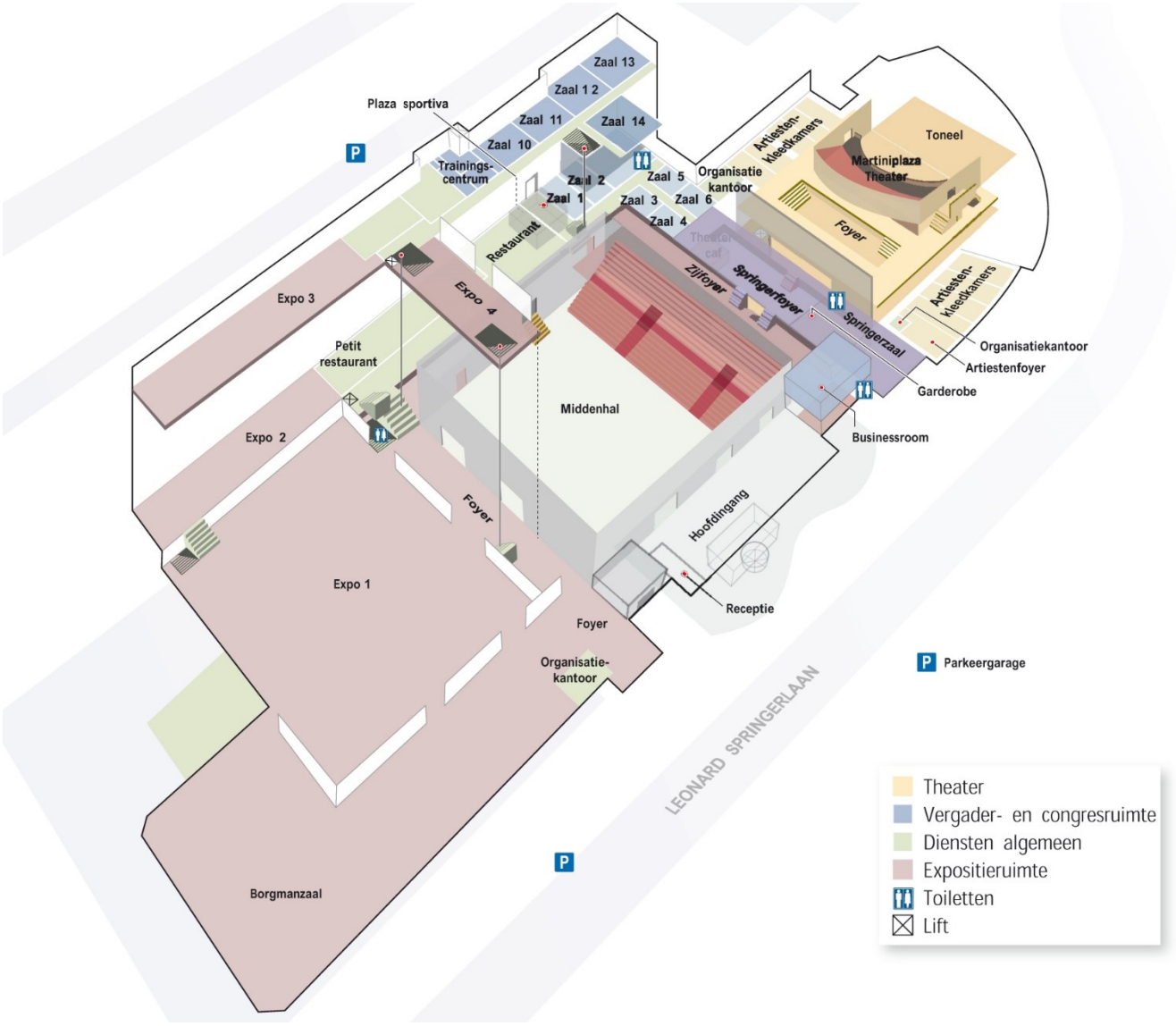

Inleveren presentaties

Wij verzoeken sprekers zo spoedig mogelijk na aankomst
de presentatie in te leveren in **zaal 4.**

Ophangen posters

De posters kunnen na aankomst worden opgehangen op de gereed staande (en genummerde) posterborden op de omloop boven de Theaterfoyer.

Locatie en tijdstippen van de maaltijden

Woensdag
Lunch: 13.00 – 14.00 uur in de Theaterfoyer
Lunch onderwijssessie Zaal 1+2 (lunchpakket) 13.00 – 14.00 uur
Walking dinner: Springerfoyer en Springerzaal 19.30 – 21.00 uur
Feestavond Springerzaal: 21.00 – 01.00 uur

Donderdag
Lunch*: 12.30 – 14.00 uur in de Theaterfoyer

* *tevens postersessie*

Bijeenkomsten voorafgaand en tijdens Bootcongres

Dinsdag 8 maart 2016

Landelijk Overleg Nier Transplantatie *Locatie: Mercure Hotel*	16.00 – 18.30
Landelijk Overleg Regionale Uitname Teams *Locatie: Apollo Hotel, Board Room*	16.00 – 18.30
Landelijke Werkgroep Transplantatie Verpleegkunde *Locatie: MartiniPlaza, zaal 1*	17.30 – 18.30
Landelijke Werkgroep Coördinatoren Donatie bij leven *Locatie: MartiniPlaza, zaal 1*	18.30 – 19.30

Woensdag 9 maart 2016

HLAi-meeting *Locatie: MartiniPlaza, zaal 3*	13.00 – 14.00
Medisch Ethische Commissie *Locatie: MartiniPlaza, theaterkantoor*	13.00 – 14.00
Ledenvergadering Nederlandse Transplantatie Vereniging *Locatie: Theaterzaal*	17.00 – 18.30

Schematisch overzicht programma
Woensdagochtend 9 maart 2016

Woensdag		**Theaterzaal**
09.30 –10.15 10.15 –10.25 10.25 –11.30		Ontvangst en registratie in Theaterfoyer Opening congres door voorzitter NTV Luuk Hilbrands en voorzitter LOC Robert Porte *Plenaire sessie I:* Thema: Grensverleggende transplantaties - Phillip Blondeel (Gent, België): Gezichtstransplantatie - Sijbrand Hofker (Groningen): Dunnedarmtransplantatie - Tallechien Tempelman en Patrick Khoe (Groningen): Buikwandtransplantatie
11.30 – 11.50	Koffiepauze Theaterfoyer	
11.50 – 12.55		*Plenaire sessie II:* Thema: Nieuwe uitdagingen in de transplantatiegeneeskunde - Boris Hogema (Sanquin Amsterdam): Hepatitis E infecties na transplantatie - Stefan Berger (Groningen): Transplantaties bij ouderen: is er een grens? - gevolgd door een tweetal abstractpresentaties
13.00 – 14.00	Lunchpauze/onderwijssessie	

Schematisch overzicht programma
Woensdagmiddag 9 maart 2016

Woensdag		**Theaterzaal**	**Zaal 1+2**	**Zaal 14**
13.00 – 14.00	Lunchpauze Theaterfoyer		*Onderwijssessie + lunchpakket* - Arnold v.d. Meer (UMCN) Donor Specific Antibodies - Aiko de Vries (LUMC) New Onset Diabetes Mellitus	
14.00 – 15.10		*Plenaire sessie III* Thema: Healthy ageing: Will you age in good health after organ transplantation? - Paul Corris (Newcastle, UK): Longterm survival after lung transplantation - Iwan van der Horst (Groningen): The heart after solid organ transplantation: diagnostics and treatment - gevolgd door een tweetal abstractpresentaties		
15.10 – 15.30	Theepauze Theaterfoyer			
		Zaal 5 + 6	**Zaal 1 + 2**	**Zaal 14**
15.30 – 17.00		*Parallelsessie IV* Basaal	*Parallelsessie V* Klinisch	*Parallelsessie VI* Patient in the lead

17.00 – 18.30		Ledenvergadering Nederlandse Transplantatie Vereniging		
19.30 – 21.00		Walking dinner Springerfoyer		
21.00 – 01.00		Feestavond met muziek Springerzaal		

Schematisch overzicht programma
Donderdagochtend 10 maart 2016

Donderdag		**Zaal 1+2**	**Zaal 5+6**	**Zaal 14**
09.00 – 10.30		*Parallelsessie VII* Basaal	*Parallelsessie VIII* Klinisch	*Parallelsessie IX* Donatie en Allocatie
10.30 – 10.50	Koffiepauze Theaterfoyer	**Na koffiepauze vervolg in Theaterzaal**		
10.50 – 12.20		*Plenaire sessie X* Thema: Machine Preservation of donor organs - Henri Leuvenink (Groningen): Principles of Machine Preservation - Gabriel Oniscu (Edinburgh, UK): Normothermic regional perfusion in DCD donors - Marcelo Cypel (Toronto, Canada): Machine perfusion of donor lungs - gevolgd door een tweetal abstractpresentaties		
12.30 – 14.00	Lunchbuffet Theaterfoyer	*Moderated Postersessie XI* Klinisch I en II Basaal I en II Donatie/Verpleegkundig/paramedisch		

Schematisch overzicht programma
Donderdagmiddag 10 maart 2016

Donderdag		**Zaal 1+2**	**Zaal 5 + 6**	**Zaal 14**
14.00 – 15.30		*Parallelsessie XII* Klinisch	*Parallelsessie XIII* Young investigators sessie Van Tx naar AEX, verder kijken dan uw promotie lang is Aan deze sessie zullen diverse sprekers een bijdrage leveren	*Parallelsessie XIV* Casuïstiek - Casus I - mevr. K de jonge (altruïstische) donor: Je bent jong en je wilt wat - Casus 2 - mevr. D De gerichte altruïstische donor: Facebook/media donor - Casus III: dhr. S Donor met overgewicht, wat zijn de risico's nu en in de toekomst
15.30 – 15.50	Theepauze Theaterfoyer			
		Theaterzaal		
15.50 – 16.55		*Plenaire sessie XV* Thema: Top 4 Best abstracts en Prijsuitreikingen - Vier beste abstracts - Uitreiking innovatie-kwaliteitsprijs 2016 - Lezing winnaar van de Astellas Trans(p)la(n)t(at)ionele Research Prijs 2015 en uitreiking prijs 2016 - Uitreiking Novartis Transplantation Awards 2016 - Uitreiking Jon J. van Roodprijs 2016, gevolgd door lezing van de prijswinnaar - Uitreiking Distinguished Research Award 2016		
16.55- 17.00	Sluiting congres door Robert Porte, voorzitter lokaal organisatiecomité			

Woensdag 9 maart 2016

Sessie I	**Plenair**	**Theaterzaal**

09.30 Ontvangst en registratie

10.15 Opening

Voorzitters: *Prof. dr. Luuk B. Hilbrands, voorzitter NTV, nefroloog Radboudumc,*
Prof. dr. Robert J. Porte, voorzitter GTC, chirurg, UMCG

Thema: ***Grensverleggende transplantaties***

10.25 **Gezichtstransplantatie**
Prof. dr. Phillip N. Blondeel, plastisch chirurg
Kliniek voor Plastische, Reconstructieve en Esthetische Chirurgie
Universitair Ziekenhuis Gent, België

10.55 **Dunnedarmtransplantatie**
Drs. Sijbrand Hofker, chirurg
Afd. Heelkunde, UMC Groningen

11.10 **Buikwandtransplantatie**
Drs. Tallechien M.T. Tempelman en Drs. Patrick C.K.H. Khoe, plastisch chirurgen, Afd. Plastische Chirurgie, UMC Groningen

11.30 Koffiepauze

Sessie II **Plenair** **Theaterzaal**

Voorzitters: *Dr. Annelies Riezebos, arts-microbioloog, UMC Groningen*
Dr. Marlies E.J. Reinders, internist-nefroloog, LUMC, Leiden

Thema: **Nieuwe uitdagingen in de transplantatiegeneeskunde**

11.50 **Hepatitis E infecties na transplantatie**
Drs. Boris Hogema,
Sanquin Amsterdam, Amsterdam

12.15 **Transplantaties bij ouderen: is er een grens?**
Dr. Stefan Berger, internist-nefroloog
Afd. Inwendige Geneeskunde, UMC Groningen

Voordrachten in het Nederlands spreektijd 7 minuten, discussietijd 3 minuten.

12.35 "I am not Sherlock Holmes": suspicions, secrecy and silence of transplant professionals in the organ trade (p. 58)
F. Ambagtsheer[1], L. van Balen[1], W. Weimar[1], [1]Dept of Internal Medicine, Transplantation and Nephrology, Erasmus MC, Rotterdam, The Netherlands

12.45 Mesenchymal stem cells maintain immunomodulatory capacity after cell death (p. 59)
F. Luk[1], S.F.H. de Witte[1], M. Franquesa[1], S.S. Korevaar[1], T. Strini[1], F.J.M.F. Dor[2], M.G.H. Betjes[1], C.C. Baan[1], M.J. Hoogduijn[1], [1]Dept of Nephrology and Transplantation and Dept of Internal Medicine, [2]Dept of Transplant Surgery and Dept of Surgery, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

12.55 Lunchpauze

Woensdag 9 maart 2016

Onderwijssessie — Zaal 1+2

Voorzitters: *Marion J.C. Wessels, MA, verpleegkundig specialist, UMC Utrecht*
Dr. Luc J.W. van der Laan, Universitair Hoofddocent, Erasmus MC

13.00 **Donor Specific Antibodies**
Dr. Arnold van der Meer, transplantatie-immunoloog
Afd. Lab Medische Immunologie, Radboudumc, Nijmegen

13.30 **New Onset Diabetes Mellitus**
Dr. Aiko P.J. de Vries, internist-nefroloog
Afd. Nefrologie, UMC Leiden

Plenaire sessie III – Plenair — Theaterzaal

Voorzitters: *Dr. Nicolle H.R. Litjens, post-doc, Erasmus MC*
Dr. Erik A.M. Verschuuren, internist-klinisch immunoloog, UMCG

Thema: **Healthy ageing:**
Will you age in good health after organ transplantation?

14.00 **Long term survival after lung transplantation**
Prof. dr. Paul Corris, Professor of Thoracic Medicine
Department of Respiratory Medicine, Newcastle University, UK

14.30 **The heart after solid organ transplantation: diagnostics and treatment**
Dr. Iwan van der Horst, cardioloog-intensivist
Intensive Care Volwassenen, UMC Groningen

Plenaire sessie III – Plenair **Theaterzaal**

Voordrachten in het Engels, spreektijd 7 minuten, discussietijd 3 minuten.

14.50 Self-monitoring renal function after transplantation: a clinical trial on safety and usability (p. 60)

C. van Lint[1]; S. van Dijk[1,5]; M. van Diepen[2], W. Wang[3]; W-P. Brinkman[3]; T. Rövekamp[4]; M. Neerincx[3]; T. Rabelink[1] and P. van der Boog[1] [1]Dept. of Nephrology, Leiden University Medical Centre; [2]Dept. of Epidemiology, Leiden University Medical Centre; [3]Faculty of Computer Science, Delft University of Technology; [4]Technology in Healthcare, Prevention and Health, TNO, Leiden; [5]Dept. of Health, Medical and Neuropsychology and Behavioural Sciences, Leiden University.

15.00 Steroid-free maintenance immunosuppression or calcineurin inhibitor minimization compared to standard quadruple immunesuppression in kidney transplantation Interim analysis of the ALLEGRO trial (p. 61)

M.S. van Sandwijk[1], A.P.J. de Vries[2], S.J. Bakker[3], I.J.M. ten Berge[1], S.P. Berger[3], J.W. de Fijter[2], J.J. Homan van der Heide[1], M.M. Idu[1], C. Krikke[3], K.A.M.I. van der Pant[1], M.E. Reinders[2], J. Ringers[2], N.C. van der Weerd[1], F.J. Bemelman[1#] and J.S. Sanders[3#]. Renal Transplant Unit[1], Academic Medical Center, Amsterdam, Department of Nephrology[2], Leiden University Medical Center, Department of Nephrology[3], University Medical Center Groningen, The Netherlands. *[#]Both authors contributed equally to this work.*

15.10 Theepauze

Parallelsessie IV – Basaal — Zaal 5+6

Voorzitters: *Dr. Martin. J. Hoogduijn, wetenschappelijk medewerker, Erasmus MC*
Prof. dr. Cees. van Kooten, onderzoeker, LUMC

Voordrachten in het Engels, spreektijd 7 minuten, discussietijd 3 minuten.

15.30 MicroRNA profiles in graft preservation solution are associated with early allograft dysfunction after liver transplantation (p. 62)
J.W. Selten[1], C.J. Verhoeven[1], H.P. Roest[1], R.W.F. de Bruin[1], J. de Jonge[1], J.N.M. IJzermans[1], L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus MC, Rotterdam, The Netherlands

15.40 Defective post-reperfusion metabolic recovery directly associates with incident delayed graft function in human kidney transplantation (p. 63)
L.G.M. Wijermars[1], A.F. Schaapherder[1], D.K. de Vries[1], L. Verschuren[1], R.C.I. Wüst[1], S. Kostidis[1], O.A. Mayboroda[1], F. Prins[1], J. Ringers[1], J. Bierau[1], J.A. Bakker[1], T. Kooistra[1], J.H.N. Lindeman[1], [1]Dept of Surgery, Leiden University Medical Center, Leiden, The Netherlands

15.50 Orthotopic liver transplantation following dual machine perfusion in the mouse (p. 64)
M. Fujiyoshi[1], T.A. Berendsen[1], R. van Rijn[1], R. Porte[1], [1]Dept of Hepatobiliary Surgery and Liver Transplantation, University Medical Center Groningen, Groningen, The Netherlands

16.00 Serum miRNAs as potential biomarkers for the bronchiolitis obliterans syndrome after lung transplantation (p. 65)
K. Budding[1], M. Rossato[1,2], E.A. van de Graaf[3], T.R.D.J. Radstake[1,2], H.G. Otten[1], [1]Laboratory of Translational Immunology, [2]Dept of Rheumatology & Clinical Immunology, [3]Dept of Respiratory Medicine, University Medical Center Utrecht, Utrecht, The Netherlands

Parallelsessie IV – Basaal **Zaal 5+6**

16.10 Retrograde flushing of the pulmonary vein during explantation: lymphocyte composition in the perfusate and impact on outcome after lung transplantation (p. 66)
K. Budding[1], E.A. van de Graaf[2], T. Kardol-Hoefnagel[1], E.-J.D. Oudijk[3], H.G. Otten[1], [1]Laboratory of Translational Immunology, and [2]Dept of Respiratory Medicine, University Medical Center Utrecht, Utrecht, [3]Center of Interstitial Lung Diseases, St. Antonius Hospital, Nieuwegein, The Netherlands

16.20 Technique for ex vivo lung perfusion (EVLP) of lungs from brain-dead donor rats and testing the effect of prednisolone treatment (p. 67)
J. van Zanden[1], H. Leuvenink[2], E. Verschuuren[3], S. Veldhuis[2], P. Ottens[2], M. Erasmus[1], M. Hottenrott[1], [1]Dept of Cardiothoracic Surgery, [2]Dept of Surgery, and [3]Dept of Pulmonary Diseases, University Medical Center Groningen, Groningen, The Netherlands

16.30 ER stress and loss of GRP78 expression provides a link between renal ischemia/reperfusion injury and the urinary metabolome (p. 68)
T. Pacchiarotta[1], P. van der Pol[2], J.W. de Fijter[2], N. Schlagwein[2], D.J. van Gijlswijk[2], O.A. Mayboroda[1], C. van Kooten[2], [1]Centre for Proteomics and Metabolomics, and [2]Dept of Nephrology, Leiden University Medical Centre, Leiden, The Netherlands

16.40 Slow induction of brain death leads to decreased renal function and increased hepatic apoptosis in rats (p. 69)
R. Rebolledo[1,2], D. Hoeksma[1*], C.M.V. Hottenrott[3], Y. Bodar[1], P.J. Ottens[1], J. Wiersema-Buist[1], H.G.D. Leuvenink[1], [1]Dept of Surgery, University Medical Center Groningen, Groningen, The Netherlands, [2]Physiopathology Program, Institute of Biomedical Sciences, Faculty of Medicine, University of Chile, Chile, [3]Dept of Cardiothoracic Surgery, University Medical Center Groningen, Groningen, The Netherlands*

16.50 Samenvatting door sessie voorzitters

17.00 Einde sessie, NTV ledenvergadering in de Theaterzaal

Parallelsessie V – Klinisch — Zaal 1+2

Voorzitters: *Dr. Dennis A. Hesselink, internist-nefroloog, Erasmus MC*
Dr. Marieke Roemeling, MDL-arts i.o., UMC Groningen

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

15.30 Improvement of gynaecological screening of female renal transplant recipients by self-sampling for HPV detection (p. 70)
F. Hinten[1], L. Hilbrands[2], K. Meeuwis[3], M. van Bergen-Verkuyten[4], B. Slangen[5], M. van Rossum[3], J. Rahamat-Langendoen[4], L. Massuger[1], J. de Hullu[1], W. Melchers[4], [1]Dept of Obstetrics and Gynaecology, [2]Dept of Nephrology, [3]Dept of Dermatology, and [4]Dept of Medical Microbiology, Radboud University Medical Center, Nijmegen, [5]Dept of Obstetrics and Gynaecology, Maastricht University Medical Centre, Maastricht, The Netherlands

15.40 Fractional excretion of NGAL instead of 99mTcMAG3 renography to monitor resolution of delayed graft function (p. 71)
J.R. Bank[1], M.E.J. Reinders[1], L. Noordermeer[1], M.J.K. Mallat[1], S.W. van der Kooij[1], C. van Kooten[1], J.W. de Fijter[1], [1]Dept of Nephrology, Leiden University Medical Center, Leiden, The Netherlands

15.50 Long-term effects of living kidney donation on renal function, blood pressure and survival (p. 72)
M.H. de Borst[1], M.F.C. de Jong[1], S.J.L. Bakker[1], R.T. Gansevoort[1], G. Navis[1], S.P. Berger[1], [1]Dept of Internal Medicine, Division of Nephrology, University Medical Center Groningen, Groningen, The Netherlands.

16.00 Predicted Indirectly ReCognizable HLA Epitopes presented by HLA-DRB1 (PIRCHE-II) are related to HLA-antibody formation during pregnancy (p. 73)
K. Geneugelijk[1], G. Hönger[2], H.W. van Deutekom[3], K.A. Thus[1], C. Keşmir[3], I. Hösli[4], S. Schaub[5] and E. Spierings[1], [1]Laboratory for Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Laboratory for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland, [3]Dept of Theoretical Biology and Bioinformatics, Utrecht University, Utrecht, [4]Dept for Obstetrics and Fetomaternal Medicine, University Hospital Basel, Basel, Switzerland, [5]Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland

Parallelsessie V – Klinisch **Zaal 1+2**

16.10 MicroRNAs in urinary sediments as non-invasive tool to detect acute rejection after kidney transplantation (p. 74)
E.M. Gielis[1,2], J.D.H. Anholts[2], J.W. de Fijter[3], I. Bajema[4], S. Heidt[2], F.H.J. Claas[2], M. Eikmans[2], [1]Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Belgium, [2]Dept of Immunohematology and Blood Transfusion, [3]Dept of Nephrology, and [4]Dept of Pathology , Leiden University Medical Center, Leiden, The Netherlands

16.20 Elevated intragraft expression of innate immunity and cell death-related markers characterizes deceased donor conditions and is a risk factor for adverse graft outcome (p. 75)
J. Yang[1], G. Haasnoot[1], C. van Kooten[2], M. Mallat[2], H. de Fijter[2], I. Bajema[3], F.H.J. Claas[1], M. Eikmans[1], [1]Dept of Immunohematology and Blood Transfusion, [2]Dept of Nephrology, and [3]Dept of Pathology, Leiden University Medical Center, Leiden, The Netherlands

16.30 Fecal microbiota transplantation against intestinal Extended Spectrum beta-Lactamase producing Enterobacteriaceae colonization in renal transplant and non-transplant patients (p. 76)
R. Singh[1], S.E. Geerlings[2], P.F. de Groot[3], M. Nieuwdorp[3], C.J. Hodiamont[4], R.J.M. ten Berge[1], F.J. Bemelman[1], [1]Division of Nephrology, Renal transplant Unit, [2]Div. of Infectious Diseases, and [3]Divof Vascular Medicine, Dept of Internal Medicine, [4]Dept of Medical Microbiology, Academic Medical Center, University of Amsterdam, The Netherlands

16.40 Resting energy expenditure in end-stage cystic fibrosis patients before and after lung transplantation (p. 77)
F.M. Hollander[1,2], A. Kok[1], N.M. de Roos[3], G. Belle-van Meerkerk[2], E.A. van de Graaf[2], [1]Division of Internal Medicine and Dermatology, Dept of Dietetics, and [2]Cystic Fibrosis and Lung Transplantation Center, University Medical Center Utrecht, Utrecht, [3]Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands

Woensdag 9 maart 2016

16.50 Pancreas donor quality and donor risk indices in pancreas allocation in the Eurotransplant region (p. 78)
C.A.T. van Leeuwen[1,2], W.H. Kopp[1,2], E. de Vries[1], J. de Boer[1], H. Putter[3], W. Schareck[4], U. Samuel[1], A.E. Braat[2], [1]Eurotransplant International Foundation, Leiden, The Netherlands, [2]Dept of Surgery, and [3]Dept of Medical Statistics, Leiden University Medical Center, Leiden, The Netherlands, [4]University Hospital Rostock, Rostock, Germany

17.00 Einde sessie, NTV ledenvergadering in de Theaterzaal

Parallelsessie VI – Patiënt in the lead — Zaal 14

Voorzitters: Dr. Stefan P. Berger, internist-nefroloog, UMC Groningen
Drs. Coby H. Annema, Verpleegkundig onderzoeker, UMC Groningen

15.30 – 17.00 uur

Sessie met patiëntenverenigingen:
shared decision making en anonimiteit

Abstract *Voordracht in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.*

Anonymity in deceased organ donation in The Netherlands: a gap between law and practice (p. 79)
D.G. Georgieva[1], E.T.M. Schiks[1], B.J.J.M. Haase-Kromwijk[1], Nederlandse Transplantatie Stichting, Leiden, The Netherlands

Panel discussie

17.00 Einde sessie, NTV-ledenvergadering in de Theaterzaal

Ledenvergadering NTV — Theaterzaal

17.00 Algemene ledenvergadering
Vergaderstukken vanaf 1 maart beschikbaar via
www.transplantatievereniging.nl

Walking dinner	**Springerfoyer**

19.30 Ontvangst en walking dinner

Feestavond	**Springerzaal**

21.00 Feestavond met band: Groove Department

Parallelsessie VII – Basaal, immunologie Zaal 1+2

Voorzitters: *Dr. Hennie G. Otten, medisch immunoloog, UMC Utrecht*
Dr. Laura B. Bungener, medisch immunoloog, UMC Groningen

Voordrachten in het Engels, spreektijd 7 minuten, discussietijd 3 minuten.

09.00 IL-21 receptor antagonist ATR-107: pioneer in decreasing humoral immunity in an allogeneic setting (p. 80)
K. de Leur[1,2], F.J.M.F. Dor[2], M. Dieterich[1], J.N.M. IJzermans[2], M.G. Betjes[1], R.W. Hendriks[3], C.C. Baan[1], [1]Dept of Internal Medicine, [2]Dept of Surgery, Division of HPB & Transplant Surgery, and [3]Dept of Pulmonary Medicine, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

09.10 Increase of highly differentiated CD4+CD28null T-cells is associated with a reduced risk for early acute renal transplant rejection (p. 81)
B. Dedeoglu[1], R.W.J. Meijers[1*], M. Klepper[1], D.A. Hesselink[1], C.C. Baan[1], N.H.R. Litjens[1], M.G.H. Betjes[1], *Both authors contributed equally to this work, [1]Dept of Internal Medicine, Section of Nephrology and Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands*

09.20 Tissue priming of plasmacytoid dendritic cells enhances their phagocytosis and lowers the threshold for subsequent Toll-like receptor 7/9 activation (p. 82)
J.M. Ruben[1], G. Garcia-Romo[1], E. Breman[1], S.W. van der Kooij[1], S.W.A. Kamerling[1], A. Redeker[2], R. Arens[2], C. van Kooten[1], Dept of Nephrology[1], and [2]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Centre, Leiden, The Netherlands

09.30 Premature ageing of T cells In end-stage renal disease patients does not predict infectious complications after renal transplantation (p. 83)
B. Dedeoglu[1], R.W.J. Meijers[1], M. Klepper[1], D.A. Hesselink[1], C.C. Baan[1], N.H.R. Litjens[1], M.G.H. Betjes[1], [1]Dept of Internal Medicine, Section Transplantation and Nephrology, Erasmus University Medical Centre, Rotterdam, The Netherlands

Parallelsessie VII – Basaal **Zaal 1+2**

09.40 End-stage renal disease does not impair the large-scale generation of potent alloantigen-specific regulatory T cells for immunotherapy (p. 84)
N.H.R. Litjens[1], K. Boer[1], J.M. Zuijderwijk[1], M. Klepper[1], A.M.A. Peeters[1], W. Verschoor[1], R. Kraaijeveld[1], C.C. Baan[1], M.G.H. Betjes[1], [1]Dept of Internal Medicine, Nephrology and Transplantation, Erasmus University Medical Centre, Rotterdam, The Netherlands

09.50 Belatacept does not inhibit plasmablast formation supported by follicular T helper cells, but favors the development of transitional regulatory B cells in kidney transplant patients (p. 85)
G.N. de Graav[1], D.A. Hesselink[1], M. Dieterich[1], R. Kraaijeveld[1], W. Weimar[1], C.C. Baan[1], [1]Dept of Internal Medicine, Section Transplantation and Nephrology, Erasmus University Medical Centre, Rotterdam, The Netherlands

10.00 Antigenic targets of local antibodies produced in Ectopic Lymphoid Structures in Cardiac Allografts (p. 86)
M.M.H. Huibers[1], J.M.T. Beerthuijzen[1], A.J. Gareau[2], E. Siera-de Koning[1], J. van Kuik[1], E.G. Kamburova[3], N. de Jonge[4], T.D.G. Lee[5,6 7], H.G. Otten[3], R.A. de Weger[1], [1]Dept of Pathology, [4]Dept of Cardiology, and [3]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Dept of Internal Medicine, University of Manitoba, Canada, [5]Dept of Pathology, [6]Dept of Surgery, and [7]Dept of Microbiology and Immunology, Dalhousie University, Halifax, Canada

10.10 A CD59 promotor polymorphism in donor lungs correlates with a higher risk for chronic rejection after lung transplantation (p. 87)
K. Budding[1], E.A. van de Graaf[2], T. Kardol-Hoefnagel[1], J.C.A. Broen[1,3], J.M. Kwakkel-van Erp[2], E.-J.D. Oudijk[4], D.A. van Kessel[4], C.E. Hack[1,3], and H.G. Otten[1], [1]Laboratory of Translational Immunology, [2]Dept of Respiratory Medicine, and [3]Dept of Rheumatology and Dermatology, University Medical Center Utrecht, Utrecht, [4]Center of Interstitial Lung Diseases, St. Antonius Hospital, Nieuwegein, The Netherlands

10.20 Samenvatting door sessie voorzitters

10.30 Koffiepauze

Parallelsessie VIII – Klinisch — Zaal 5+6

Voorzitters: *Dr. Robert A. Pol, vaat- en transplantatiechirurg, UMC Groningen*
Dr. Wojaiech G. Polak, chirurg, Erasmus MC

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

09.00 Center volume is associated with outcome following pancreas transplantation within the Eurotransplant region (p. 88)
W.H. Kopp[1,2], M. van Meel[2], H. Putter[3], U. Samuel[2], H. Arbogast[4,6], W. Schareck[5,6], J. Ringers[1,6], A.E. Braat[1], [1]Dept of Surgery, Division of Transplantation, and [3]Dept of Statistics, Leiden University Medical Center, Leiden, The Netherlands, [2]Eurotransplant International Foundation, Leiden, The Netherlands, [4]Klinikum Großhadern, Chirurgische Klinik und Poliklinik, Munich, Germany, [5]University Hospital Rostock, Rostock, Germany, [6]Eurotransplant Pancreas Advisory Committee

09.10 Use of extended criteria donor organs is a risk factor for pancreas graft thrombosis (p. 89)
C.A.T. van Leeuwen[1], W.H. Kopp[1], H. de Kort[2], J.W. de Fijter[3], H. Putter[4], A.G. Baranski[1], A.F.M. Schaapherder[1], J. Ringers[1], A.E. Braat[1], [1]Dept of Surgery, Leiden University Medical Center, Leiden, [2]Academic Medical Center, Amsterdam, [3]Dept of Nephrology, and [4]Dept of Statistics, Leiden University Medical Center, Leiden, The Netherlands

09.20 Influence of donor warm ischemia time on development of acute kidney injury after DCD liver transplantation (p. 90)
M. Kalisvaart[1], J.E. de Haan[2], D.A. Hesselink[3], W.G. Polak[1], B.E. Hansen[4], J.N.M. IJzermans[1], H.J. Metselaar[4], J. de Jonge[1], [1]Dept of Surgery, Division of Transplant Surgery, [2]Dept of Intensive Care, [3]Dept of Internal Medicine, Division of Nephrology and Renal Transplantation, and [4]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

Parallelsessie VIII – Klinisch **Zaal 5+6**

09.30 Low-pressure pneumoperitoneum facilitated by deep neuromuscular blockade during laparoscopic donor nephrectomy is associated with reduced length of hospital stay (p. 91)
D. Özdemir-van Brunschot[1], G.J. Scheffer[1], M. van der Jagt[1], H. Langenhuijsen[3], A. Dahan[4], J.E. Mulder[2], S. Willems[2], L.B. Hilbrands[5], C.J. van Laarhoven[1], F.A. d'Ancona[1], M.C. Warlé[1], [1]Dept of Surgery, [2]Dept of Anesthesiology, [3]Dept of Urology, and [5]Dept of Nephrology, Radboud University Medical Center, Nijmegen, [4]Dept of Anesthesiology, Leiden University Medical Centre, Leiden, The Netherlands

09.40 A Short Period of Oxygenated Hypothermic Machine Perfusion Prior to Normothermic Machine Perfusion Improves Bile Output and Bile Composition of Extended Criteria Donor Livers (p. 92)
A.P.M. Matton[1,2], Y. de Vries[1,2], R. van Rijn[1,2], A.C. Westerkamp[1,2], L.C. Burlage[1,2], N. Karimian[1,2], A.S.H. Gouw[3], T. Lisman[1], R.J. Porte[2], [1]Surgical Research Laboratory, and [2]Section of Hepatobiliary Surgery and Liver Transplantation, Dept of Surgery, and [3]Dept of Pathology, University of Groningen, Groningen, The Netherlands

09.50 Hepatocyte- and Cholangiocyte-derived MicroRNAs in Perfusate and Bile during Ex-Situ Normothermic Machine Perfusion of Human Donor Livers (p. 93)
A.P.M. Matton[1,2], H.P. Roest[3], C.J. Verhoeven[3], N. Karimian[1,2], S. op den Dries[1,2], M.E. Sutton[1,2], J. de Jonge[3], L.J.W. van der Laan[3], R.J. Porte[2], [1]Surgical Research Laboratory, and [2]Section of Hepatobiliary Surgery Surgery and Liver Transplantation, Dept of Surgery, University of Groningen, University Medical Center Groningen, [3]Dept of Surgery, Erasmus University Medical Centre, Rotterdam, The Netherlands

10.00 Evaluation of in-hospital complications after liver transplantation with the comprehensive complication index: potential benefit of DCD grafts in post alcoholic cirrhosis? (p. 94)
M. Kalisvaart[1], J.E. de Haan[2], W.G. Polak[1], B.E. Hansen[3], J.N.M. IJzermans[1], H.J. Metselaar[3], J. de Jonge[1], [1]Dept of Surgery, Division of Transplant Surgery, [2]Dept of Intensive Care, and [3]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

Parallelsessie VIII – Klinisch — Zaal 5+6

10.10 The relationship between health literacy, self-management and complications after kidney transplantation (p. 95)
L. Maasdam[1], M.C. van Buren[1], M. Tielen[1], M. Cadogan[1], W. Weimar[1], E.K. Massey[1], [1]Dept of Internal Medicine, Kidney Transplant Unit, Erasmus Medical Center, Rotterdam, The Netherlands

10.20 Samenvatting door sessie voorzitters

10.30 Koffiepauze

Parallelsessie IX – Donatie en allocatie — Zaal 14

Voorzitters: Dr. Marion J. Siebelink, programmamanager UMC Groningen Transplantatie Centrum
Dr. Raechel J. Toorop, vaat- en transplantatiechirurg, UMC Utrecht

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

09.00 Predictors for longer-term health-related quality of life of living kidney donors: A prospective multicenter study (p. 96)
L. Wirken[1,2], H. van Middendorp[1,2], C.W. Hooghof[3], J.S. Sanders[4], R.E. Dam[5], K.A.M.I. van der Pant[6], E.C.M. Berendsen[7], H. Wellink[8], P. Ulrichts[9], A.J. Hoitsma[3], L.B. Hilbrands[3], A.W.M. Evers[1,2], [1]Health, Medical and Neuropsychology Unit[1], Leiden University, Leiden, [2]Dept of Medical Psychology, and [3]Dept of Nephrology, Radboudumc, Nijmegen, [4]Dept of Internal Medicine, University Medical Center Groningen, Groningen, [5]Dept of Nephrology, Leiden University Medical Center, Leiden, [6]Dept of Internal Medicine/Nephrology, Academic Medical Center, Amsterdam, [7]Dept of Nephrology, University Medical Centre Utrecht, Utrecht, [8]Dept of Nephrology, VU University Medical Center, [9]Dept of Internal Medicine/Nephrology, Maastricht University Medical Center, The Netherlands

Parallelsessie IX – Donatie en allocatie **Zaal 14**

09.10 Overweight young female donors have a lower post-donation reserve capacity (p. 97)
M. van Londen[1], G.J. Navis[1], M.H. de Borst[1], A.T. Lely[2], [1]Dept of Nephrology, University Medical Center Groningen, Groningen, [2]Dept of Gynaecology and Obstetrics, University Medical Center Utrecht, Utrecht, The Netherlands

09.20 Pregnancy outcomes in a Dutch living kidney donation population (p. 98)
M.C. van Buren[1], C.A.J. Oudmaijer[1], L. Maasdam[1], M. Tielen[1], M.G.H. Betjes[1], J. van de Wetering[1], [1]Dept of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands

09.30 The development of a nurse-led self-management intervention for kidney transplant recipients using intervention mapping: The ZENN-study (p. 99)
D.K. Beck[1], J.W. Grijpma[1], M. Tielen[1], M.C. de Haan–van Buren[1], J.M.J. Been-Dahmen[3], M.A.C. Peeters[3], M.W.F. van den Hoogen[1], T. van Gelder[1], J. van Busschbach[2], A. van Staa[3,4], M. Betjes[1], W. Weimar[1], E.K. Massey[1], [1]Dept of Internal Medicine, and [2]Dept of Psychiatry, Erasmus Medical Center Rotterdam, [3]Research Centre Innovations in Care, Rotterdam University, [4]Institute of Health Policy & Management (iBMG), Erasmus University Rotterdam, The Netherlands

09.40 Living elderly kidney donors: more investigations, lesser kidneys (p. 100)
L.L. de Haan[1], F.C.H. D'Ancona[2], H.L. Langenhuijsen[2], M. vd Jagt[3], M. Warle[3], Ph.M.M. Dooper[1], H.J. Kloke[1], Dept of Nephrology[1], Dept of Urology[2], and Dept of Surgery[3], Radboud University Medical Centre, Nijmegen, The Netherlands

09.50 Mortality of young biliary atresia patients listed for liver transplantation: results from the Eurotransplant registry (p. 101)
H.P.J. van der Doef[1], P.F. van Rheenen[1], M. van Rosmalen[2], X. Rogiers[2], H.J. Verkade[1], [1]Groningen Transplant Center, Dept of Pediatrics, University of Groningen, University Medical Center Groningen, [2]Eurotransplant, Leiden, The Netherlands

Parallelsessie IX – Donatie en allocatie — Zaal 14

10.00 Infections and their impact on waiting list survival in patients with end stage liver disease (p. 102)
L.J.M. Alferink[1], C.A.M. Schurink[2], W.G. Polak[3], R.M. De Man[1], B.E. Hansen[1 4], H.J. Metselaar[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Medical Microbiology and Infectious Diseases, [3]Dept of Surgery, and [4]Dept of Public Health, Erasmus University Medical Center, Rotterdam The Netherlands

10.10 Non-anastomotic biliary strictures are more severe after transplantation of donation after circulatory death, compared to donation after brain death livers (p. 103)
Y. de Vries[1], C.I. Buis[1], S.V.K. Mahesh[2], A.P. Van den Berg[3], R.J. Porte[1], [1]Dept of Surgery and Liver Transplantation, [2]Dept of Radiology, and [3]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands

10.20 Samenvatting door sessie voorzitters

10.30 Koffiepauze

Sessie X Plenair — Theaterzaal

Voorzitters: Prof. dr. L.W. Ernst van Heurn, chirurg, AMC / VUmc Amsterdam
Dr. Cyril Moers, chirurg, UMC Groningen

Thema: Machine Preservation of donor organs

10.50 **Principles of Machine Preservation**
Prof. dr. Henri Leuvenink, onderzoeker
Afd. Chirurgie, UMC Groningen

11.00 **Normothermic regional perfusion in DCD donors**
Mr. Gabriel Oniscu, Consultant Transplant Surgeon and Honorary Clinical Senior Lecturer, Transplant Unit,
Royal Infirmary of Edinburgh, Edinburgh, U.K.

Sessie X **Plenair** **Theaterzaal**

11.30 **Machine perfusion of donor lungs**
Dr. Marcelo Cypel, Thoracic Surgeon
Division of Thoracic Surgery, University of Toronto, Canada

Abstracts *Voordrachten in het Engels, spreektijd 7 minuten, discussietijd 3 minuten.*

12.00 Oxygenated hypothermic machine perfusion after static cold storage improves endothelial function of extended criteria donor livers (p. 104)
L.C. Burlage[1,2], N. Karimian[1,2], A.C. Westerkamp[1,2], N. Visser[2], S. Op den Dries[1,2], M.E. Sutton[1,2], A.P.M. Matton[1,2], R. Van Rijn[1,2], J. Adelmeijer[2], A.S.H. Gouw[3], T. Lisman[1,2], R.J. Porte[1], [1]Dept of Surgery, Section of Hepatobiliary Surgery and Liver Transplantation, [2]Surgical Research Laboratory, and [3]Dept of Pathology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

12.10 Normothermic Machine Perfusion of Donor Livers Using a Novel Hemoglobin Based Oxygen Carrier Solution, Eliminating the Need for Human Blood Products (p. 105)
A.P.M. Matton[1,2], L.C. Burlage[1,2], R. van Rijn[1,2], S.A. Karangwa[1,2], Y. de Vries[1,2], M.M.W. Nijsten[3], S. Op den Dries[1,2], M. Sutton[1,2], A. Westerkamp[1,2], T. Lisman[1], R.J. Porte[2], [1]Surgical Research Laboratory, [2]Section of Hepatobiliary Surgery and Liver Transplantation, Dept of Surgery, and [3]Dept of Critical Care, University. of Groningen, Groningen, The Netherlands

12.30 Lunchbuffet en postersessies

Postersessie XI Klinisch I

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

12.30 – 13.00

Moderator: Dr. Jan Stephan F. Sanders, internist/nefroloog, UMC Groningen

1. Intima Media Thickness (IMT) and Major Adverse Cardiac Events (MACE) in patients after kidney transplantation (p. 120)
M. van Dijk[1], A. M. van Roon[1], F.J. Bemelman[2], J.W. de Fijter[3], A.P.J. de Vries[3], J.J. Homan van der Heide[2], J.S. Sanders[1], [1]Dept of Nephrology, University Medical Center Groningen, Groningen, [2]Dept of Nephrology, Academic Medical Center, Amsterdam, [3]Dept of Nephrology, University Medical Center Leiden, Leiden, The Netherlands

2. Incidence, risk factors and treatment of incisional hernia after kidney transplantation; an analysis of 1564 consecutive patients (p. 121)
L.S.S. Ooms[1], J. Verhelst[1*], J. Jeekel[2], J.N.M. IJzermans[1] , J.F. Lange[1], T. Terkivatan[1], [1]Dept of Surgery, and [2]Dept of Neuroscience, Erasmus University Medical Center, Rotterdam, The Netherlands*

3. Suprapubic ureteric stenting in kidney transplantation; does the type of stent matter? (p. 122)
L.S.S. Ooms[1], L.G. Spaans[1], M.G.H. Betjes[2], J.N.M. IJzermans[1], T. Terkivatan[1], [1]Dept of Surgery, Division of Transplant Surgery, and [2]Dept of Internal Medicine, Division of Nephrology, Erasmus Medical Center, University Medical Center Rotterdam, The Netherlands

4. One year post-VZV booster: still equal response in renal transplant recipients compared to healthy persons (p. 123)
M.M.L. Kho[1], W. Weimar[1], M.J. Boer-Verschragen[1], A.A. van der Eijk[2], N.M. van Besouw[1], [1]Dept of Internal Medicine – Nephrology and Transplantation, and [2]Dept of Viroscience, Erasmus Medical Center, Rotterdam, The Netherlands

5. Treatment with tacrolimus versus cyclosporine A is a delicate balance between BK virus replication and rejection in renal transplant recipients (p. 124)
L. Gard[1], W. van Doesum[2*], H.G.M. Niesters[1], W.J. van Son[2], A. Diepstra[3], C.A. Stegeman[2], A. Riezebos-Brilman[1], J.S.F. Sanders[2], [1]Dept of Medical Microbiology, Division of Clinical Virology, [2]Dept of Internal Medicine, Division of Nephrology, and [3]Dept of Pathology, University of Groningen, University Medical Centre Groningen, Groningen, The Netherlands.* **Contributed equally to this work.*

Postersessie XI Klinisch I

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

13.00 – 13.30

Moderator: Dr. A.P.J. de Vries, nefroloog, LUMC

6. Is it clinically relevant to perform a protocol MAG3 scan postoperative?: A retrospective monocentric study (p. 125)
B. Schmitjes[1], A. van der Zande[1], M.W.F. van den Hoogen[2], [1]Medical student, and [2]Dept of Internal Medicine, Renal Transplantation Unit, Erasmus Medical Center, Rotterdam The Netherlands

7. Predictors of postoperative cardiovascular complications until three months after kidney transplantation (p. 126)
M.C. Slot[1,2], J. van de Wetering[1], M.M.L. Kho[1], M.G.H. Betjes[1], J.I. Roodnat[1], [1]Dept of Kidney Transplantation, Erasmus Medical Center, Rotterdam, [2]Dept. of Nephrology, VU Medical Center, Amsterdam, The Netherlands

8. A successful approach to kidney transplantation in patients with secondary hyperoxaluria (p. 127)
J.I. Roodnat[1], A.M.E. de Mik-van Egmond[2], W.J. Visser[2], S. Berger[3], W.A.G. van der Meijden[4], F. Knauf[5], M. van Agteren[1], M.G.H. Betjes[1], E.J. Hoorn[1], [1]Dept of Internal Medicinem, and [2]Dept of Dietetics, Erasmus University Medical Center, Rotterdam, The Netherlands, [3]Dept of Internal Medicine, University Hospital Groningen, The Netherlands, [4]Dept of Internal Medicine, Radboud University, Nijmegen, The Netherlands, [5]Dept of Nephrology and Hypertension, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Germany

9. Barriers and facilitators in regular gynaecological screening of female renal transplant recipients (p. 128)
F. Hinten[1], R. Hermens[2], K.A.P. Meeuwis[3], M. van der Linden[1], L.F.A.G. Massuger[1], W.J.G. Melchers[4], L.B. Hilbrands[5], J.A. de Hullu[1], [1]Dept of Obstetrics and Gynaecology, [2]Dept of IQ Healthcare, [3]Dept of Dermatology, [4]Dept of Medical Microbiology, and [5]Dept of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands

10. HPV prevalence before and after renal transplantation in females with end-stage renal disease (p. 129)
F. Hinten[1], L. Hilbrands[2], K. Meeuwis[3], J. IntHout[4], W.G.V. Quint[5], A.J. Hoitsma[2], L. Massuger[1], W. Melchers[6], J. de Hullu[1], [1]Dept of Obstetrics and Gynaecology, [2]Dept of Nephrology, [3]Dept of Dermatology, [4]Dept of Health Evidence, [6]Dept of Medical Microbiology, Radboud University Medical Center, Nijmegen, [5]Delft Diagnostic Laboratory, Delft, The Netherlands

Postersessie XI Klinisch I

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

13.30 – 14.00

Moderator: Prof. dr. Jaap Homan van der Heide, nefroloog, AMC

11. Donor comprehension of provided information during informed consent process in live donor nephrectomy; does it matter what we tell donors? A pilot study (p. 130)
K. Kortram[1], E.Q.W. Spoon[1], C.W.N. Looman[2], H.J.A.N. Kimenai, J.N.M. IJzermans[1], F.J.M.F. Dor[1], [1]Dept of Surgery, Division of HPB & Transplant Surgery, [2]Dept of Public Health, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

12. Towards a standardized informed consent procedure for live donor nephrectomy: What do surgeons tell potential donors? (p. 131)
K. Kortram[1], J.N.M. IJzermans[1], F.J.M.F. Dor[1], [1]Dept of Surgery, Division of HPB & Transplant Surgery, Erasmus MC University Medical Center, Rotterdam, The Netherlands Netherlands

13. Peri-operative events and complications in minimally-invasive live donor nephrectomy: what should we tell potential donors? A systematic review and meta-analysis (p. 132)
K. Kortram[1], J.N.M. IJzermans[1], F.J.M.F. Dor[1], [1]Dept of Surgery, Division of HPB & Transplant Surgery, Erasmus MC University Medical Center, Rotterdam, The Netherlands

14. Which way to stent the ureter? – comparison of 2 ways of urinary drainage in pediatric kidney transplantation (p. 133)
A.S. ter Haar[1], R.S. Parekh[4], R.W.J. Leunissen[1], J. van den Hoek[2], A. Lorenzo[5], D. Hebert[4], M.G. Keijzer-Veen[1,3], K. Cransberg[1], [1]Dept of Pediatric Nephrology, and [2]Dept of Pediatric Urology, Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands, [3]Dept of Pediatric Nephrology, University Medical Center Utrecht-WKZ Utrecht, The Netherlands, [4]Dept of Pediatric Nephrology, and [5]Dept of Pediatric Urology, The Hospital for Sick Children, Toronto, Canada

15. Circulatory support and the immediate graft function in pediatric kidney transplantation (p. 134)
M. Pheninckx[1], A.M. Terpstra[1], C.E.J. Sloots[2], A. Gonzalez Candel[3], H. de Jong[1], E.A.M. Cornelissen[4], A.H. Bouts[5], M. Voet-Lindner[6], K. Cransberg[1], [1]Dept of Pediatric Nephrology, [2]Dept of Pediatric Surgery, and [3]Dept of Pediatric Anesthesiology, Erasmus University Medical Center, Rotterdam, [4]Dept of Pediatric Nephrology, Radboud University Medical Centre, Nijmegen, [5]Dept of Pediatric Nephrology, Academic Medical Centre, Amsterdam, [6]Dept of Pediatric Anesthesiology, Radboud University Medical Centre, Nijmegen, The Netherlands

Postersessie XI Klinisch II

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

12.30 – 13.00

Moderator: Prof. dr. Herold Metselaar, MDL-arts, Erasmus MC Rotterdam

16. Systematic review and meta-analysis of the impact of computed tomography assessed skeletal muscle mass on outcome in patients awaiting or undergoing liver transplantation (p. 135)
J.L.A. van Vugt[1], S. Levolger[1], R.W.F. de Bruin[1], J. van Rosmalen[2], H.J. Metselaar[3], J.N.M. IJzermans[1], [1]Dept of Surgery, [2]Dept of Biostatistics, and [3]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

17. Optimizing microRNA biomarker detection in liver graft presservation solution by counteracting heparin-mediated inhibition (p. 136)
H.P. Roest[1], J.W. Selten[1], C.J. Verhoeven[1], R.W.F. de Bruin[1], J. de Jonge[1], J.N.M. IJzermans[1], L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus Medical Center–University Medical Center, Rotterdam, The Netherlands

18. Pretransplant HRCT Characteristics are Associated with Worse Outcome of Lung Transplantation for Cystic Fibrosis Patients (p. 137)
G. Belle-van Meerkerk[1,2], P.A. de Jong[3], H.W. de Valk[2], T. Neefjes[3], F.A. Pameijer[3], J.M. Kwakkel-van Erp[1], E.A. van de Graaf[1], [1]Dept of Respiratory Medicine, [2]Dept of Internal Medicine, and [3]Dept of Radiology[3], University Medical Centre Utrecht, Utrecht, The Netherlands

19. Effect of recipient length and type of diagnosis on waiting time for lung transplantation candidates (p. 138)
L.H. Rijsman[1], K. Aamri[1], R.C.A. Meijer[1], G. van Aarnhem[1], E. Oudijk[2], J.M. Kwakkel-van Erp[1], E.A. van de Graaf[1], P.Zanen[1], B. Luijk[1], [1]Dept of Respiratory Medicine, University Medical Center Utrecht, Utrecht, [2]Dept of Respiratory Medicine, St. Antonius Hospital, Nieuwegein, The Netherlands

Postersessie XI Klinisch II

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

20. High incidence of herpes zoster after kidney, liver, heart and lung transplantation (p. 139)
N.M. van Besouw[1], S. Roest[2], D.M. Bovée[1], H.J. Metselaar[3], R.A.S. Hoek[4], J.J. van Weezel[4], A.A. van der Eijk[5], W. Weimar[1], O.C. Manintveld[2], M.M.L. Kho[1], [1]Dept of Internal Medicine-Nephrology & Transplantation, [2]Dept of Cardiology, [3]Dept of Gastroenterology and Hepatology, [4]Dept of Respiratory Medicine, and [5]Dept of Viroscience, Erasmus University Medical Center, Rotterdam, The Netherlands

Postersessie XI Klinisch II

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

13.00 – 13.30

Moderator: Drs. Christina Krikke, chirurg, UMC Groningen

21. Plasma alemtuzumab levels show great interpatient variability, but are not associated with late acute rejection in simultaneous pancreas-kidney recipients (p. 140)
J.R. Bank[1], M.J.K. Mallat[1], C.M. Jol-van der Zijde[2], R.G. Bredius[2], P.J.M. van der Boog[1], A.E. Braat[3], J. Ringers[3], M.E.J. Reinders[1], J.W. de Fijter[1], [1]Dept of Nephrology, [2]Dept of Pediatrics, and [3]Dept of Surgery, Leiden University Medical Center, Leiden, The Netherlands

22. Development of donor specific antibodies after islet-after-kidney transplantation (p. 141)
M.F. Nijhoff[1,2], H. Bouwsma[2], H.J.W. de Fijter[2], T.A. Rabelink[2], D.L. Roelen[3], E.J.P. de Koning[1,2], [1]Dept of Endocrinology, Dept of Nephrology and Transplantation, and [3]Dept of Immunology, Leiden University Medical Centre, Leiden, The Netherlands

Postersessie XI Klinisch II

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

23. The role of methylprednisolone in the rescue of functional graft loss after islet rejection (p. 142)
M.F. Nijhoff[1,2], H. Bouwsma[2], J. Ringers[3], J.W. de Fijter[2], T.A. Rabelink[2], E.J.P. de Koning[1,2], [1]Dept of Endocrinology, [2]Dept of Nephrology and Transplantation, and [3]Dept of Surgery, Leiden University Medical Centre, Leiden, The Netherlands

24. Islet Donor Risk Score: an evidence-based IEQ prediction model (p. 143)
J.B. Doppenberg[1], W.H. Kopp[2], H. Putter[3], A.E. Braat[2], M.A. Engelse[1], E.J.P. de Koning[1], [1]Dept of Internal Medicine, [2]Dept of Surgery, and [3]Dept of Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, The Netherlands

25. Identification of non-HLA antibody targets in kidney transplantation for a new diagnostic assay (p. 144)
L.A. Michielsen[1], H.G. Otten[2], M.M. Krebber[1], A.D. van Zuilen[1], M.C. Verhaar[1], [1]Dept of Nephrology and Hypertension, [2]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands

Postersessie XI Klinisch II

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

13.30 – 14.00

Moderator: Dr. Arjan van Zuilen, nefroloog, UMCU

26. IVIG and high dose steroid treatment of transplant glomerulopathy effectively slows progression of loss of renal allograft function (p. 145)
K.A. Sablik[1], C.W.N. Looman[2], M.C. Clahsen-van Groningen[3], J. Damman[3], D.L. Roelen[4], M. van Agteren[1], M.G.H. Betjes[1], [1]Dept of Nephrology and Transplantation, [2]Dept of Biostatistics, and [3]Dept of Pathology, Erasmus University Medical Center, Rotterdam, [4]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands

Postersessie XI Klinisch II

27. Discontinuation of mycophenolate mofetil does not significantly change blood pressure in renal transplant patients: results of the TacMono study (p. 146)
A.E. de Weerd[1], M. Boer-Verschragen[1], E.J. Hoorn[1], M.G.H. Betjes[1], [1]Dept of Nephrology, Erasmus Medical Center, Rotterdam, The Netherlands

28. Pregnancy in patients with a renal transplant: role of immune-suppressive drugs in pregnancy outcome (p. 147)
D. Feyaerts[1], O.W.H. van der Heijden[2], H. Zweers[2], B. van Cranenbroek[1], I. Joosten[1], H.W. van Hamersvelt[3], R.G. van der Molen[1], [1]Dept of Laboratory Medicine, [2]Dept of Obstetrics and Gynaecology, and [3]Dept of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands

29. Influence of donor factors and operative technique on surgical outcome in a cohort comprising 18 years of mini-incision and laparoscopic kidney donation (p. 148)
K. Ramdhani[1], A Haasnoot[1], A.E. Braat[1], A.G. Baranski[1], V.A.L. Huurman[1], [1]Dept of Transplant Surgery, Leiden University Medical Center, Leiden, The Netherlands

Postersessie XI Basaal I

Poster presentaties in het Engels, spreektijd 3 minuten, discussietijd 1 minuut.

12.30 - 13.00

Moderator: Dr. Ron W.F de Bruin, wetenschappelijk onderzoeker, Erasmus MC, Rotterdam

30. Whole blood phospho-specific flowcytometry reveals the influence of immunosuppressive drugs on monocyte activation after kidney transplantation (p. 149)
N.M. Kannegieter[1], D.A. Hesselink[1], R. Kraaijeveld[1], G.N. de Graav[1], M.G.H. Betjes[1], W. Weimar[1], C.C. Baan[1], [1]Dept of Internal Medicine, Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands

Postersessie XI Basaal I

31. TNFR2-agonist facilitates high purity expansion of human Treg starting from low purity isolated Treg (p. 150)
X. He[1], S. Landman[1], S. Bauland[2], J. van den Dolder[3], H.J.P.M. Koenen[1], I. Joosten[1*], *Bots authors contributed equally to this work, [1]Dept of Laboratory Medicine, Laboratory of Medical Immunology, Radboud University Medical Center, Nijmegen, [2]Sanavisie, Mill, [3]Hycult Biotech, Uden, The Netherlands*

32. CD86-expression on monocytes and B cells as a tool for therapeutic drug monitoring of belatacept (p. 151)
G.N. de Graav[1], D.A. Hesselink[1], W. Verschoor[1], M. Dieterich[1], T. van Gelder[1], W. Weimar[1], C.C. Baan[1], [1]Dept of Internal Medicine, Section Transplantation and Nephrology, Erasmus Medical Center, Rotterdam, The Netherlands

33. High numbers of pre-transplant donor-specific IL-21 producing cells predicts acute rejection after kidney transplantation (p. 152)
N.M. van Besouw[1], R. de Kuiper[1], M.C. Clahsen[1], Y. Wu[1], J.N.M. IJzermans[1], D.A. Hesselink[1], C.C. Baan[1], [1]Dept of Internal Medicine-Nephrology & Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands.

34. Characterization of Polyomavirus BK-specific CD8+ T cells in renal transplant recipients suffering from viral reactivation (p. 153)
M.C. van Aalderen[1,2], E.B.M. Remmerswaal[1,2], K.M. Heutinck[1,2], A. ten Brinke[3], K.A.M.I. van der Pant[2], N.C. van der Weerd[2], F.J. Bemelman[2], M.C. Feltkamp[4], R.A.W. van Lier[3], I.J.M. ten Berge[1,2], [1]Dept of Experimental Immunology, and [2]Renal Transplant Unit, Division of Internal Medicine, Academic Medical Centre, Amsterdam, [3]Sanquin Research, Amsterdam, [4]Dept of Medical Microbiology, Leiden University Medical Centre, Leiden, The Netherlands

Postersessie XI Basaal 1

Poster presentaties in het Engels, spreektijd 3 minuten, discussietijd 1 minuut.

13.00 – 13.30

Moderator: Dr. Nicolle H.R. Litjens, post-doc, Erasmus MC Rotterdam

35. The role of syndecan-1 in the interaction between dendritic cells and T cells (p. 154)
M. Kouwenberg[1], L Hilbrands[1], J van der Vlag[1], [1]Dept of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands

36. Endogenous Interleukin-37 diminishes CXCL1 release by dendritic cells upon stimulation with TLR ligands (p. 155)
W.P.C. Pulskens[1], L.A. Joosten[2], C.A. Dinarello[2,3], L.B. Hilbrands[1], J. van der Vlag[1], [1]Dept of Nephrology, and [2]Dept of General Internal Medicine, Radboud University Medical Center, Nijmegen, The Netherlands, [3]Dept of Medicine, University of Colorado, Denver, Aurora, CO USA

37. End stage renal disease patients have a skewed T cell receptor Vbeta repertoire (p. 156)
L. Huang[1], A.W. Langerak[2], I.L.M. Wolvers-Tettero[2], R.W.J. Meijers[1], C.C. Baan[1], N.H.R. Litjens[1], M.G.H. Betjes[1], [1]Dept of Internal Medicine, Section Nephrology and Transplantation, [2]Dept of Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands

38. The impact of allograft rejection on DNA methylation after kidney transplantation (p. 157)
K. Boer[1], L.E.A. de Wit[1], D.A. Hesselink[1], L.J. Hofland[2], M.G.H. Betjes[1], C.C. Baan[1], [1]Dept of Internal Medicine, Nephrology and Transplantation, and [2]Dept of Endocrinology, Erasmus University Medical Center, Rotterdam, The Netherlands

39. Immunosuppressive medication and DNA methylation of the Interferon-gamma promoter in T cells (p. 158)
F.S. Peters[1], A.M.A. Peeters[1], L.J. Hofland[2], M.G.H. Betjes[1], K. Boer[1], C.C. Baan[1], [1]Dept of Internal Medicine, Nephrology and Transplantation, and [2]Dept of Endocrinology, Erasmus University Medical Center, Rotterdam, The Netherlands

Postersessie XI Basaal 1

Poster presentaties in het Engels, spreektijd 3 minuten, discussietijd 1 minuut.

13.30 – 14.00

Moderator: Prof. dr. Irma Joosten, immunoloog, Radboudumc, Nijmegen

40. Is the Kidney Donor Risk Index a predictor of graft failure in the Dutch Kidney transplantation population? (p. 159)
M.F.J. van der Heide[1], J.W. de Fijter[2], L. Wijermars[1], H. Putter[3], A.F.M. Schaapherder[1], V.A.L. Huurman[1], [1]Dept of Transplant Surgery, [2]Dept of Nephrology, and [3]Dept of Medical Statistics, Leiden University Medical Center, Leiden, The Netherlands

41. Mesenchymal stromal cells undergo major changes during therapeutic application (p. 160)
M.J. Hoogduijn[1], S.F.H. de Witte[1], F. Luk[1], M.C.G.N. van den Hout-van Vroonhoven[2], L. Ignatowicz[3], R. Catar[4], T. Strini[1], S.S. Korevaar[1], W.F.J. van IJcken[2], M.G.H. Betjes[1], M. Franquesa[1], G. Moll[4,5,6], C.C. Baan[1] Nephrology and Transplantation[1], Dept. of Internal Medicine, and Center for Biomics[2], Erasmus MC, Rotterdam, Netherlands; Dept. of Dermatology and Venerology[3], Lund University, Sweden; Dept. of Nephrology and Intensive Care Medicine[4], and Berlin-Brandenburg School for Regenerative Therapies[5] (BSRT), Charité Universtätsmedizin Berlin, Germany; [6]Division of Therapeutic Immunology (TIM), Dept. of Laboratory Medicine (LABMED), Karolinska Institutet, Stockholm

42. Optimizing the immunogenicity and immunomodulatory properties of MSC (p. 161)
S.F.H. de Witte[1], M. Franquesa[1], T. Strini[1], S.S. Korevaar[1], F. Luk[1], S.J. Elliman[2], P.N. Newsome[3], M. Gargesha[4], D. Roy[4], A.M. Merino Rodriguez[1], C.C. Baan[1], M.J. Hoogduijn[1], [1]Dept of Internal Medicine, Nephrology and Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Orbsen Therapeutics Ltd., Galway, Ireland, [3]Dept of NIHR Liver Biomedical Research Unit and Centre for Liver Research, University of Birmingham, UK, [4]BioInVision Inc., Mayfield Village, OH, USA

Postersessie XI Basaal I

43. The delicate balance between fraud and patient care (p. 162)
B.G. Hepkema[1], L. Bungener[1], C. Roozendaal[1], A.Lambeck[1], B.J. Kroesen[1], S. Berger[2], [1]Dept of Laboratory Medicine, Transplantation Immunology, and [2]Dept of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

Postersessie XI Basaal II

Poster presentaties in het Engels, spreektijd 3 minuten, discussietijd 1 minuut.

12.30 – 13.00

Moderator: Prof. dr. Carla C. Baan, hoofd transplantatie laboratorium, Erasmus MC Rotterdam

44. A Novel, Rapid, Efficient, Automated, Pancreatic Islet Isolation Technique (p. 163)
J.B. Doppenberg[1], M.A. Engelse[1], E.J.P. de Koning[1], [1]Dept of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands

45. Preliminary results of isolated islets after hypothermic machine perfusion of human donor pancreata (p. 164)
M. Leemkuil[1], J.B. Doppenberg[2], R.J. Ploeg[3], C. Krikke[1], E.J.P. de Koning[2,4], M.A. Engelse[2], H.G.D. Leuvenink[1], [1]Dept of Surgery, University Medical Center Groningen, Groningen, The Netherlands, [2]Dept of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands, [3]Oxford Transplant Center, Oxford, United Kingdom,, [4]Hubrecht Institute for Development Biology and Stem Cell Research, Utrecht, The Netherlands

46. Tacrolimus (Tac), rather than cyclosporine (CsA), interacts with insulin resistance (IR) to alter key transcription factors for β-cell identity & function without altering NFAT localization (p. 165)
J. Triñanes[1,2], A.E. Rodriguez[2], E.J.P. de Koning[1], J.W. de Fijter[1], F. Carlotti[1], A. Torres[2], E. Porrini[2], A.P.J. de Vries[1], [1]Dept of Nephrology, Leiden University Medical Center, Leiden, The Netherlands, [2]Center for Biomedical Research of the Canary Islands, University of La Laguna, Spain

Postersessie XI Basaal II

47. Immunosuppressive drugs do not interfere with direct-acting antivirals for treatment of HCV recurrence (p. 166)
P.E. de Ruiter[1], Y. Gadjradj[1], J. de Jonge[1], J. Kwekkeboom[2], R.W. de Bruin[1], H.J. Metselaar[2], J.N.M. IJzermans[1], L.J.W. van der Laan[1], [1]Dept of Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands

48. Characterisation of peribiliary glands in a new model: precision-cut bile duct slices (p. 167)
I.E.M. de Jong[1,2], A.P.M. Matton[1,2], R. Iswandana[3], S. Suriguga[3], T. van Haaften[3], J. Wiersema-Buist[1], D. Oosterhuis[3], T. Lisman[1], P. Olinga[3], R.J. Porte[2], [1]Surgical Research Laboratory, [2]Dept of Surgery, Section of Hepatobiliary Surgery and Liver Transplantation, and [3]Dept of Pharmacy, Pharmaceutical Technology and Biopharmacy, University of Groningen, Groningen, The Netherlands.

Postersessie XI Basaal II

Poster presentaties in het Engels, spreektijd 3 minuten, discussietijd 1 minuut.

13.00 – 13.30

Moderator: Prof. dr. E.J.P. de Koning, internist, Leids Universitair Medisch Centrum

49. Quality of donor lung grafts: A comparative study between fast and slow brain death induction models in rats (p. 168)
M. Hottenrott[1], J. van Zanden[1], R. Rebolledo[2], D. Hoeksma[2], J. Bubberman[2], J. Burgerhof[3], A. Breedijk[4], B. Yard[4], M. Erasmus[1], H. Leuvenink[2], [1]Dept of Cardiothoracic Surgery, [2]Dept of Surgery, and [3]Dept of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [4]Dept of Internal Medicine, V. Clinic, University Medical Center Mannheim, Mannheim, Germany

Postersessie XI Basaal II

50. Association between a donor TARC/CCL17 promotor polymorphism and impaired clinical outcome after lung transplantation (p. 169)
K. Budding[1], E.A. van de Graaf[3], J. van Setten[2], O.A. van Rossum[1], T. Kardol-Hoefnagel[1], E.-J.D. Oudijk[4], C.E. Hack[1,5], and H.G. Otten[1], [1]Laboratory of Translational Immunology, [2]Dept of Cardiology, [3]Dept of Respiratory Medicine, [5]Dept of Rheumatology and Dermatology, University Medical Center Utrecht, Utrecht, [4]Center of Interstitial Lung Diseases, St. Antonius Hospital, Nieuwegein, The Netherlands

51. Inadequate upregulation of anti-oxidative mechanisms in brain-dead rat kidneys (p. 170)
D. Hoeksma[1], R. Rebolledo[1,2], C.M.V. Hottenrot[3], Y. Bodar[1], P.J. Ottens[1], J. Wiersema-Buist[1], H.G.D. Leuvenink[1], [1]Dept of Surgery, [3]Dept of Cardiothoracic Surgery, University Medical Center Groningen, Groningen, The Netherlands, [2]Physiopathology Program, Institute of Biomedical Sciences, Faculty of Medicine, University of Chile, Chile

Postersessie XI Donatie

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

12.30 – 13.00

Moderator: Drs. Tineke Wind, transplantatiecoördinator, Maastricht UMC

52. Systematic review of current clinical DCD heart transplantation practice and its implications for the Dutch DCD protocol (p. 171)
M.E. Erasmus[1], [1]University Medical Center Groningen, Groningen, The Netherlands

53. Unexpected donation after circulatory death (uDCD) – A great potential for new organs? (p. 172)
L.H. Venema/A.Brat[1], B. Bens[2], D. van der Vliet[3], T. Tromp[3], W.C. de Jongh[4], M.E.C. van der Haak-Willems[4], M. Erasmus[5], C. Krikke[1], [1]Dept of Surgery, and [2]Dept of Emergency Medicine, University Medical Center Groningen, Groningen, [3]Dept of Surgery, Radboud University Medical Center, Nijmegen, [4]Dept of Surgery, Maastricht University Medical Center, Maastricht, [5]Dept of Thoracic Surgery, University Medical Center Groningen, Groningen, The Netherlands

Postersessie XI Donatie

54. Afname van weefseldonoren door daling aantal overledenen in ziekenhuizen? (p. 173)
A.H. Brunsveld-Reinders[1], C.H. Vrijenhoek[1], E.M. den Hollander[1], P.E. Vorstius Kruijff[2], J.G.C. Blok-Singerling[3], Y.W. Anthonio-Rog[4], M.S. Huijzer-den Toom[5], E. de Jonge[1], [1]Leiden University Medical Center, Leiden, [2]Amphia Hospital, Breda, [3]Bronovo Hospital, Den Haag, [4]Haga Hospital, Den Haag, [5]Haaglanden Medical Center, Den Haag, The Netherlands

55. Significant more consent for organ donation for doctors trained in 'Communication about Donation' (p. 174)
N.E. Jansen[1], A.J. Hoitsma [1], H. Rodenburg[1], B. Schaefer[1], B.J.J.M. Haase-Kromwijk[1], [1]Dutch Transplant Foundation, Leiden, The Netherlands

Postersessie XI Donatie

Poster presentaties in het Nederlands, spreektijd 3 minuten, discussietijd 1 minuut.

13.00 – 13.30

Moderator: Cees Brugman, donatiecoördinator, UMCG

56. Towards a standardized informed consent procedure for live donor nephrectomy: the PRINCE (Process of Informed Consent Evaluation) project: study protocol for a nationwide prospective cohort study (p. 175)
K. Kortram[1], E.Q.W. Spoon[1], S.Y. Ismail[1], F.C.H. d'Ancona[2], M.H.L. Christiaans[3], L.W.E. van Heurn[4], H.S. Hofker[5], A.W.J. Hoksbergen[6], J.J. Homan van der Heide[4], M.M. Idu[4], C.W.N. Looman[1], S.A. Nurmohamed[6], J. Ringers[7], R.J. Toorop[8], J. van de Wetering[1], J.N.M. IJzermans[1], F.J.M.F. Dor[1], [1]Erasmus University Medical Center, Rotterdam, [2]Radboud University Medical Center, Nijmegen, [3]Maastricht University Medical Center, Maastricht, [4]Academic Medical Center, Amsterdam, [5]University Medical Center Groningen, Groningen, [6]VUmc, Amsterdam, [7]Leiden University Medical Center, Leiden, [8]Utrecht University Medical Center, Utrecht, The Netherlands

Postersessie XI Donatie

57. Raising awareness of unspecified live kidney donation: an ELPAT view (p. 176)
L. Burnapp[1], K. Van Assche[2], A. Lennerling[3], D. Slaats[4], D. Van Dellen[5], N. Mamode[1], F. Citterio[6], W.C. Zuidema[4], W. Weimar[4], F.J.M.F. Dor[7], [1]Guys Hospital, London, UK, [2]Free University of Brussels, Brussels, Belgium, [3]Sahlgrenska University Hospital, Göteborg, Sweden, [4]Erasmus Medical Center, Rotterdam, The Netherlands, [5]Manchester Royal Infirmary, Manchester, UK, [6]Catholic University, Rome, Italy, [7]Erasmus Medical Center, Rotterdam, The Netherlands

58. Inclusion of compatible donor-recipient pairs in the Dutch kidney exchange programme: a new challenge (p. 177)
M. de Klerk[1], W.C. Zuidema[1], J. van de Wetering[1], E. Massey[1], W. Weimar[1], M.G.H. Betjes[1], [1]Dept of Internal Medicine, Section of Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands

59. Transplantatieverpleegkundigen in een perifeer dialysecentrum geven een aantoonbare kwaliteitsverbetering van de transplantatievoorbereiding (p. 178)
I.C.M. Mensink-Eijkelkamp[1], M. Dijkstra-Oskam[1] en M. Gritters van den Oever[2], [1]Dept of Nefrology, Medisch Spectrum Twente, Enschede, The Netherlands

Parallelsessie XII – Klinisch — Zaal 1+2

Voorzitters: *Dr. Marije C. Baas, nefroloog, Radboudumc, Nijmegen*
Dr. Dries E. Braat, chirurg, UMC Leiden

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

14.00 Highly sensitized patients transplanted via the Eurotransplant Acceptable Mismatch program have excellent long-term graft survival (p. 106)
S. Heidt[1], M.D. Witvliet[1], G.W. Haasnoot[1], F.H.J. Claas[1], [1]Eurotransplant Reference Laboratory, Leiden University Medical Center, Leiden, The Netherlands

14.10 BK polyomavirus seroreactivity of kidney donors predicts viremia and nephropathy in recipients (p. 107)
H.F. Wunderink[1], E. van der Meijden[1], C.S. van der Blij-de Brouwer[1], M.J.K. Mallat[2], G.W. Haasnoot[3], E.W. van Zwet[4], E.C.J. Claas[1], J.W. de Fijter [2], A.C.M. Kroes[1], F. Arnold[5], A. Touzé[5], F.H.J. Claas[3], J.I. Rotmans[2#], M.C.W. Feltkamp[1#], [1]Dept of Medical Microbiology, [2]Dept of Nephrology, [3]Dept of Immunohematology and Blood Transfusion, and [4]Dept of Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, The Netherlands, [5]UMR INRA ISP1282, Université François Rabelais, Tours, France. [#] Both authors contributed equally to this paper*

14.20 Increasing Donor Age on the Risk of Permanent Pacing After Orthotopic Heart Transplantation (p. 108)
K. Caliskan[1], F. Akca[1], A. Constantinescu[1], O. Manintveld[1], S. Akin[1], O.Birim[2], T. Szili-Torok[1], [1]Dept of Cardiology, and [2]Dept of Cardiothoracic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

14.30 Pretransplant donor specific HLA antibodies in 4770 renal transplant recipients: A preliminary analysis of the PROCARE cohort (p. 109)
E.G. Kamburova[1], B.W. Wisse[1], I. Joosten[2], W.A. Allebes[2], A. van der Meer[2], L.B.Hilbrands[3], M.C. Baas[3], E. Spierings[1], C.E. Hack[1], F. van Reekum[4], A.D. van Zuilen[4], M.C. Verhaar[4], M.L. Bots[5], A.C.A.D. Drop[1], L. Plaisier[1], M.A.J.Seelen[6], J.S.F.Sanders[6], B.G. Hepkema[7], A.J. Lambeck[7], L.B. Bungener[7], C. Roozendaal[7], M.G.J. Tilanus[8], J. Vanderlocht[8], C.E. Voorter[8], L.Wieten[8], E. van Duijnhoven[9], M. Gelens[9], M. Christiaans[9], F. van Ittersum[10], A. Nurmohamed[10], N.M. Lardy[11], W.T. Swelsen[11],

K.A.M.I. van Donselaar-van der Pant[12], N.C. van derWeerd[12], I.J.M. ten Berge[12], F.J. Bemelman[12], A.J. Hoitsma[13], J.W. de Fijter[14], M.G.H. Betjes[15], D.L. Roelen[16], F.H.J. Claas[16], H.G. Otten[1], Part of Profiling Consortium of Antibody Repertoire and Effector functions (PROCARE), [1]Laboratory of Translational Immunology, [4]Dept of Nephrology and Hypertension, and [5]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Utrecht, [2]Dept of Laboratory Medicine - Medical Immunology, and [3]Dept of Nephrology, Radboud University Medical Center, Nijmegen, [6]Dept of Nephrology, and [7]Dept of Laboratory Medicine, University Medical Center Groningen, Groningen, [8]Dept of Transplantation Immunology, and [9]Dept of Nephrology, Maastricht, University Medical Center, Maastricht, [10]Dept of Nephrology, VU University Medical Center, Amsterdam, [11]Dept of Immunogenetics, Sanquin, Amsterdam, [12]Renal Transplant Unit, Dept of Internal Medicine, Academic Medical Center, Amsterdam, [13]NOTR/NTS, Leiden, [14]Dept of Nephrology, and [16]Dept of Immunohaematology and Blood Transfusion, Leiden University Medical Center, Leiden, [15]Dept of Nephrology, Erasmus Medical Center, Rotterdam, The Netherlands

14.40 Kidney transplantation from deceased donors for recipients over the age of 75 compared with recipients between 65 and 74 of age – A Dutch Cohort Study (p. 110)

H. Peters-Sengers[1], J.J. Homan van der Heide[1], M.B.A. Heemskerk[2], I.R.J.M. ten Berge[1], M.M. Idu[3], M.G.H. Betjes[4], A.D. van Zuilen[5], M.H. Christiaans[6], L.B. Hilbrands[7], A.P.J. de Vries[8], A.S. Nurmohamed [9], S.P. Berger[10], F.J. Bemelman[1], [1]Dept of Nephrology, Academic Medical Center, Amsterdam, [2]Organ Centre, Dutch Transplant Foundation, Leiden, [3]Dept of Surgery, Academic Medical Center, Amsterdam, [4]Dept of Nephrology, Erasmus University Medical Center, Rotterdam, [5]Dept of Nephrology, University Medical Center Utrecht, Utrecht, [6]Dept of Nephrology, Leiden University Medical Center, [7]Dept of Nephrology, Radboud University Medical Center, Nijmegen, [8]Dept of Nephrology, Leiden University Medical Center, [9]Dept of Nephrology, VU Medical Center, Amsterdam, [10]Dept of Nephrology, University Medical Center Groningen, Groningen, The Netherlands

Parallelsessie XII – Klinisch **Zaal 1+2**

14.50 Evaluating the waiting policy in patients with malignancies prior to renal transplantation: acceptable risks of recurrence after transplantation (p. 111)
J. van de Wetering[1], J. Kal-van Gestel[1], C. Konijn[2], T. Luth[3], W. Weimar[1], A. Hoitsma[2], M. Betjes[1], [1]Dept of Internal Medicine, Erasmus Medical Center, Rotterdam, [2]Nederlandse Transplantatie Stichting, Leiden, [3]Integraal Kanker Centrum Nederland, Utrecht., The Netherlands

15.00 Levels of VEGF-C, PLGF and Follistatin at 12 months post transplantation are associated with increased risk for long term progressive renal dysfunction (p. 112)
G.J. Dreyer[1], J.W. de Fijter[1], D.M. Briscoe[2], K.P. Daly[2], M.E.J. Reinders[1*], [1]Dept of Nephrology, Leiden University Medical Center, Leiden, The Netherlands, [2]Transplantation Research Center, Boston Children's Hospital, Boston, Massachusetts, *Both authors contributed equally to this work*

15.10 Pubertal maturation and T cells in renal transplant recipients (p. 113)
A.M. Terpstra[1,2,3,4], A.W. Langerak[5], C.C. Baan[2], H. de Jong[1], M.G.H. Betjes[2], T. van Gelder[2], A.C.S. Hokken-Koelega[1], E.A.M. Cornelissen[3], A.H. Bouts[4], J.I. Roodnat[2], K. Cransberg[1], [1]Dept of Paediatrics, Erasmus Medical Center–Sophia Children's Hospital, Rotterdam, [2]Dept of Internal Medicine, Erasmus Medical Center, Rotterdam, [3]Dept of Paediatrics, Radboud University Medical Centre, Nijmegen, [4]Dept of Paediatrics, Academic Medical Centre, Amsterdam, [5]Dept of Immunology, Erasmus Medical Center, Rotterdam, The Netherlands

15.20 Good functionality but lower yield after islet isolation from donation after circulatory death pancreata (p. 114)
J.B. Doppenberg[1], H. Putter[2], M.F. Nijhoff[1], M.A. Engelse[1], E.J.P. de Koning[1], [1]Dept of Internal Medicine, and [2]Dept of Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, The Netherlands

15.30 Theepauze

Parallelsessie XIII – Young investigators Zaal 5+6

Voorzitters: Anne C. van Erp, Laura C. Burlage en Drs. Aukje Brat

14.00 **Young investigators sessie**
Van Tx naar AEX, verder kijken dan uw promotie lang is

In het jaar 2015 volbracht de ruimtevaart de eerste verkenningsvlucht naar dwergplaneet Pluto. Apple kondigde de komst van de Iphone 7 aan, met functies waarvan u nog niet weet ze nodig te zullen hebben.
Dit terwijl de transplantatiegeneeskunde nog gebruik maakt van lang beproefde technieken. Deze technieken werken goed, maar toch doen wij allen onderzoek naar verbetering ervan.
Echter, hoeveel hiervan haalt de praktijk? Gaan we wel vooruit? Blijven we niet hangen in wat 'goed' en vertrouwd is? Welke visie en dromen hadden onderzoekers 30 jaar geleden? Kan dit ons inspireren voor de toekomst?
We dagen u uit om met ons over de grenzen van een vierjarige PhD heen te kijken en de vraag te stellen: hoe zouden wij de toepkomst graag zien?

Allerlei vragen die langskomen in deze sessie, bedoeld voor alle jonge onderzoekers om eens een stapje buiten de eigen wetenschapsniche te maken en te kijken wat er tot nu toe bereikt is en nog veel belangrijker, wat we met zijn allen nog kunnen bereiken.

Tijdens deze sessie zal prof. dr. G. Kootstra in retrospectief zijn visie met ons delen in een voordracht getiteld 'Research gebaseerd op fantasierijke dromen', waarna dr. M.A. Engelse (LUMC) in prospectief zijn visie voor de toekomst hierop zal laten volgen.

15.30 Theepauze

Parallelsessie XIV – Casuïstiek nierdonatie bij leven Zaal 14

Voorzitters: *Janneke Vervelde, coördinator nierdonatie bij leven, AMC*
Dr. Diederik Kimenai, chirurg, Erasmus MC

Sprekers: Ellen Jansen, verpleegkundig specialist i.o., nefrologie, UMCG
Dr. Margriet de Jong, internist-nefroloog, UMCG
Dr. Gerbrig J. Versteegen, medisch psycholoog, UMCG

Interactieve sessie

14.00 **Casus I**: mevr. K
De jonge (altruïstische) donor:
Je bent jong en je wilt wat

14.30 **Casus II**: mevr. D
De gerichte altruïstische donor:
Facebook / media donor

15.00 **Casus III:** dhr. S
Donor met overgewicht, wat zijn de risico's nu en in de toekomst

15.30 Theepauze

Sessie XV - Plenair — Theaterzaal

Voorzitters:. Prof. dr. Robert J. Porte, chirurg UMCG, namens loc UMCG
Dr. Marlies E.J. Reinders, nefroloog LUMC, namens bestuur NTV

Top 4 beste abstracts

Voordrachten in het Nederlands, spreektijd 8 minuten, discussietijd 2 minuten.

15.50 Increasing the number of potential organ donors with 37%: a prospective observational multicenter study on unrecognized potential organ donors outside the intensive care unit (p. 115)
M. Witjes[1], A. Kotsopoulos[2], I. Herold[3], L. Otterspoor[3], K. Simons[4], J. van Vliet[5], M. Blauw[5], B. Festen[6], J. Eijkenboom[7], B. Post[1], W.F. Abdo[1], [1]Dept of Intensive Care, Radboud University Medical Center, Nijmegen, [2]Dept of Intensive Care, St. Elisabeth Hospital, Tilburg, [3]Dept of Intensive Care, Catharina Hospital, Eindhoven, [4]Dept of Intensive Care, Jeroen Bosch Hospital, 's-Hertogenbosch, [5]Dept of Intensive Care, Rijnstate, Arnhem, [6]Dept of Intensive Care, Gelderse Vallei, Ede, [7]Dept of Intensive Care, Máxima Medical Centre, Veldhoven, The Netherlands

16.00 Anonymity in live kidney donation reconsidered: patients' and donors' experiences, preferences and attitudes (p. 116)
D. Slaats[1], A. Lennerling[2], K.A.M.I. van der Pant[3], I.M. Dooper[4], R.A. M. Meijer[5], P.T.R. Ulrichts[6], J.M. Wierdsma[7], C. Schrauwers[8], J. van de Wetering[1], W. Weimar[1], M.G.H. Betjes[1], W.C. Zuidema[1], N. Mamode[9], F.J.M.F. Dor[10], E.K. Massey[1]. [1]Dept of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Dept of Transplantation, Sahlgrenska University Hospital, Göteborg, Sweden, [3]Dept of Internal Medicine/Nephrology, Academic Medical Center, Amsterdam, The Netherlands, [4]Dept of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands, [5]Dept of Nephrology, University Medical Center Groningen, Groningen, The Netherlands, [6]Dept of Nephrology, University Medical Center Maastricht, Maastricht, The Netherlands, [7]Dept of Nephrology, University Medical Ceneter Utrecht, Utrecht, The Netherlands, [8]Dept of Nephrology, VUmc Amsterdam, The Netherlands, [9]Dept of Transplantation, Guys Hospital, London, UK, [10]Dept of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

Sessie XV - Plenair **Theaterzaal**

16.10 Hypothermic machine perfusion is also beneficial for deceased donor kidneys when cold ischemic time is short and a short cold ischemic time is also beneficial when kidneys are machine perfused (p. 117)

J.J.H.F.M. Kox[1], C. Moers[2], D. Monbaliu[3], A. Strelniece[4], J. Treckmann[5], I. Jochmans[3], H.G.D. Leuvenink[2], L.W.E. van Heurn[1], J. Pirenne[3], A. Paul[5], R.J. Ploeg[2,6], [1]Dept of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands, [2]Dept of Surgery, University Medical Center Groningen, Groningen, The Netherlands, [3]Abdominal Transplant Surgery, University Hospital Leuven, Belgium, [4]Eurotransplant, Leiden, The Netherlands, [5]General, Visceral and Transplantation Surgery, University Hospital Essen, Germany, [6]Oxford Transplant Centre, U.K.

16.20 The use of human liver scaffolds for stem cell-driven graft engineering (p. 118)

M.M.A. Verstegen[1], K. van der Heijden[2], S. van den Hoek[1], R. de Bruin[1], J. IJzermans[1], L.J.W. van der Laan[1], J. de Jonge[1], [1]Dept of Surgery, and [2]Dept of Cardiology – Biomedical Engineering, Erasmus Medical Center, Rotterdam, The Netherlands

16.30 Sessie met prijsuitreikingen

Prijsuitreikingen **Theaterzaal**

Voorzitters: *Prof. dr. Luuk Hilbrands*
Dr. Marlies Reinders

16.30 Uitreiking innovatie-kwaliteitsprijs 2016
door Louise Maasdam, voorzitter LWTV

16.32 Astellas Trans(p)la(n)t(at)ionele Research Prijs
Lezing door prijswinnaar 2015: Liselotte Ooms, Erasmus MC

Uitreiking prijs 2016 door Prof. dr. Luuk Hilbrands

16.42 Uitreiking Novartis Transplantation Awards 2016
door Dr. A.D. (Arjan) van Zuilen, internist-nefroloog UMC Utrecht, voorzitter Novartis Transplant Advisory Board (NTAB)
categorieën: klinische transplantatiegeneeskunde en basaal wetenschappelijk onderzoek

16.45 Uitreiking Jon J. van Roodprijs 2016
gevolgd door een lezing van de prijswinnaar

16.55 Uitreiking Distinguished Research Award 2016
door Prof. dr. Luuk Hilbrands

17.00 Sluiting door Robert Porte

ABSTRACTS

"I am not Sherlock Holmes": suspicions, secrecy and silence of transplant professionals in the organ trade

F. Ambagtsheer[1], L. van Balen[1], W. Weimar[1], [1]Dept of Internal Medicine, Transplantation and Nephrology, Erasmus MC, Rotterdam, The Netherlands

In 2013 we circulated an anonymous survey amongst 546 Dutch transplant professionals (TPs) (response rate: 241/44%) about their experiences with patients who purchased kidneys abroad. We found that of the 100 (42%) TPs who treated patients who traveled to a country outside the European Union for a kidney transplant, 31 (31%) were certain and 65 (65%) had suspicions that patients had bought kidneys. To gain more insight into TPs' experiences with these patients, we also conducted in-depth anonymous interviews with 41 TPs (24 male), of whom 29 nephrologists, 5 nurse practitioners, 5 social workers, one research coordinator and one transplant surgeon. The interviews took place at 6 transplant centres and 12 non-university hospitals according to a topic list that addressed TPs' opinions and their behaviour towards these patients. Most TPs (n=30) suspected that patients bought kidneys abroad. They described their suspicions as having a "gut feeling" that patients purchased kidneys. Eighteen TPs emphasized that patients did not tell them how the kidney was obtained and from whom. Nonetheless, 12 TPs did treat patients who told them that they had purchased the kidney. Twenty-four TPs said that they refrain from "interrogating" their patients about their alleged purchase to avoid harming the relationship with their patients (n=12), because the questioning serves no medical purpose (n=10) or because they did not want to know or were not interested in their patients' alleged purchases (n=9). Almost all TPs (n=38) understand why patients buy organs. Nevertheless many (n=25) also condemn their patients for purchasing organs. Eleven TPs indicated that purchase does not justify a breach of their secrecy oath. Many TPs (n=24) do not consider it their duty to investigate or report their patients' purchase and emphasized that this is the responsibility of law enforcement. Seven TPs however would consider reporting their patients. Only 2 TPs mentioned the importance of doctors as gatekeepers who may be in the position to report organ trade to national authorities. TPs' reluctance to enquire after their patients' possible kidney purchase and the absence of disclosure by TPs may explain why prosecutions of the crime hardly exist and why the crime persists. TPs should become more active in reporting organ trafficking networks, such as the names of the centres or transplant staff that facilitate (illegal) transplants.

Mesenchymal stem cells maintain immunomodulatory capacity after cell death

F. Luk[1], S.F.H. de Witte[1], M. Franquesa[1], S.S. Korevaar[1], T. Strini[1], F.J.M.F. Dor[2], M.G.H. Betjes[1], C.C. Baan[1], M.J. Hoogduijn[1], [1]Dept of Nephrology and Transplantation and Dept of Internal Medicine, [2]Dept of Transplant Surgery and Dept of Surgery, Erasmus MC, University Medical Center, Rotterdam, The Netherlands.

Mesenchymal stem cells (MSC) are widely studied as cell therapeutic agent after solid organ transplantation. However, MSC therapy comes with safety concerns and in vitro expansion of MSC is labor intensive and time consuming. Moreover, full elucidation of mechanisms of action of MSC therapy is lacking. Identification of key cellular or soluble components that are responsible for the effects of MSC will result in a better understanding of MSC therapeutic activity and might give the opportunity to generate these components as an alternative to the use of live cells. MSC were isolated and expanded from adipose tissue of healthy kidney donors. In order to discriminate between immunomodulation via cell-cell interaction or via secreted factors MSC were inactivated by heating for 30 minutes at 50 °C. Heat inactivated (HI)-MSC preserved their immuno-phenotype, but lost the ability to secrete soluble factors. 3x10^5 HI- and viable MSC were used to treat lipopolysaccharide (LPS) induced sepsis mice. The immunemodulatory interaction between MSC and different immune cell types was evaluated by co-culturing MSC with peripheral blood mononuclear cells and MACS purified B cells and monocytes. Cell proliferation and cell phenotype was determined by flow cytometry. Cytokine levels were measured with ELISA. MSC and HI-MSC drastically reduced circulating levels of pro-inflammatory IFN-γ and increased anti-inflammatory IL-10 after LPS induced sepsis. In vitro, living MSC reduced T cell proliferation in a dose dependent manner whereas HI-MSC had no effect. both HI- and living MSC inhibited B cell memory formation but only viable MSC were capable to induce IL-10 producing regulatory B cells. However, both living and HI-MSC significantly suppressed TNF-α production by LPS stimulated monocytes in vitro. This indicates that monocytes respond in a similar fashion to dead MSC and living MSC and partly explains how MSC exert their immunosuppressive effect after infusion. These results demonstrate that MSC modulate immune responses via two mechanisms. One is mediated by active interactions between viable MSC and immune cells. The other depends on modulation of monocyte function, which requires the presence but not viability of MSC. Both mechanism may contribute to the potential of MSC for immunotherapy in solid organ transplantation.

Self-monitoring renal function after transplantation: a clinical trial on safety and usability

C. van Lint[1]; S. van Dijk[1,5]; M. van Diepen[2], W. Wang[3]; W-P. Brinkman[3]; T. Rövekamp[4]; M. Neerincx[3]; T. Rabelink[1] and P. van der Boog[1] [1]Dept. of Nephrology, Leiden University Medical Centre; [2]Dept. of Epidemiology, Leiden University Medical Centre; [3]Faculty of Computer Science, Delft University of Technology; [4]Technology in Healthcare, Prevention and Health, TNO, Leiden; [5]Dept. of Health, Medical and Neuropsychology and Behavioural Sciences, Leiden University.

Background: Enabling patients to monitor kidney function at home could decrease the high frequency of outpatients visits and improve speed of rejection detection. In this RCT, the safety and usability of self-monitoring creatinine and blood pressure with the support of a Disease Management System (DMS) during the first year post-transplantation was investigated. Methods: The intervention group used a Statsensor® Xpress™ to measure creatinine and a WatchBP® Home to measure blood pressure during the first year post-transplantation. Measurements were registered in a web-based system using a traffic light analogy to support interpretation of creatinine trends. The control group received usual care. Kidney function, blood pressure, quality of life and number of outpatients contacts (minutes spent) of both groups were assessed. Creatinine trends measured at home were compared to clinically relevant increases (>10%) measured in the hospital laboratory. A subsample of intervention patients (n=20) was interviewed on self-monitoring experiences. Results: In total 119 patients were included (77% response rate). A significant reduction in outpatient contacts was observed: 283 (SD 12) and 322 (SD 9) outpatient minutes spent for intervention and control group, respectively (p. 01). No differences were found for eGFR, blood pressure and quality of life. For 36 out of 71 laboratory-based creatinine increases, sufficient home-based creatinine measurements were available for trend comparison. A similar trend was observed between home-based and laboratory-based measurements in 78% of the cases. Self-monitoring enhanced early detection of rejection in 3 out of 5 cases, no rejections were missed. Satisfaction was high: 95% of the interviewed patients would recommend self-monitoring to other patients and 75% would have liked to extend self-monitoring creatinine beyond 1 year. Conclusions: This RCT shows that self-monitoring renal function after transplantation is highly appreciated by patients and enables number of outpatient visits to be significantly reduced without compromising on quality of care. With possibly improving the detection rate of relevant creatinine increases (e.g. due to increased measurement frequency), self-monitoring kidney function can play a useful role in post-transplantational care.

Steroid-free maintenance immunosuppression or calcineurin inhibitor minimization compared to standard quadruple immune-suppression in kidney transplantation Interim analysis of the ALLEGRO trial

M.S. van Sandwijk[1], A.P.J. de Vries[2], S.J. Bakker[3], I.J.M. ten Berge[1], S.P. Berger[3], J.W. de Fijter[2], J.J. Homan van der Heide[1], M.M. Idu[1], C. Krikke[3], K.A.M.I. van der Pant[1], M.E. Reinders[2], J. Ringers[2], N.C. van der Weerd[1], F.J. Bemelman[1#] and J.S. Sanders[3#]. Renal Transplant Unit[1], Academic Medical Center, Amsterdam, Department of Nephrology[2], Leiden University Medical Center, Department of Nephrology[3], University Medical Center Groningen, The Netherlands. [#]Both authors contributed equally to this work.

Background The determination of the immunosuppressive regimen delivering maximum efficacy with minimal toxicity in kidney transplant recipients is a continuing challenge. Methods In this multicenter, investigator-driven, open-label trial, 295 kidney transplant recipients with a low to intermediate immunological risk were randomized to (1) standard triple maintenance immunosuppression (prednisolone, mycophenolic acid and tacrolimus after basiliximab and methylprednisolone induction) versus (2) steroid-free maintenance immune-suppression or (3) calcineurin inhibitor minimization after six months. The primary endpoint was kidney function, measured as MDRD, creatinine clearance and proteinuria. Secondary endpoints included death, primary nonfunction, graft failure, biopsy proven rejections, discontinuation of study medication for more than six weeks, serious adverse events and cardiovascular risk factors (blood pressure, lipid profile and diabetes). In addition, a composite endpoint reflecting treatment failure, i.e. death, graft loss, rejection and discontinuation of study medication for more than six weeks was defined. The total study duration was two years, with a prespecified interim analysis at six months. Results In this interim analysis, there were no differences in MDRD (43.2 vs 45.0 ml/min/1.73m^2), creatinine clearance (58.5 vs 58.3 ml/min) or proteinuria (0.20 vs 0.19 g/day) between the corticosteroid withdrawal (CSWD) group and the chronic corticosteroid therapy (CCS) group. This was true for all donor subtypes (living, DBD and DCD). There were also no significant differences in the individual secondary outcomes of death (1.0 in the CSWD vs 1.5% in the CCS group), primary nonfunction (4.1% vs 1.5%), graft failure (3.1% vs 1.5%), rejection (18.6% vs 14.1%), type of rejection and discontinuation of study medication (19.6% vs 12.6%). Treatment failure occurred more often in the CSWD group (hazard ratio 1.65, p = 0.027), but this group experienced fewer serious adverse events (44 vs 57 per 100 patients, p = 0.048) due to a lower rate of infections. The cardiovascular profile in the CSWD group was also more favorable, with an improved diastolic blood pressure and an improved lipid profile. CONCLUSION Steroid-free maintenance immunosuppression is a safe option for low to intermediate risk living, DBD and DCD kidney transplant recipients.

MicroRNA profiles in graft preservation solution are associated with early allograft dysfunction after liver transplantation

J.W. Selten[1], C.J. Verhoeven[1], H.P. Roest[1], R.W.F. de Bruin[1], J. de Jonge[1], J.N.M. IJzermans[1], L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus MC, Rotterdam, The Netherlands

Introduction: Early allograft dysfunction (EAD) after liver transplantation (LT) is associated with inferior patient and graft survival and is more prevalent with increasing cold ischemia times and decreased initial graft quality. However, the possibility of predicting EAD and hereby minimizing the clinical consequences, remains difficult in practice. Recent animal and human studies highlight the potential of hepatocyte-derived microRNAs (HDmiRs) in serum as sensitive, stable an specific biomarkers of liver injury. The aim of this study is to investigate whether HDmiRs in cell-free graft preservation solution are predictive of the development of EAD after liver transplantation. Methods: Graft preservation solutions of 83 prospective liver grafts at the end of cold ischemia time were analyzed after heparinase treatment. RT-qPCR was performed for four miRNAs, including miRNA-122 and miR-148a. MircoRNA profiles were compared between patients who developed EAD or primary non-function (PNF) (n=48) with the patients without EAD or PNF (n=35). Results: In our cohort, EAD was associated with grafts from donation after cardiac death (DCD) donors, higher donor age (>65), male donors and female recipients (p=0.004; p=0.037; p=0.03; p=0.03). Levels of miR-122 were shown to be higher in preservation solution samples from EAD/PNF grafts (p<0.005), and from DCD donors (p=0.001). Higher levels of miR-122 in preservation solution during transplantation was associated with increased levels of ASAT and ALAT (<2000 U/L) in the week after transplantation and was related to a decreased graft survival (p=0.05). Furthermore, increased miR-148a was associated with DCD grafts (p=0.001) and decreased long term patient survival (p=0.034). Conclusion: This study demonstrates that HDmiRs in graft preservation solutions may successfully be applied to assess the liver function following transplantation. Increased levels of miR-122 and miR-148a are related to the development of EAD/PNF and long term graft and patient survival. Further research is required for the predictive value of tissue-specific HDmiRs and graft function in perfusion liquids during machine preservation.

Defective post-reperfusion metabolic recovery directly associates with incident delayed graft function in human kidney transplantation

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Delayed graft function (DGF) following kidney transplantation detrimentally affects long-term graft function and survival. DGF is a manifestation of ischemia reperfusion (I/R) injury, yet up to this point there is no medical therapy that alleviates DGF. Preclinical studies characterize metabolic defects due to mitochondrial damage as driver of I/R injury. In this clinical study, we tested whether these preclinical findings translate to the context of DGF. A comprehensive approach that included sequential establishment of arteriovenous concentration differences over the graft along with metabolomic and genomic analysis in paired tissue biopsies shows that a post reperfusion metabolic incompetence precedes DGF. This report is based on sequential studies. A total of 85 patients were enrolled. Twelve patients refused to give informed consent and 7 patients were excluded due to cancelled surgery. Grafts with later DGF fail to recover aerobic respiration as reflected by persistently low tissue glucose/lactate ratio (mean(±s.e.m.): 0.2(±0.06) in +DGF vs. 0.9(±0.16) in controls ($P<0.0039$) [Figure 1a] and persistent lactate and hypoxanthine release from the graft 30 minutes after reperfusion [resp. Figure 2 and Figure 1b], which was absent in controls (mean(±s.e.m.): 1.7(±0.67) mmol lactate/l ($P<0.000038$) and 12.17(±4.63) µmol hypoxanthine /l $P<0.0024$ respectively). Evaluation of metabolic function shows that failure to instigate aerobic respiration upon reperfusion relates to extensive mitochondrial damage (e.g disorganized christae and fragmentation). Pre-treatment of human kidney tissue with the mitochondrial stabilizing peptide SS-31 preserves mitochondrial function during simulated I/R ($P<0.016$). In conclusion, DGF is preceded by a profound post-reperfusion metabolic deficit. Strategies aimed at preventing DGF should focus on preservation of both mitochondrial integrity and optimal use of functioning anaerobic metabolic networks of the graft.

Orthotopic liver transplantation following dual machine perfusion in the mouse

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Introduction Ex vivo Machine perfusion of explanted organs can improve the utilization of grafts derived from extended criteria donors and donors after circulatory death. To effectively study and improve clinical machine perfusion, we developed a murine model of hypothermic dual machine perfusion and orthotopic liver transplantation. This model enables a host of benefits ranging from high-throughput screening of pharaceutical enhancements to using knockout technology to elucidate fundamental pathological processes during liver transplantation. Methods Machine perfusion: The perfusion machine comprised of two independent perfusion circuits for portal venous and arterial perfusion and a perfusate temperature control system. We harvested livers from five Male C57BL/6 mice aged 9–12 weeks, preserving the hepatic arteries (HA), superior mesenteric artery (SMA), and abdominal aorta, preserving sufficient length of the supra-hepatic vena cava (SHVC), infra-hepatic vena cava (IHVC), and portal vein (PV). After vascular cuffs were attached to the IHVC and PV, the graft was connected to the portal and venous perfusion port, respectively. Dual machine perfusion was performed at 4oC for 30 minutes using William's medium E based perfusion solution. The PV flow rate was set at 4ml/min, the arterial flow rate at 0.5ml/min. Liver transplantation: The recipient procedure (n=5) was started after 30 minutes of MP. Upon graft introduction into the recipient abdomen, portal blood flow was established first, after which the IHVC was anastomosed using a cuff technique. Arterial reconstruction was then performed using side-to-end anastomosis between the abdominal aorta of the graft and recipient. The bile duct was reconstructed using an intraluminal stent. Results During hypothermic dual machine perfusion, all perfusion parameters remained within normal range. The mean total perfusion time was 82 minutes. All recipient mice recovered from anesthesia after the operation. The 3-day survival rate was 80% (4/5). Conclusion Herein we established a novel murine model of hypothermic dual machine perfusion, which was confirmed with orthotopic liver transplantation. This model is suitable for a wide range of both fundamental and clinically applied research, which will be vital to optimizing the benefits of machine perfusion.

Serum miRNAs as potential biomarkers for the bronchiolitis obliterans syndrome after lung transplantation

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Introduction Lung transplantation (LTx) is the last treatment for patients suffering from endstage lung diseases. Survival post-LTx is hampered by the development of the bronchiolitis obliterans syndrome (BOS), hallmarked by fibrotic complications, of which the clinical diagnosis is based on a surrogate marker, FEV1 decline, and is often late. Therefore, there is clinical need for novel biomarkers for BOS development at an earlier stage.
Methods We hypothesized that selected miRNAs could serve as stratification markers for patients who do or do not develop BOS post-LTx. We analyzed serum levels of selected pro-fibrotic (miR-21,miR-155), anti-fibrotic (miR-29a) and fibrosis-unrelated (miR-103,miR-191) miRNAs in endstage lung disease patients and during follow-up in a cohort of LTx patients.
Results When stratified per lung disease, we observed significant elevated circulatory miRNA serum levels for all investigated miRNAs in both chronic obstructive pulmonary disease and interstitial lung disease patients compared to healthy controls. Only miR-103 was increased for cystic fibrosis patients. Levels of all miRNAs analyzed were significantly increased in the serum of BOS+ vs. BOS- patients. Additionally, levels of miR-21 and miR-103 were significantly higher in BOS+ patients prior to the clinical diagnosis of BOS. Similar observations were made for miR-155 and miR-191.
Conclusion: We demonstrate that a selected group of miRNAs is elevated in end-stage lung disease and in BOS+ patients compared to BOS- patients. This difference is present prior to the clinical diagnosis of BOS. However, further research is justified on the prognostic value of circulating miRNAs in BOS and lung conditions in general.

Retrograde flushing of the pulmonary vein during explantation: lymphocyte composition in the perfusate and impact on outcome after lung transplantation

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Introduction Lung transplantation (LTx) remains the final treatment option for patients suffering from endstage lung diseases. Lung preservation is essential for transplantation outcome. Studies have shown a beneficial effect of retrograde flushing on early graft dysfunction and bronchial complications, but there is no concordance in literature. Consequently, antegrade lung perfusion is still the standard method of practice in most centers for LTx procedure.
Methods We investigated total PBMC numbers and the cellular composition in the collected perfusate after retrograde flushing. Furthermore, we studied the influence of the combined antegrade and retrograde flushing procedure on LTx outcome.
Results Total cell numbers varied between samples (max. 8.0x108,n=47), but showed a significant correlation, p=0.0005, between PBMC numbers in the flush and amount of perfusion fluid analyzed. The percentage of T (p=0.0027) and B cells (p=0.0010) was decreased in the perfusate, whereas the percentage of NK cells was significantly higher compared to the circulation (p=0.0043). Kaplan-Meier analyses showed no differences on the incidence of chronic rejection or survival in the first 4 years post-LTx between pre- and post-retrograde flush patient groups. However, we observed a significant higher number of patients with episodes of acute rejection (p=0.039).
Conclusion High numbers of NK cells are present in lung tissue which are removed from the graft via retrograde flushing, which has a beneficial effect on outcome after LTx. Although clinical validation of our observations is essential, the addition of retrograde flushing during organ preservations can be valuable for LTx outcome.

Technique for ex vivo lung perfusion (EVLP) of lungs from brain-dead donor rats and testing the effect of prednisolone treatment

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Ex vivo lung perfusion (EVLP) systems have become an important tool to treat marginal brain dead donor lungs with pulmonary edema. Some centers have successfully increased their donor lung pool using EVLP while graft survival has remained comparable to standard brain dead donor lung transplantation. This is probably the result of a comparable immune response after transplantation. Therefore, an easily reproducible and stable rat lung perfusion system is an important tool to test new treatment opportunities to limit the immune response and possibly support the regeneration of donor lungs. Heart-lung blocks were procured from Lewis rats three hours after acute traumatic brain death induction, and were subsequently cold preserved for one hour. Thereafter, lungs were placed for six hours in the normothermic EVLP model. Lungs were ventilated with a pressure controlled ventilation adjusted to a tidal volume (VT) of 7 ml/kg of body weight, a PEEP of 5 cmH2O, a frequency of 60 and a FiO2 of 21%. Perfusion was performed with a modified Steen solution and cefuroxime at a maximal pulmonary arterial pressure of 13 mmHg. As intervention we study the effect of prednisolone (40 mg), standardly administered in the human EVLP. Ventilation parameters, lung oxygenation capacity, pH, glucose levels and flow were noted and perfusate samples collected, over time. Lungs were macroscopically scored and tissue was stored for wet/dry ratio, qPCR and patho-histological analysis. Judged by ventilation parameters, lung oxygenation capacity and flow, a stable rat EVLP system was developed. Preliminary analysis suggest that addition of prednisolone in the EVLP system results in a better macroscopic appearance, ventilation parameters and lung oxygenation capacity. We hope to also soon be able to present the effect of prednisolone on immune activation in the lung. This model will be an important tool to test new treatment opportunities for brain death induced immune activation of donor lungs. Since prednisolone is known to have an anti-inflammatory effect, it might be beneficial to exclude it when testing future treatment opportunities in the rat EVLP.

ER stress and loss of GRP78 expression provides a link between renal ischemia/reperfusion injury and the urinary metabolome

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Ischemia/reperfusion injury (IRI) profoundly impacts graft survival following kidney transplantation. Epithelial injury is one of the earliest histological alterations of IRI and is especially observed in the corticomedullary junction. In this region oxygen tension is lowest whereas epithelial cells are metabolically very active. Therefore we hypothesized that urinary metabolomics could be a tool for non-invasive assessment of IRI-induced changes. We used a rat IRI model in combination with the protective effect of therapeutic inhibition of Mannan-binding lectin (MBL). Samples (serum, urine, tissue) were collected at 2, 5 and 24 h post ischemia/reperfusion (I/R) and the urinary metabolic profiles were analysed using a GC-MS platform. We demonstrate that this IRI model is characterized by early epithelial injury and an increased expression of KIM-1, NGAL, IL-6 and rise in serum creatinine. Moreover, already at 2 hours a strong reduction of GRP78 protein expression is observed, specifically in the corticomedullary junction. Loss of GRP78, a regulator of the ER-stress response, was accompanied by induction of downstream mediators spliced-XBP1 and CHOP expression. Inhibition of MBL in vivo protected tubular cells from rapid loss of GRP78 expression and consequent tubular injury. Exploratory data analysis of the urinary metabolic profiles showed a dominant effect of time, but not of the protective treatment. The use of PLS regression models in combination with all injury markers as response variables, only revealed a significant association between metabolic changes in urine and expression of GRP78. Exploring the variable importance of projection values we have identified a number of metabolites, including alpha-ketoglutarate, aconitic acid, uric acid, hippuric acid and desaminotyrosine which were significantly contributing to the model and were affected by protective anti-MBL treatment. In conclusion, we show that loss of GRP78 and induction of the ER-stress response is a very early process in IRI, specifically taking place in the corticomedullary junction. Using a combination of statistical models and specific intervention we could link the metabolic trajectory to the recovery process and show that metabolomics is a valuable tool for the evaluation of IRI at cellular and tissue level.

Slow induction of brain death leads to decreased renal function and increased hepatic apoptosis in rats

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Introduction: Donor brain death (BD) is an independent risk factor for graft survival in recipients. While in some patients BD results from a fast increase in intracranial pressure, usually associated with trauma, in others intracranial pressure increases more slowly. The speed of intracranial pressure increase may be a possible risk factor for renal and hepatic graft dysfunction. This study aims to assess the effect of speed of BD induction on renal and hepatic injury markers. Methods: BD induction was performed in 64 mechanically ventilated male Fisher rats by inflating a 4.0F Fogarty catheter in the epidural space. Rats were observed for 0.5 h, 1 h, 2 hrs, or 4 hrs following BD induction. Slow induction was achieved by inflating the balloon-catheter at a speed of 0.015 ml/min until confirmation of BD. Fast induction was achieved by inflating the balloon at 0.45 ml/min for 1 minute. Plasma, kidney and liver tissue were collected for analysis. Results: Slow BD induction led to higher plasma creatinine at all time points compared to fast induction. Furthermore, slow induction led to increased renal mRNA expression of IL-6, and renal MDA values after 4 hrs of BD compared to fast induction. Hepatic mRNA expression of TNF-α, Bax/Bcl-2, and protein expression of caspase-3 was significantly higher due to slow induction after 4 hrs of BD compared to fast induction. PMN infiltration was not different between fast and slow induction in both renal and hepatic tissue. Conclusion: Slow induction of BD leads to poorer renal function compared to fast induction. Also, renal inflammatory and oxidative stress markers were increased. Liver function was not affected by speed of BD induction but hepatic inflammatory and apoptosis markers increased significantly due to slow induction compared to fast induction. These results provide initial proof that speed of BD induction influences detrimental renal and hepatic processes.

Improvement of gynaecological screening of female renal transplant recipients by self-sampling for HPV detection

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Background: Female renal transplant recipients (RTRs) have increased risk for developing human papillomavirus (HPV) related (pre)malignancies of the lower genital tract. Annual cervical screening is advised for RTRs, but the participation rate is low. The aim of this study is to investigate whether HPV self-sampling is suitable for gynaecological screening of RTRs to increase participation rate.

Methods: A large prospective cohort study with 253 RTRs, who were transplanted at Radboud university medical center or Maastricht University Medical Centre, was performed. All participants received an Evalyn Brush®, a device for a cervico-vaginal self-sample, and questionnaires were sent to assess the experience with this device. High risk (hr)HPV presence was determined with the high sensitive SPF_{10}-$LiPA_{25}$ system and clinically validated GP5+/6+ PCR. HrHPV positive tested (SPF_{10}-$LiPA_{25}$ system) patients underwent gynaecologic examination.

Results: More than 90% of the patients rated their experience with the Evalyn Brush® as good to excellent and 77% preferred self-sampling over a physician taken sample. Thirty-five of 217 RTRs (16%) tested hrHPV positive with SPF_{10}-$LiPA_{25}$ system and 22 (10%) tested positive with the GP5+/6+ PCR. Eleven hrHPV positive patients with SPF_{10}- $LiPA_{25}$ system had clinically relevant gynaecological abnormalities and they all also tested positive with GP5+/6+ PCR.

Conclusions: Self-sampling is clinically applicable in gynaecological screening and is preferred by female RTRs. Therefore, self-sampling could be implemented with the aim to increase the participation rate of female RTRs in yearly gynaecological screening.

Fractional excretion of NGAL instead of 99mTcMAG3 renography to monitor resolution of delayed graft function

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Introduction: Kidneys transplanted from extended criteria donors have a higher prevalence of delayed graft function (DGF). Early identification of factors that prolong duration of DGF may improve clinical outcome and prevent invasive procedures. The standard in our center to monitor resolution of DGF is a renography with ^{99m}Tc labelled mercaptoacetyltriglycine (MAG_3). Since ischemia/reperfusion injury results in impaired extraction of $^{99m}TcMAG_3$ via the organic anion transporter, but also in impaired reabsorption of NGAL by PTECs (luminal side), we hypothesize that the excretion of fractional NGAL (FE-NGAL) can replace MAG_3 scans to follow resolution of functionally defined DGF(1) (fDGF). *Methods:* 92 consecutive DCD transplant recipients were included, all received IL2-RB induction and maintenance therapy with steroids, MMF and delayed-CsA introduction at day 4. Before introduction of CsA on day-4 and at day-10, MAG_3 scans were performed and tubular function slope (TFS) score (2) was calculated. Daily FE-NGAL was calculated using urinary and serum NGAL. Statistical analysis included positive and negative predictive values (PPV and NPV). *Results:* In DCD recipients a day-4 TFS score >1.5 could distinguish patients with mild fDGF (≤7 days) from patients with moderate/severe fDGF (>7 days), with PPV of 93.4% and NPV of 63.3%. Day-4 FE-NGAL <2.5% could even better distinguish patients with mild fDGF from those with moderate/severe fDGF (PPV=92.6%, NPV=100%). Also in patients with residual native kidney diuresis (>1L) FE-NGAL was highly distinctive (PPV=85.7%, NPV=100%). However, for the prediction of moderate (7-20 days) versus severe fDGF (≥21 days), both TFS and FE-NGAL had limited value (PPV=45.6% and 40.5%, NPV=100% and 87.5%, respectively). Furthermore, preliminary results suggest that sequential FE-NGAL may help to identify patients with additional CNI-toxicity and/or rejection. *Conclusion:* In this cohort of DCD recipients FE-NGAL better distinguished patients with mild fDGF from those with moderate/severe fDGF compared to standard follow-up using $^{99m}TcMAG_3$ renography, also in patients with preserved residual diuresis. Sequential FE-NGAL may prove to be a useful non-invasive biomarker to guide optimal timing of a renal allograft biopsy in recipients with DGF and additional CNI toxicity and/or acute rejection.

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Long-term effects of living kidney donation on renal function, blood pressure and survival

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Introduction: Studies addressing the impact of kidney donation on clinical outcomes have yielded conflicting results, at least in part due to inadequate matching with controls. Methods: We analyzed data from 610 living kidney donors and matched controls derived from a general population-based cohort (PREVEND), who did not have diabetes or micro- or macroalbuminuria at baseline (n=7296). We performed 1:1 propensity matching by age, sex, body mass index (BMI), systolic blood pressure (BP), antihypertensive use, and eGFR at baseline. We also analyzed measured GFR (mGFR) by iothalamate clearance before donation (n=432), and at 3 months (n=406), 5 years (n=192) and 10 years (n=58) after donation. Results: At baseline, donors were 51±10 yrs old, 49% were men, 16% used antihypertensive drugs, systolic BP was 129±15 mmHg, BMI was 25±6 kg/m2 and eGFR was 89±15 ml/min/1.73 m2; these parameters were highly similar in non-donors (all P>0.05). During follow-up for 10.3 [4.5-10.8] years, 7 donors and 56 non-donors died. The all-cause mortality risk in donors was lower than in matched non-donors (hazard ratio 0.27 [95% CI 0.12-0.60], P=0.001). This association remained similar after adjustment for age, sex, BMI, systolic BP, and eGFR. In a subgroup of individuals with 4-year follow-up data (197 donors and 483 non-donors), BMI (27±4 vs 26±4 kg/m2), BP (127±16 vs 129±20 mmHg) and antihypertensive use (24% vs 20%) were similar among both groups (all P>0.05), whereas eGFR was lower in donors (67±14 mL/min/1.73 m2) than in non-donors (86±17 mL/min/1.73 m2). mGFR was 116±22 mL/min before donation, was reduced to 73±13 mL/min (P<0.001) at 3 mo post-donation and stabilized at 5 yrs (80±19 mL/min) and 10 yrs (77±16) after donation. None of the donors developed an mGFR <30 mL/min/1.73 m2. Conclusion: Live kidney donation is a safe procedure in carefully selected patients and seems associated with a lower all-cause mortality risk compared with matched individuals in the general population.

Predicted Indirectly ReCognizable HLA Epitopes presented by HLA-DRB1 (PIRCHE-II) are related to HLA-antibody formation during pregnancy

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Pregnancy can prime maternal immune responses against inherited paternal HLA of the fetus. This frequently leads to the production of child-specific HLA antibodies. We previously showed that predicted T-helper epitopes derived from donor HLA and presented by recipient HLA class-II (PIRCHE-II) are associated with antibody response after kidney transplantation. The aim of this study is to evaluate the role of PIRCHE-II in the formation of child-specific HLA antibodies during pregnancy. A total of 301 mother-child pairs were HLA-typed and maternal blood samples were analyzed for the presence of child-specific HLA antibodies. Child-specific antigens were classified as either immunogenic HLA or non-immunogenic HLA based on the presence of specific antibodies and correlated to PIRCHE-II numbers. Immunogenic HLA contained higher numbers of PIRCHE-II than non-immunogenic HLA. Moreover, the probability of antibody production during pregnancy increased with the number of PIRCHE-II. However, this correlation was absent in pregnancies that were preceded by one or more miscarriages. Our data suggest that the number of PIRCHE-II is related to the formation of child-specific HLA antibodies during pregnancy. Furthermore, a previous miscarriage and a previous successful full-term pregnancy have a different immunological impact on a subsequent successful pregnancy. Present confirmation of the role of PIRCHE-II in antibody formation outside the transplantation setting suggests that the PIRCHE-II concept is universal.

MicroRNAs in urinary sediments as non-invasive tool to detect acute rejection after kidney transplantation

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MicroRNAs in urine are suitable targets for non-invasive detection of acute rejection (AR), since they represent relatively stable analytes. Indeed, we found that PCR signals for several microRNAs in both sedimentary cells and isolated exosomes remained stable in urine collected freshly from 4 renal transplant patients at the bedside, when these urine samples had been incubated for up to 24 hours at room temperature. Next, within the transplant period 2007-2014 we set up a discovery-validation strategy to identify microRNAs that are associated with incidence of AR. First, 742 microRNAs were profiled by qPCR in urinary sediment of 8 recipients with AR and in 8 recipients with stable graft function. As validation, 10 microRNAs were analyzed in urinary sediments of 140 recipients with AR: morphologically indicative of borderline (n=5), cellular (n=67), vascular (n=37) or humoral rejection (n=31). Biopsies were negative for SV40. The group was compared with urinary sediment from 64 recipients, who had a surveillance biopsy taken showing no morphologic alterations indicative of rejection. RNA was extracted from the sediments, and a spike-in was added to the RNA to check efficiency of the cDNA reaction. MicroRNA levels were corrected for 3 reference microRNAs. In the discovery set, 32 microRNAs were differentially expressed ($P<0.05$) between groups, of which 20 were significantly lower in the AR group. Some microRNAs matched with what was found in previous profiling studies in transplant biopsies and urines. In the validation set, most pronounced differences in the AR group compared to controls (all $P<0.00001$) were found for miR-25-3p (1.9-fold), miR-126-3p (2.9-fold), miR-142-5p (0.40-fold), miR-155-5p (3.1-fold), and miR-615-3p (0.23-fold). The latter four together distinguished AR from controls in a multivariate logistic regression model with a sensitivity of 90.0% and a specificity of 81.0%. Measurement of microRNAs in urinary sediment of kidney transplant patients may help to non-invasively identify acute graft rejection.

Elevated intragraft expression of innate immunity and cell death-related markers characterizes deceased donor conditions and is a risk factor for adverse graft outcome

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Background: The innate immune response, including the Toll-like receptors (TLRs) and the complement system, is increasingly being recognized in allograft injury after kidney transplantation. We aimed to establish the relationship between innate immune gene expression at the moment of implantation or acute rejection and graft outcome. Method: A total of 19 genes, including TLRs, complement components and regulators, and apoptosis-related genes, were analyzed at the mRNA level by qPCR in 123 biopsies with acute rejection (AR) and paired pre-implantation biopsies (n=75), within the first 6 months post-transplant. Expression levels before transplantation were tested in relation to the type of donor (deceased or living; making up 78% and 22%, respectively, of the group) and occurrence of delayed graft function (DGF). The expression levels during AR were investigated for association with steroid-responsiveness and graft loss. Results: Before transplantation, expression of C2, C3, and the Bax/Bcl2 ratio were significantly higher ($P<0.01$) in tissue samples from deceased donors as compared to living donors. Within the deceased donor group there were no associations between gene expression and DGF. During AR, all TLRs and C2 and C3 showed increased expression compared with pre-implantation conditions whereas three complement regulators and C4 and Bcl2 showed decreased expression. During AR, expression of none of the genes was associated with steroid response. However, relatively high TLR4 expression and Bax/Bcl2 ratio at time of AR were related to adverse graft outcome. Fifteen patients with a high Bax/Bcl2 ratio in their deceased donor graft (higher than that in the living donor group) had significantly ($P<0.05$) worse death-censored graft survival (61.3%) at 6-year post-transplant compared to those with a low ratio (89.4%) and those with a living donor graft (95.8%). In Cox regression analysis, TLR4 and Bax/Bcl2 ratio in the deceased donor group predicted outcome independently of previously identified clinical risk factors of graft loss. Conclusion: The elevated expression of C2, C3, and Bax/Bcl2 ratio in deceased donor transplants supports the notion that complement and apoptosis pathway activity is already enhanced before kidney transplantation. The relationship of high Bax/Bcl2 ratio during AR with graft loss may point to an adverse effect of intragraft cell death, and thereby possibly enhanced immunogenic danger signals, on graft outcome.

Fecal microbiota transplantation against intestinal Extended Spectrum beta-Lactamase producing Enterobacteriaceae colonization in renal transplant and non-transplant patients.

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Introduction: Infections by Extended Spectrum beta-Lactamase (ESBL) producing Enterobacteriaceae is causing significant morbidity among patients resulting in frequent hospitlizations and the need of longstanding intravenous antibiotic use. Patients with recurrent antibiotic exposure and renal transplant patients are at risk for colonization by ESBL producing Enterobacteriaceae. Van Nood et.al. (New England Journal of Medicine 2013) demonstrated that fecal microbiota transplantation (FMT) is highly effective against Clostridium difficile colitis with overall success rate of 94%. AIMS: To evaluate the effectiveness of FMT against intestinal colonization by ESBL producing Enterobacteriaceae. METHODS: We performed a proof of principle study in renal transplant and non-transplant patients with intestinal colonization by ESBL producing Enterobacteriaceae confirmed by rectal swab culture. These patients underwent FMT with feces of a healthy donor, administered through a nasoduodenal tube. All patients underwent full colon lavage with cetomacrogol one day prior to FMT. Follow-up after FMT consisted of rectal culture on ESBL taken at week 1, 2, 4 and 12 after FMT. If the ESBL producing Enterobacteriaceae still persisted, a second FMT was performed. RESULTS: In total, 4 renal transplant and 11 non-transplant patients with intestinal ESBL producing Enterobacteriaceae colonization underwent FMT. In the renal transplant group: 1 renal transplant patient was successfully decolonized after the first FMT whereas another after a second FMT. The other two are still in follow-up. In the non-transplant group (n=11); 2 patients (18.2%) were decolonized after the first FMT and another 2 (18.2%) after the two FMT procedures. ESBL persistence occurred in 5 non-transplant patients (45.4%) whereas two patients (18.2%) are still in follow-up. Two patients have more than a year follow-up after successful decolonization after FMT; these two remained ESBL-free. Side effects: 4 out of 15 patients (26.7%) reported self-limiting mild abdominal cramps during FMT. No nausea or vomiting occurred. Conclusion: FMT to eradicate ESBL producing Enterobacteriaceae seems to be less efficacious than FMT to treat Clostridium difficile and has an overall success rate of 40%.

Resting energy expenditure in end-stage cystic fibrosis patients before and after lung transplantation

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Background & aims: Resting energy expenditure (REE) is increased in patients with cystic fibrosis (CF) with end-stage lung disease due to chronic inflammation and pulmonary infections. It is expected that energy expenditure will be lower after lung transplantation (LTx) because the inflammation will decrease. We therefore assessed REE in pre-LTx CF and post-LTx CF patients. We also studied the agreement between measured and predicted REE.
Methods: Included were 12 pre-LTx CF patients (9 women, median age 31.6 years IQR 23.3-40.0) and 12 post-LTx CF patients (6 women, median age 33.5 years, IQR 22.3-40.3). REE was measured in a fasted state using indirect calorimetry. Values were compared with predicted REE calculated by formulas of Harris Benedict (HB 1919 and 1984), Schofield and World Health Organization (WHO) 1985. A calculated REE between 90% and 110% of REE measured was considered adequate.
Results: Mean REE measured by indirect calorimetry was 1735 kcal (SD 251) pre-LTx and 1650 kcal (SD 235) post-LTx (p=0.40). REE expressed per kg Fat Free Mass (FFM) was 40.5 kcal/kg in pre-LTx CF patients, which was about 15% higher than the 34.3 kcal/kg in post-LTx CF patients (p=0.01). Prediction equations underestimate REE in at least 75% of pre-LTx and 33% of post-LTx CF patients. The predicted REE using the four different prediction formulas did not differ significant from each other. REE expressed per kg Fat Free Mass (FFM) was 40.5 kcal/kg in pre-LTx CF patients, which was about 15% higher than the 34.3 kcal/kg in post-LTx CF patients (p=0.01). Conclusions: After lung transplantation the REE per kg FFM is decreased in patients with CF. Prediction equations underestimate REE in end-stage CF patients. REE per kg FFM is lower post-LTx than pre-LTx in CF patients. Measurement of REE is recommended for LTx CF patients, especially pre-LTx to optimize energy requirements for improving the nutritional status.

Pancreas donor quality and donor risk indices in pancreas allocation in the Eurotransplant region

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Background Pancreas donor selection and recognition, as well as optimal organ allocation are important to cope with increasing organ shortage. The Pancreas Donor Risk Index (PDRI) might be a useful tool, however contains logistical factors that do not necessarily reflect donor quality. The Preprocurement Pancreas Allocation Suitability Score (P-PASS) was developed in 2008 to predict pancreas acceptance and might not be fully applicable. Methods All donors reported to Eurotransplant from 2004 until 2014 were included. PDRI logistical factors were set to reference, to purely reflect donor quality (PDRIdonor). PDRI and P-PASS association with allocation outcome was studied using area under the receiver operating characteristic curve (AUROC). Regional differences in donor quality were also investigated. Results In the study period 23 851 donors, of which 10 444 pancreas donors, were reported. From 6090 (58.3%) donors the pancreas was accepted by a transplant center and from 2947 (28.2%) donors the pancreas was transplanted. P-PASS was inferior to PDRIdonor in its ability to predict organ reporting, acceptance and transplantation: AUC 0.63, 0.67 and 0.73 for P-PASS vs. 0.78, 0.79 and 0.84 for PDRIdonor, respectively. Furthermore, there were significant differences in donor quality amongst the different Eurotransplant countries, both in reported donors, as well as in transplanted organs. Conclusions PDRI is a powerful predictor of allocation outcome and should be preferred over P-PASS. Proper donor selection and recognition and possibly a more liberal approach towards inferior quality donors may increase donation and transplantation rates.

Anonymity in deceased organ donation in The Netherlands: a gap between law and practice

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Introduction In The Netherlands there is a gap between legislation and practice regarding anonymity in deceased organ donation. The Dutch law is in accordance with European Directives and states that anonymity can be revoked if the donor or recipient gives written consent to do so. The donor family does not have the legal right to give consent for revealing any information. In practice, numerous professionals reveal information of the donor to the recipient without the correct consent and vice versa. This consent is not necessary for exchange of information under the law, for example the Medical Treatment Agreement Act. Is this legally required consent even feasible and desirable in practice?
Argumentation In the healthcare sector it is not allowed to reveal information from the medical record of the donor or recipient without his or her written consent. Revoking identity is not limited to personal data which makes the identification of donor or recipient possible. It is also not allowed to give non-identifiable information of the donor such as age. This is based on the ethical principal that the recipient has to be protected against emotional contact and claims from the donor family. This has its consequences for practice. Non-identifiable information of the recipient such as gender is given, since it is known that this information can have a positive impact on the experience of the donor family on the donation process. This analysis of the law shows that consent from recipient is necessary. Currently, the donor family is informed about the age and gender of the recipient through a letter, without the permission from the recipient. It has also consequences for current initiatives that aim to revoke anonymity between donor and recipient are not allowed, since the law forbids donor family to give consent instead of the donor.
Conclusion The Dutch law with regard to anonymity in deceased organ donation is clear. Even information such as name of the donor can be released by practitioners if the donor has given his written consent. In practice, non-identifiable information is spread without consent. It is not feasible to ask every potential donor consent to spread his age and gender after dead. It is therefore questionable whether it is desirable to ask for this consent. Practice and legislation differ, and therefore policy has to be developed to fill the existing gap. Further discussion on this subject is necessary.

IL-21 receptor antagonist ATR-107: pioneer in decreasing humoral immunity in an allogeneic setting

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Background and aims: Antibody-mediated rejection is an immunological restriction contributing to high rates of allograft dysfunction. The extent of this humoral immune response is often underestimated. It does not only result in the formation of circulating donor-specific antibodies (DSAs), but also involves interaction between CD4+CXCR5+ T follicular helper (Tfh) cells and CD19+CD27+ memory B cells, leading to immunoglobulin-producing plasmablasts. Within this process, IL-21 acts as primary cytokine. Here, we investigated the effect(s) of the IL-21R antagonist ATR-107 on IL-21/IL-21R controlled phosphorylation of STAT3, and on Tfh-mediated B cell help upon allogeneic stimulation. Methods: Phospho-flow cytometry was used to determine the phosphorylation level of IL-21 stimulated peripheral CD4+ and CD8+ T cells in pre-transplant blood of kidney transplant patients. Mixed lymphocyte reactions (MLRs) were performed with FACS sorted CD4+CXCR5+ Tfh cells and CD19+CD27+ memory B cells stimulated with alloantigen. B cell differentiation and immunoglobulin class switching were analysed by flow cytometry. Both approaches were performed in the presence or absence of ATR-107 (10ug/ml). Results: ATR-107 inhibited the phosphorylation of STAT3 in a dose-dependent manner in both CD4+ and CD8+ T cells. After MLR, a significant CD27+CD38+ plasmablast population was detected (14.28±3.78%), which was significantly reduced in the presence of ATR-107 (3.14±0.64%, $p<0.01$). Inhibition of plasmablast differentiation was associated with impaired immunoglobulin class switching measured by decreased proportions of membrane bound IgG on memory B cells (from 13.12±5.07% to 2.23±1.05%, $p<0.05$). Conclusion: In conclusion, interrupting the interaction between Tfh and memory B cells via the IL-21/IL-21R pathway may be a promising and novel approach to reduce B cell-mediated alloreactivity in organ transplantation.

Increase Of Highly Differentiated CD4+CD28null T-Cells Is Associated With A Reduced Risk For Early Acute Renal Transplant Rejection

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Background: End-stage renal disease patients have a dysfunctional, prematurely aged peripheral T-cell system. Here we hypothesized that the degree of premature T-cell ageing before kidney transplantation predicts the risk for early acute allograft rejection (EAR). Methods: 222 living donor kidney transplant recipients were prospectively analyzed. EAR was defined as biopsy proven acute allograft rejection within 3 months after kidney transplantation. The differentiation status of circulating T cells, the relative telomere length and the number of recent thymic emigrants (RTE; defined as CD31+ naive T cells) were determined as T-cell ageing parameters. Results: Of the 222 patients analyzed, 30 (14%) developed an EAR. The donor age and the historical panel reactive antibody score were significantly higher ($p=0.024$ and $p=0.039$ respectively) and the number of related donor kidney transplantation was significantly lower ($p=0.018$) in the EAR group. EAR-patients showed lower CD4+CD28null T-cell numbers ($p<0.01$) and the same trend was observed for CD8+CD28null T-cell numbers ($p=0.08$). No differences regarding the other ageing parameters were found. A multivariate Cox regression analysis showed that higher CD4+CD28null T-cell numbers was associated with a lower risk for EAR (HR: 0.65, $p=0.028$). A Kaplan-Meier analysis showed that patients with high numbers of CD4+CD28null T-cells (>36.67 cells/µl) had a significantly higher EAR free survival than patients with intermediate (4.33–36.67 cells/µl) and low (<4.33 cells/µl) numbers of these cells ($p=0.008$ and $p=0.009$ respectively). In vitro, a significant lower percentage of alloreactive T cells was observed within CD28null T cells ($p<0.001$). Conclusion: Immunological ageing-related expansion of highly differentiated CD28null T cells is associated with a lower risk for EAR.

Tissue priming of plasmacytoid dendritic cells enhances their phagocytosis and lowers the threshold for subsequent Toll-like receptor 7/9 activation

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Plasmacytoid dendritic cells (pDC) have a pivotal role in clearing viral infections, and can regulate tolerance or immunity depending on their activation status. We have previously demonstrated a strong influx of pDC in the tubulointerstitium of human renal allograft rejection biopsies. In experimental transplant models, pDC were demonstrated to be activators of indirect alloreactivity, suggesting they should be able to take up donor antigens. In this study, we investigated the capacity and requirements of human pDC to ingest and present donor antigen. In absence of any stimulus pDC were unable to ingest apoptotic cells (AC) (mean 2%), which was only slightly increased after activation using TLR9 ligand CpG (mean 15%), in consensus with previous reports. However, priming pDC by conditioned medium (CM) derived from human kidney cell lines, as well as primary tubular epithelial cells, and subsequent TLR9 ligation using CpG or cytomegalovirus, strongly induced the capacity to ingest AC (mean 44%). Priming by CM led to phosphorylation of the key transcription factor Interferon Regulatory Factor-7, in absence of IFNα production. Importantly, upon priming 10-fold lower concentrations of CpG were required to get optimal TLR9 activation. Consequently, activated primed pDC produced vast amounts of IFNα (mean 5,354 vs 475 pg/mL) and the chemokines CCL4 and CXCL10. Moreover, priming increased pDC phenotypic maturation (CD40/80/83/86 and CCR7) and TLR7/9 expression, compared to non-primed pDC. As a functional consequence, primed pDC induced a vigorous allogeneic T cell proliferation as compared to their non-primed counterparts (mean 60% vs 4%), as well as inducing a strong TH1 skewing (e.g. IFNγ mean 2,268 vs 60 pg/mL). Using a CD4 T cell clone with indirect specificity, pDC were capable of indirect antigen presentation. In conclusion, we show that factors produced by renal epithelial cells enable the phagocytic capacity of pDC following TLR9 ligation. Moreover, this tissue priming lowers the TLR9 activation threshold by one order of magnitude. Subsequently, TLR9 ligation by CpG or CMV strongly enhances their function as antigen presenting cells, and could explain the observed relation between viral and allogeneic immunity.

Premature Ageing Of T Cells In End-Stage Renal Disease Patients Does Not Predict Infectious Complications After Renal Transplantation

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Background: ESRD patients have a prematurely aged T-cell system, which may contribute to the uremia-associated immune deficiency. In this study we tested the hypothesis that the characteristics of premature T-cell ageing, assessed prior to and within the first year after renal transplantation (RT), are associated with the risk for infections after RT. Methods: We prospectively studied 188 living donor RT-recipients during their first year of transplantation. The peripheral T cells were analyzed before, and 3 and 6 months after transplantation, for the content of recent thymic emigrants (RTE), the relative telomere length (RTL) and differentiation status. We assessed T-cell differentiation status by immunophenotyping, RTL was determined as a measure for proliferative history and RTE were identified by the expression of CD31 within the naïve T cell pool. These parameters were related to the occurrence of opportunistic infections (OI) and serious infections (SI). Results: Of the 188 RT-recipients, 84 (45%) developed an infection during the first year after RT and were defined as the infection group. Within this group, 50 (60%) patients developed an OI and 53 (63%) developed an SI. The majority of the infections (85%) occurred within the first 6 months after RT, and within this period the majority (66%) of the infections occurred within the first 3 months after RT. T-cell ageing parameters assessed prior to RT were not associated with the risk for infection during the first 6 months. The CD4+ and CD8+ memory T-cell compartments showed a significant decrease within the first 3 months after RT in both groups ($p<0.001$). The CD4+ memory T cells increased between T=3 and T=6, only reaching statistical significance for the infection group ($p=0.015$). The amount of CD8+ memory T cells increased significantly in both groups ($p<0.001$), but reached baseline levels only in the infection group. In the infection group the percentage of CD8+CD28null T cells increased significantly ($p=0.024$) between T=3 and T=6, almost resulting in a larger value than at baseline ($p=0.061$). The RTL of the CD8+ T-cell population only increased significantly in the infection group between T=0 and T=3 ($p=0.018$), and remained similar thereafter. The observed differences in the post-RT dynamics in several T cell subsets and RTL was a consequence of an infectious episode. Conclusion: Parameters of uremia-associated premature ageing of peripheral T-cells do not predict post-transplant infections.

End-stage renal disease does not impair the large-scale generation of potent alloantigen-specific regulatory T cells for immunotherapy

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Background. Alloantigen-specific natural occurring regulatory T cells (nTregs) have the potential to offer a more targeted approach of immunosuppression and are the cell type of interest for inducing tolerance in kidney transplantation. We have recently developed an expansion protocol for highly enriched nTregs thereby obtaining sufficient numbers of potent nTregs for immunotherapy. Patients suffering from end-stage renal disease (ESRD) have a dysfunctional T cell immune system but it is not known how this affects nTreg function and expansion potential. In this study, frequencies, phenotype, expansion capacity, stability and function of nTregs from ESRD patients were compared to those from healthy individuals (HI). Material and Methods. Flow cytometry-based isolated nTregs of both ESRD patients (either not or on renal replacement therapy, RRT) and HI were expanded using (donor-derived) allogeneic mature monocyte-derived dendritic cells (moDC) and extensively characterized by analysis of the demethylation status of the TSDR of the FOXP3 gene and the expression of typical nTreg markers, i.e. FOXP3, HELIOS and CTLA4. In addition, the suppressive capacity of allogeneic mature moDC-expanded nTregs was tested in a mixed lymphocyte reaction (MLR). Results. Compared to age- and gender-matched HI, similar frequencies of nTregs were present within the circulation of ESRD patients either not or on RRT, i.e. median percentages nTregs within CD4+ T cells amounted to 5.6, 5.2 and 5.9, respectively. The isolated nTregs of ESRD patients could be equally well or even better expanded using allogeneic mature moDC, i.e. median fold expansions after 10-11 days amounted to 12.6 and 30.2 (ESRD patients not or on RRT, respectively) versus 8.7 (HI). Extensive phenotypical characterization did not reveal significant differences. The demethylation status of the TSDR was maintained or even further promoted as was the expression of characteristic nTregs markers. In addition, even at low ratios of Tregs: Teffectors (i.e. 1:320), the median percentage of inhibition of donor-alloantigen-induced proliferation by allogeneic mature moDC-expanded nTregs of ESRD patients either not or on RRT was similar to HI. Conclusion. Circulating nTregs of ESRD patients either not or on RRT can be highly enriched and alloantigen-specific expanded to numbers needed for clinical applications. Phenotype, stability and functionality of these alloreactive nTregs is similar to results obtained from HI.

Belatacept does not inhibit plasmablast formation supported by follicular T helper cells, but favors the development of transitional regulatory B cells in kidney transplant patients

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The costimulatory inhibitor belatacept effectively blocks T-B cell interaction in animal transplant models. We studied the functional follicular T helper cells (TFH)-B cell interaction in belatacept-treated patients to determine the effects of this drug in human kidney transplantation.
The presence of CXCR5+PD-1+CD4+ TFH cells, CD19+CD27+CD38++ plasmablasts and CD19+CD24++CD38++ transitional B cells was assessed in the circulation of belatacept-treated and tacrolimus-treated patients (n=40), and in vitro after donor antigen re-stimulation in the presence and absence of therapeutic concentrations of belatacept (10 µg/mL) or tacrolimus (10 ng/mL). PBMCs were obtained 3 months after transplantation or during an acute rejection episode (before additional therapy was given). The proportion of TFH-cells and their allogeneic IL-2 and IL-21 production were measured as well as the differentiation of B cells into TNFα-producing effector plasmablasts and transitional IL-10+ regulatory B cells (Bregs). In belatacept-treated patients, the frequency of circulating TFH cells was low before transplantation (0.6 cells/µL), and did not change after. The number of circulating plasmablasts and transitional B cells dropped under belatacept treatment (from 0.3 to 0.2 cells/µL, p=0.006, and from 1.5 cells/µL to 0.2 cells/µL, p=0.001, respectively). For these B cell populations, similar observations were made for tacrolimus-treated patients. After in vitro re-stimulation with donor antigen, a 10-fold increase of TFH cells was observed, which was ~30% inhibited by belatacept, p=0.001, and ~50% by tacrolimus, p<0.001. Intracellular IL-2 and IL-21 production by these activated memory T cells was not suppressed by belatacept or tacrolimus. Interestingly, in belatacept-treated patients during rejection (n=11) a higher proportion of donor-antigen re-stimulated TFH cells produced IL-21 than in stable belatacept-treated patients (n=9), 39% vs. 22%, respectively, p=0.01. Stimulated B cells differentiated into TNFα-producing plasmablasts, a process not inhibited by belatacept, but only by tacrolimus. Unlike tacrolimus, however, belatacept favored the differentiation into IL-10 producing transitional B cells, i.e. Bregs. No differences were found in B cell differentiation between rejectors and non-rejectors. In short, in vitro belatacept favors a regulatory profile of B cells, but fails to inhibit the donor-reactive TFH-B cell interaction after human kidney transplantation.

Antigenic targets of local antibodies produced in Ectopic Lymphoid Structures in Cardiac Allografts

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Background: Cardiac allograft vasculopathy (CAV) is an immune-mediated vascular pathology that limits the survival of cardiac transplants; antibody and cellular-mediated events have been implicated in this process. Ectopic lymphoid structures (ELS) surrounding coronary arteries can be observed in patients with evident CAV and are active, antibody-producing immune structures. The aim of this study was to investigate the antigenic targets of the antibodies produced in the ELS.
Methods: Epicardial coronary arteries (n=56) were collected on autopsy from heart transplant patients and studied for the presence of ELS. Double immunohistochemistry was done to test whether plasma cells were positive for IgG and IgM antibodies. Clonality of plasma cells was tested using PCR and *in situ* hybridisation for kappa and lambda. IgG and IgM levels in tissue lysates of ELS were measured by ELISA, and typed for donor specificity using the Luminex platform.
Results: Plasma cells within and around ELS produce IgG or IgM antibodies. The B cells display an oligoclonal distribution. IgG and IgM levels in epicardial tissue were detected in explanted hearts (controls) but were significantly higher in cardiac transplant patients with large ELS ($p<0.05$). In 4 out of the 25 lysates from patients with ELS (16%) these contain donor specific antibodies directed towards HLA type II. In some cases HLA antibodies in the ELS were found, but not in the plasma/serum, suggesting local production instead of diffusion into the tissue.
Conclusion: Patients with ELS exhibit actively antibody producing plasma cells with no clonal expansion. Interestingly, these locally produced antibodies are in some cases directed against the donor HLA-II type. Local antibody-mediated rejection has major consequences for the graft that might be hard to detect in the systemic circulation.

A CD59 promotor polymorphism in donor lungs correlates with a higher risk for chronic rejection after lung transplantation

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Introduction Complement activation primarily leads to membrane attack complex formation and subsequent target cell lysis. Protection against self-damage is regulated by complement regulatory proteins, including CD46, CD55, and CD59. Within their promotor regions, single nucleotide polymorphisms (SNPs) are present that could influence transcription.
Methods We analyzed these SNPs and investigated their influence on protein expression levels on PBMCs and donor derived primary endothelial cells. Furthermore, we analyzed the effect of this SNP configuration on sensitivity to complement mediated cell lysis and subsequent cytokine secretion.
Results A single SNP configuration in the promotor region of *CD59* was found correlating with lower CD59 expression on lung endothelial cells ($p=0.016$) and monocytes ($p=0.013$). Lung endothelial cells with this SNP configuration secreted more pro-fibrotic cytokines IL-6 ($p=0.047$) and FGF-β ($p=0.036$) upon exposure to sublytical complement activation than cells with the opposing configuration, whereas monocytes were more susceptible to antibody-mediated complement lysis ($p<0.0001$). Analysis of 137 lung transplant donors indicated that this *CD59* SNP configuration correlates with impaired long-term survival ($p=0.094$) and a significantly higher incidence of the bronchiolitis obliterans syndrome ($p=0.046$) in the recipient.
Conclusion: These findings support a role for complement in the pathogenesis of this post-transplant complication and are the first to show a deleterious association of a donor *CD59* promotor polymorphism in lung transplantation.

Center volume is associated with outcome following pancreas transplantation within the Eurotransplant region

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Introduction Outcome following all kinds of surgery depends on several factors, amongst these the annual volume-outcome relationship. This might also be the case in a highly complex field of pancreas transplantation. No study has investigated this relationship in a European setting. Methods All consecutive pancreas transplantations from January 2008 until December 2013 were included. Donor, recipient and transplant related factors were analyzed for their association with patient and graft survival. Centers were classified in equally sized groups as being low volume (<5 transplantations on average each year in the 5 preceding years), medium volume (5-13/year) or high volume (≥ 13/year). Results In the study period, 1276 pancreas transplantations were included. Mean duration of follow up was 3.2 (SD 1.8) years. Low volume centers performed 396 (32.6%) transplantations, medium volume 425 (35%) transplantations and high volume 393 (32.4%) transplantations. Unadjusted 1 year patient survival was associated with center volume and was best in high volume centers, compared to medium and low volume: 96.5%, 94% and 92.3%, respectively (p=0.002). Pancreas donor risk index (PDRI) was highest in high volume centers: 1.38 vs. 1.21 in medium and 1.25 in low volume centers, (p<0.001). Unadjusted 1 year death censored pancreas graft survival did not differ significantly between volume categories: 86%, 83.2% and 81.6%, respectively (p=0.110). However, after multivariate Cox-regression analysis, higher PDRI (HR 1.61, p=0.002), retransplantation (HR 1.90, p<0.001) and higher recipient BMI (HR 1.04, p=0.044) were independent risk factors for pancreas graft failure. High center volume was protective for graft failure (HR 0.65, p=0.014) compared to low center volume. Medium volume was protective compared to low volume, albeit not statistically significant (HR 0.87, p=0.367). Conclusion Patient and graft survival following pancreas transplantation is better in higher volume centers. High volume centers have good results, even though they transplant organs with the highest risk.

Use of extended criteria donor organs is a risk factor for pancreas graft thrombosis

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Introduction Despite improvements in perioperative management of pancreas transplantation recipients, graft thrombosis remains a serious threat. Scarcity of organs forces transplant professionals to accept more extended criteria organs. This use of high-risk organs might lead to an increased number of graft thrombosis. Furthermore, in the literature the association of graft thrombosis with antibody mediated rejection (AMR) has been described. Methods All consecutive pancreas transplantation performed from 2004 until 2014 were analysed. Primary endpoint was the incidence of graft thrombosis within 90 days after transplantation. Influence of donor risk was analysed. Secondary endpoints were bleeding and reoperation. Thrombosis due to proven AMR was not considered thrombosis. AMR was defined as C4d positivity on histological examination and present donor specific antibodies (DSA). Suspicion of AMR was defined as positive C4d or DSA. Results 211 consecutive pancreas transplantations were performed (185 SPK, 24 PAK, 2 PTA). Mean pancreas donor risk index (PDRI) was 1.36 (SD 0.44). Two female recipients had thrombosis due to AMR. Complete graft thrombosis occurred in 15/211 cases (7.1%). In 53/211 patients (25.1%) a reoperation had to be performed, this was in 15/53 cases (28.3%) for bleeding. Graft thrombosis risk was 2.3% for standard criteria donors and 10.6% for extended criteria donors (p=0.028). Multivariate analysis showed that an extended criteria donor pancreas is an independent risk factor for graft thrombosis (HR 4.7, p=0.042) and also, female recipients were at increased risk (HR 3.9, p=0.021). AMR was suspected (not proven) in 0/4 male recipients and 4/10 female recipients (p=0.251). Conclusion Graft thrombosis is the main cause of early graft failure, however, for standard criteria donors, the risk of thrombosis is low (2.3%). Extended criteria donors have an increased risk for graft thrombosis. Risk of thrombosis is also higher in female recipients, possibly explained by the higher prevalence of suspected AMR.

Influence of Donor Warm Ischemia Time on Development of Acute Kidney Injury after DCD Liver Transplantation

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Introduction Acute kidney injury (AKI) after liver transplantation (LT) is observed in over 50% of the donation after circulatory death (DCD) recipients. This phenomenon has been attributed to the additional donor warm ischemia time (DWIT) with subsequent increase of hepatic ischemia/reperfusion injury (IRI). As of today, various definitions of DWIT are used and little is known about its influence on the development of postoperative AKI. Our objective was to analyze the impact of DWIT on development and severity AKI after DCD LT. Methods Development of AKI, according to AKIN criteria, after DCD LT in our hospital was retrospectively assessed from July 2008 until April 2015. DWIT was divided into two periods: donor agonal phase (time from saturation <80% or MAP <50 mmHg to asystole) and absolute DWIT (time from asystole to start of cold perfusion). A multivariable logistic regression model (using backward likelihood estimation) with all clinical relevant donor, recipient, and intraoperative factors was created to identify factors associated with development of AKI. Postoperative peak serum aspartate amino-transferase (AST) was used as a surrogate marker for hepatic IRI. Results Seventy DCD recipients were included of whom 40 (57%) developed AKI. Agonal phase was longer in the AKI group (15 vs. 11 min; p=0.020). Surprisingly, absolute DWIT was shorter in the AKI group (15 vs. 18 min; p=0.050). Mean donor agonal phase however, correlated well with severity of AKI (no AKI, 11 min; AKIN 1, 13 min; AKIN 2, 16 min; AKIN 3, 20 min; p=0.014). This correlation was not observed for the mean absolute DWIT (no AKI, 18 min; AKIN 1, 16 min; AKIN 2, 16 min; AKIN 3, 17 min; p=0.205). The multivariable logistic regression model identified donor agonal phase as an independent factor associated with AKI (OR 1.104; 95% CI 1.014-1.203; p=0.023). Also peak serum AST increased with length of donor agonal phase (p=0.002), but was not congruent with absolute DWIT (p=0.374). Conclusion Our results suggest that not absolute DWIT, but length of donor agonal phase has an important influence on development and severity of AKI after DCD LT. Moreover, the severity of hepatic IRI also increases with length of donor agonal phase. This study provides new insight on the importance of the agonal phase on the severity of AKI and hepatic IRI after DCD liver transplantation.

Low-pressure pneumoperitoneum facilitated by deep neuromuscular blockade during laparoscopic donor nephrectomy is associated with reduced length of hospital stay

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Background: The use of low intra-abdominal pressure (<10 mmHg) reduces postoperative pain scores after laparoscopic procedures. We hypothesize that the use of low-pressure pneumoperitoneum -facilitated by deep neuromuscular blockade- improves the early quality of recovery after laparoscopic donor nephrectomy. Methods: 64 living donors scheduled for LDN were randomly assigned to low- (6mmHg) or standard (12mmHg) pressure pneumo-peritoneum. A deep neuromuscular block was used in both groups. Surgeons, anesthesiologists and the research team were blinded for the allocation of treatment. Surgical conditions were rated by the surgical rating scale (SRS); ranging from 1 (very poor) to 5 (optimal). If the SRS was below 4 (good) at any point during the procedure, the intra-abdominal pressure was increased step-wise. The primary outcome measure was the overall score on the quality of recovery-40 questionnaire at postoperative day 1. Results: Eight procedures (24%), initially started with low-pressure, were converted to a standard pressure (≥10mmHg). There was a tendency towards a better quality of recovery-40 score on day 1 in the low-pressure group (p=0.06). Overall pain scores and analgesic consumption did not differ between the low- and standard pressure group. Low-pressure PNP was associated with earlier mobilization and physical independence (p<0.05) and a lower deep intra-abdominal pain score at day 2 (p=0.02). In the low-pressure group, 15 patients (45%) were discharged at day 2 as compared to 7 patients (20%) in the standard pressure group (p=0.03). Conclusion: The use of low-pressure pneumoperitoneum during LDN is associated with a shorter length of hospital stay. This finding is mainly driven by earlier mobilization and physical independence.

A Short Period of Oxygenated Hypothermic Machine Perfusion Prior to Normothermic Machine Perfusion Improves Bile Output and Bile Composition of Extended Criteria Donor Livers

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Introduction: A short period of end-ischemic oxygenated hypothermic machine perfusion (HMP) can restore cellular adenosine triphosphate (ATP) energy stores in donor livers prior to transplantation. Hepatic bile production is highly dependent on transmembrane ATP-binding cassette (ABC) transporters in both hepatocytes and cholangiocytes. Given the significant arterial supply of oxygen to cholangiocytes and the central role of ATP in bile production, HMP was hypothesized to improve the quantity and quality of bile produced by donor livers after subsequent normothermic reperfusion. Methods: Eighteen human donor livers declined for transplantation were preserved with static cold storage (median 8.1 hrs). Six of these livers underwent 2 hours of oxygenated HMP, followed by ex vivo functional assessment during 6 hours of normothermic machine perfusion (NMP). Controls were 12 livers that underwent functional assessment during 6 hours NMP without first undergoing oxygenated HMP. Bile volume and composition, as well as gene expression of relevant ABC transporters (BSEP, MDR3, CYP7A1, AE2 and CFTR) were compared. Results: Cumulative bile production during NMP was significantly higher in HMP preserved livers, compared to controls (at 6 hrs NMP: 33.8 vs. 8.2 ml/kg liver; p=0.019). Biliary secretion of bile salts, phospholipids and bicarbonate during NMP was higher in the HMP group, compared to controls (bile salts: 0.060 vs. 0.003 mmol/kg liver, p=0.052; phospholipids: 0.019 vs. 0.003 mmol/kg liver, p=0.053; bicarbonate during last 30 min: 477 vs. 175 mmol/kg/30 min liver, p=0.089). There were no differences in gene expression of the ABC transporters between groups. Conclusion: A short period of 2 hours oxygenated HMP after conventional static cold storage results in significantly higher bile output and increased biliary secretion of bile salts, phospholipids and bicarbonate after subsequent warm reperfusion. This enhanced secretory function is likely explained by increased function of the ATP-dependent bile transporters.

Hepatocyte- and Cholangiocyte-derived MicroRNAs in Perfusate and Bile during Ex-Situ Normothermic Machine Perfusion of Human Donor Livers

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Introduction: MicroRNAs are gaining increasing attention for their use as bio-markers for tissue injury and biological factors. Normothermic machine perfusion (NMP) enables viability assessment of donor livers prior to transplantation, and we investigated whether the release of hepatocyte- and cholangiocyte-derived microRNAs (HDmiRs and CDmiRs, respectively) during NMP of human donor livers is predictive for hepatocytic and cholangiocytic function and viability. Methods: After a median cold preservation time of 8.4 hrs, 18 donor livers that were declined for transplantation were subjected to 6 hrs of NMP. Perfusion solution contained red blood cells, fresh frozen plasma and nutrients. Perfusate and bile samples were taken at 2 and 6 hrs of NMP for quantification of miRNA by qRT-PCR assays for HDmiRs 122 and 148a, and for CDmiRs 30e and 222. Ct values were used to calculate relative expression levels (2-(Ct)). Pearson correlations were performed between the microRNAs and biliary bilirubin (marker for hepatocytic function), AST in perfusate (hepatocytic injury), biliary bicarbonate (biliary function) and biliary LDH (biliary injury). Results: Biliary bilirubin levels correlated moderately negatively with both HDmiRs in perfusate ($r<-0.58$, $p<0.05$) and with HDmiR148a and CDmiR222 in bile ($r<0.53$, $p<0.05$) at 6 hrs NMP. All miRs measured in perfusate correlated very strongly with AST in perfusate ($r>0.89$, $p<0.005$) at 2 hrs of NMP and only HDmiRs correlated very strongly ($r>0.82$, $p<0.005$) at 6 hrs NMP. At 2 hrs NMP, only CDmiRs correlated very strongly with AST in perfusate ($r>0.84$, $p<0.005$), at 6 hrs all miRs correlated very strongly ($r>0.80$, $p<0.005$). Biliary bicarbonate did not correlate with HD or CDmiRs in bile or perfusate. Biliary LDH correlated very strongly with CDmiRs in bile ($r>0.80$, $p>0.05$) at 2 hrs and strongly with all miRs at 6 hrs ($r>0.75$, $p<0.005$). Biliary LDH correlated strongly with HDmiRs in perfusate at 2 and 6 hrs NMP ($r>0.68$, $p<0.05$). Conclusion: This study suggests hepatocyte- and cholangiocyte-derived miRs in perfusate and bile are reflective of hepatic and cholangiocytic injury rather than function. CDmiRs tend to be released into bile rather than into perfusate, and HDmiRs are released in bile at a later stage. Furthermore, HDmiRs in perfusate could potentially be used for assessment of biliary injury.

Evaluation of in-hospital complications after liver transplantation with the comprehensive complication index: potential benefit of DCD grafts in post alcoholic cirrhosis?

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Introduction DCD grafts are increasingly used in liver transplantation (LT) to overcome the donor shortage. These grafts are associated with more severe hepatic ischemia/reperfusion injury (IRI) and biliary complications. Due to the lack of appropriate morbidity parameters, short term recipient outcomes are still unknown. With the recently developed Comprehensive Complication Index (CCI) the postoperative morbidity after DCD LT can be compared with DBD LT. Methods All consecutive patients (excluding retransplantations and high urgency LT) who underwent LT from January 2007 until August 2015 in our center were retrospectively assessed. In-hospital complications were registered by the Clavien Dindo classification. The CCI is the cumulative result of all complications weighted by their grade in this classification. Retransplantation was scored as a IVb complication. The postoperative peak serum AST was used to quantify hepatic IRI. Results 330 recipients were included of whom 98 (30%) received a DCD graft and 232 (70%) a DBD graft. Recipient age (p=0.059), labMELD (p=0.536), and BMI (p=0.149) were comparable for both graft types. Hepatic IRI was more severe in the DCD group (median peak AST 2827 vs. 929 U/L; p=0.001) and the in-hospital retransplantation rate was higher in this group as well (9% vs. 3%; p=0.024). However, the median CCI at hospital discharge was comparable for both graft types (DCD 38.7; DBD 36.2; p=0.537). To compare the CCI for different indications for LT (viral hepatitis, biliary cirrhosis, post alcoholic cirrhosis, and 'other' group), a sub-analysis was performed. This analysis showed a comparable median CCI for DCD and DBD grafts in the viral hepatitis (p=0.538), biliary cirrhosis (p=0.537), and 'other' (p=0.353) group. In recipients with post alcoholic cirrhosis (n=59) a lower median CCI was observed when DCD grafts were used (30.2 vs. 43.6; p=0.031), while DCD and DBD recipients in this subgroup had comparable age (p=0.619), labMELD (p=0.828), and BMI (p=0.478). Conclusion This study provides new insight in the direct postoperative complications after LT. Despite more severe hepatic IRI and a higher retransplantation rate, the overall CCI was comparable in DCD and DBD LT. The lower CCI observed in DCD recipients with post alcoholic cirrhosis might have detected a subgroup suitable as recipients for DCD grafts.

The relationship between health literacy, self-management and complications after kidney transplantation

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Introduction: Health literacy (HL) and self-management (SM) may influence how patients interpret and act on post-transplant self-care, medication and lifestyle recommendations. Among a sample of our patient population 56% were re-hospitalized within one year after kidney transplantation (KT) . The aim of this study was to investigate whether HL and SM change over time and influence complications after KT. Methods: We performed a prospective cohort study. T0 was at discharge from the hospital after KT, T1 was 6 months later and T2 was 12 months later. We measured SM using an adapted Partners in Health scale (PIH, range 1-8) which has 4 subscales (after-care and knowledge, monitoring physical consequences, emotional and social consequences, healthy lifestyle) and HL using the Dutch Newest Vital Sign (NVSD, range 0-6). Change scores were calculated. Number of re-hospitalizations was summed and complications were categorized as rejection, infections and other. Regression (linear and logistic) analyses were conducted. Results: 154 patients participated. At T1 HL scores were significantly higher (p=.01) than at T0. HL did not change significantly (p=.1) between T1 and T2. After-care and knowledge significantly improved between T0 and T1 (p=.00), emotional and social consequences significantly improved between T1 and T2 (p=.01), but healthy lifestyle significantly decreased between T0 and T1 (p=.00). Higher baseline level of after-care and knowledge and monitor of physical consequences was related to a significantly higher rate of re-hospitalizations at T2 (p=.04, p=.03). Rejection was related to decreasing scores of emotional and social consequences between T0 and T1 (p=.04). Other complications were related to increasing scores of HL between T1 and T2 (p=.04). Conclusion: Evidence was found for changes in HL and SM over time. HL and SM were also found to relate to the rate of re-hospitalization, though in the opposite direction than expected. Increasing re-hospitalizations among those who improved in HL and SM skills might be explained by the fact that they respond earlier to symptoms of complications. Also, transplant-specific clinical tests to assess HL and SM is lacking. Future research on the relationship between HL, SM, kidney function and graft survival is needed.

Predictors for longer-term health-related quality of life of living kidney donors: A prospective multicenter study

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Background: Longer-term post-donation health-related quality of life (HRQoL; i.e., physical, psychological, and social-relational functioning) is comparable to that before donation and to that of the general population for the majority of living kidney donors. However, a small subgroup of donors experiences worse longer-term functioning after donation, for example showing symptoms of depression, anxiety, or persistent fatigue. Current guidelines for psychosocial screening procedures are often not evidence-based, resulting from a scarcity of research identifying possible predictors for worse longer-term functioning after donation. The current study examined an encompassing account of predictors for longer-term HRQoL of living kidney donors, including the expert opinion of transplant professionals within the screening process. Methods: HRQoL of living kidney donors was assessed before, and six and twelve months after donation in 230 donors from seven Dutch transplantation centers. Potential socio-demographic, psychological, social, and physical predictors were assessed before donation. Also, risk estimation questionnaires were filled out by transplant professionals (nephrologists, coordinating nurses, social workers, and psychologists) after the first consultation with the donors. Results: Being single, worse pre-donation physical and psychological functioning and specifically higher levels of fatigue, were related to worse longer-term physical functioning after donation. The donor-recipient relationship, worse pre-donation physical and psychological functioning, and lower levels of social support were related to worse psychological functioning after donation. Also, higher risk estimations of transplant professionals were related to worse longer-term post-donation functioning. Conclusion: The risk factors for worse longer-term HRQoL identified in the current study could be used to optimize screening procedures for living kidney donors. Furthermore, interventions for donors at risk could focus on these risk factors to prevent worse longer-term outcomes in donors with a high risk profile.

Overweight young female donors have a lower post-donation reserve capacity

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Recent work shows that young female kidney donors are at increased risk of developing gestational hypertension or preeclampsia. Absence of pregnancy-induced renal vasodilation is a hallmark of preeclampsia. We previously found that renal reserve capacity (RC) is reduced after donation in donors with high BMI, and older donors, but data in female donors of childbearing age are sparse so far. We investigated RC in 58 female donors of childbearing age (<45 years). RC was determined as the rise in glomerular filtration rate (GFR, by 125I-Iothalamate clearance) after constant dopamine infusion, 4 months prior and 2 months after live kidney donation. Median pre-donation GFR was 119 [111-132] ml/min, after dopamine stimulation GFR was 133 ml/min [120-146], with a median RC of 12 [3-17] ml/min. Although BMI was positively associated with GFR, there was no association with RC (st. beta=0.11, p=0.39). Post-donation, GFR was 78 [72-86] ml/min and 81 [76-87] after stimulation, with a RC of 3 [0-6] ml/min. Overweight donors (BMI >25) were more likely to have a RC loss of >5 ml/min (p=0.04) and BMI was inversely associated with the RC after transplantation (st. beta -0.35, p=0.02). We also observed a non-significant association of BMI with the development proteinuria (st. beta 0.25, p=0.06) at 2 months after transplantation. These data show that overweight is associated with lower post-donation reserve capacity in young female donors. We postulate that reduced renal reserve capacity can explain the increased risk of preeclampsia and gestational hypertension in overweight female kidney donors. Obesity is a well-established risk factor for preeclampsia and we propose that female kidney donors with the desire to have children especially, should be counselled to adopt a healthy lifestyle with a healthy body weight.

Pregnancy outcomes in a Dutch living kidney donation population.

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Introduction The majority of kidney transplantations in the Netherlands are performed with a kidney from a living donor. Some of the female donors might have a future pregnancy wish. For these women it is of great importance to know if donating a kidney could have a possible negative effect on their future pregnancies. Literature is sparse on this subject. Although recent studies show a significant increase in the risk of pre-eclampsia, older studies did not show this increased risk. The aim of this study was to investigate if a kidney donation affects complications in pregnancies. Methods We conducted a single center retrospective study of living kidney donors between 1981 and July 2013. Women aged 45 years or younger at time of donation were interviewed about their pregnancies before and after kidney donation. First by telephone or at our outpatient clinic, when this was not possible we send them a questionnaire by email or post. Women who had been pregnant before donation were used as control group. Results 1462 living kidney donors donated their kidney at our hospital between 1981 and July 2013. We could include 172/259 (66%) women in our study, 5 died, 11 refused, 28 moved to foreign country or had no correct address and 43 could not be reached. Median age at donation was 38 yrs (18 - 45). 110/172 (68%) women had 292 pregnancies before donation at a median age at delivery of 27 yrs, compared to 25/172 (15%) women whom had 46 pregnancies after donation and median age at delivery of 33 yrs ($p = 0.00$). 37/172 (22%) had not been pregnant at all. Before donation women reported 38/292 (13%) miscarriages compared to 14/46 (30%) after donation ($p = 0.01$) and 11/292 (4%) abortions pre-donation compared to 1 (2%) post-donation ($p = 1.00$). Hypertension was reported in 19/243 (8%) of pre-donation pregnancies compared to 11/31 (35%) pregnancies after donation ($p = 0.00$). Pre-eclampsia before donation occurred in 4/243 (2%) of the pregnancies compared to 3/31 (10%) in post donation pregnancies ($p = 0.03$). HELLP syndrome was experienced in 2 pregnancies before donation (0,2%) compared to 1 (3%) in a post donation pregnancy ($p = 0.30$). Discussion Pregnancies after kidney donation are significantly more complicated by hypertension and pre-eclampsia as compared to the pregnancies before donation. Difference in age at delivery as well as the kidney donation may contribute to this finding. Further investigations are needed to confirm these outcomes.

The development of a nurse-led self-management intervention for kidney transplant recipients using intervention mapping: the ZENN-study

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Background: Improving self-management is a potential way to optimize post-transplant outcomes. However, proven effective interventions aimed at promoting self-management after kidney transplantation are limited. The objective of this study was to describe the systematic development of a nurse-led self-management intervention for kidney transplant recipients. Methods: The Intervention Mapping approach was used in order to develop a pilot intervention which incorporates patients' needs, theories and evidence based methods. The needs of kidney transplant recipients were assessed by reviewing the literature, conducting focus groups and a Q-methodological study (step 1). Based on the needs assessment change objectives were formulated (step 2). Evidence-based methods to achieve these objectives were selected and subsequently translated into practical implementation strategies (step 3). The intervention protocol was developed accordingly (step 4). Implementation is scheduled for November 2015 – June 2016 (step 5), and feasibility will be evaluated using a pre-post questionnaire and interviews with patients and medical staff (step 6). A patient advisory committee as well as an expert steering group advised on the development throughout the process. Results: The intervention is designed to improve self-management utilizing evidence-based methods derived from health behavior change theories, principles of solution focused brief therapy and motivational interviewing. Four sessions, each of which take 15 minutes, are added to the standard medical care provided by the nurse practitioners in the outpatient clinic. In this series of sessions patients will be encouraged to develop goal setting, action planning and pursuit skills and apply these to self-management issues they currently face.
Conclusions: The intervention mapping approach provided a useful framework for integrating patients' needs, evidence and theories in intervention development.

Living elderly kidney donors: more investigations, lesser kidneys

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Introduction: over the years the number of elderly living kidney donors (LKD) has increased considerably. Elderly donors often suffer from chronic diseases that need further investigations to determine whether they can safely be approved for donation. We investigated whether these elderly donors underwent additional preoperative examinations (for example referral to a cardiologist or MAG3-scan) and whether there were more refusals for donation compared to the younger donor age group.
Methods: After an initial informative visit potential LKD without an immediately obvious contraindication for donation proceeded with medical examinations. In our NOTR database we analyzed the data of 379 potential LKD who visited the nephrologist in 2011 till 2013. Patients were divided in two age groups: 18-59 years (group 1, n=249) and 60-76 years (group 2, n=130). We investigated the outcome of the donor screening procedure at least one year after the first medical examination. Chi-square tests were used for statistical analysis.
Results: The percentage of referrals and additional investigations increased with donor age: 45% and 65% ($p< 0.001$) in group 1 and 2, respectively. The percentage of patients not accepted for donation increased from 15% to 33% ($p< 0.001$) in group 1 and 2. Refusals were highest in the subgroup above 69 years, i.e. 46%. Reasons for refusal were mainly kidney related: 6% and 19% ($p<0.01$) in group 1 and 2, respectively. The percentages of non-kidney related medical reasons contributed less to refusal in the young and old age group, i.e. 5% and 8% ($p< 0.05$). Finally, psychosocial reasons caused refusals in 4% and 6% in group 1 and 2 (NS), respectively.
Conclusion: With increasing donor age medical referrals and thus medical examinations increased significantly. The percentage of potential LKD who eventually not were approved for donating their kidney was highest in the oldest subgroup above 69 years. One could question whether this time and money consuming screening is justified in the oldest age group.

Mortality of young biliary atresia patients listed for liver transplantation: results from the Eurotransplant registry

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Introduction: Liver transplantation has become the standard treatment for children with biliary atresia (BA) who develop end stage liver disease despite Kasai portoenterostomy. Up to 50% of BA patients need a liver transplantation before the age of 5 years. The prognosis after transplantation has steadily improved, but pre-transplant mortality is also important for the overall prognosis of BA patients. The primary objectives of this study were to assess the magnitude of pre-transplant (in particular, waiting list) mortality and to identify possible risk factors. Methods: We retrospectively studied 642 patients with BA aged <5 years listed for liver transplantation in the Eurotransplant region between 2001 and 2014, and with a waiting list duration of < 1 year. In a subcohort of 365 children (84% from the period 2007-2014) we evaluated the association of pretransplant variables [dichotomous variables: age at listing (0.5 years), blood group, gender, MELD score (20) and renal replacement therapy; continuous variables: albumin, bilirubin, creatinin, and international normalized ratio (INR)] with waiting list mortality by Cox regression analysis. Result: The waiting list mortality was 4.5%, 7.5% and 8.4%, at 3, 6 and 12 months after listing for liver transplantation, respectively. Age at listing below 0.5 years [n=141, P=0.001, hazard ratio (HR) 4.1, 95% confidence interval (CI) 1.8-9.0] and MELD score above 20 (n=131, P<0.001, HR 10.2, 95% CI 4.4-23.8) were independently associated with the waiting list mortality. Other factors were not significantly associated. In 36 patients (9.9%) both risk factors were present, which coincided with waiting list mortality of 25% already at 6 months. This subgroup accounted for 32% of all pretransplant mortality in this cohort. Conclusion: Waiting list mortality of BA patients below 5 years is 8.4%, based on a large cohort in the Eurotransplant region. Age at listing below 0.5 years and a MELD at listing above 20 are associated with a strongly increased waiting list mortality. Identification of risk factors for waiting list mortality could be helpful for optimizing the allocation of donor organs.

Infections and their impact on waiting list survival in patients with end stage liver disease

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Background and aims Liver transplantation (LT) is the treatment of choice for patients with end-stage liver disease (ESLD). Unfortunately, there is a mismatch between donors and recipients, resulting in an increase of size of and mortality rate on the waiting list. In order to improve survival on the waiting list, better management of complications in ESLD leading to mortality, is needed. An important complication in cirrhotic patients is infection. We therefore assessed the impact of infections on survival on the waiting list in patients with ESLD, in context of waiting list dynamics. Methods We performed a retrospective cohort study of all adult patients listed for LT from December 2006 to December 2013 in a single center in the Netherlands. We studied type, risk factors, impact and cumulative effect of infections on withdrawal (i.e. death or clinical deterioration) of patients from the waiting list. We therefore conducted several regression models, taking competing risks on the waiting list, LT and withdrawal, and infection as time-varying covariate into account. Results We included 312 patients in this study. During follow-up 72/312 patients (23.1%) were withdrawn due to clinical deterioration or death. Infection occurred in 144/312 (46.2%) of all patients, some had multiple infections resulting in a total number of 317 infections. Infection resulted in withdrawal in 42/317 (13.2%). Site of infection, isolated micro-organism and primary liver disease were associated with infection-related withdrawal ($p=0.001$, $p=0.004$ and $p=0.046$ respectively). Hazard ratio (HR) for withdrawal in patients with infection versus no infection was 5.87 (95% confidence interval 3.56-9.66). The HR for withdrawal increased until the third infection. In a multivariate cox-proportional hazard analysis, with infection as covariate, etiology (comparing groups, $p=0.043$), age (HR1.07, $p<0.001$), MELD-score (HR1.1, $p<0.001$), serum albumin (HR0.97, $p=0.001$) and the presence of refractory ascites (HR2.21, $p=0.013$) were associated with withdrawal, taking competing risks into account. Conclusions We show that infection is the number one cause for withdrawal from the waiting list, with a HR of almost 6, in patients with ESLD. There is a cumulative effect of having multiple infections until the third infection on withdrawal. Localization of infection and type of micro-organism in infections are associated with the risk for withdrawal, as is MELD-score, refractory ascites and primary etiology.

Non-anastomotic biliary strictures are more severe after transplantation of donation after circulatory death, compared to donation after brain death livers

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Introduction. Livers from donation after circulatory death (DCD) donors are increasingly accepted for liver transplantation. Although, several studies have shown a higher incidence of non-anastomotic biliary strictures (NAS) after DCD liver transplantation, it is not well known whether NAS are more severe and widespread in DCD, compared to DBD liver recipients. Aim of this study was to compare severity and anatomical extension of NAS in DCD and DBD liver grafts based on an established radiological grading system. Patients and Methods. A total of 427 adult liver transplantations performed between 2000 and 2014 were included. Radiological imaging of the biliary tree was reviewed retrospectively using an established grading system. Severity of NAS was classified as mild, moderate or severe. Anatomical localization of NAS was categorized in 4 zones of the biliary tree. Results. Cumulative incidence of NAS was 24% in DCD and 15% in DBD liver recipients. Moreover, NAS were more severe in DCD compared to DBD liver recipients (p=0.032). Severe biliary abnormalities were observed in 22.6 % of DBD and 47.6 % of DCD liver recipients. In addition, within the biliary tree, anatomical localization of NAS were more widespread in DCD, compared to DBD liver recipients. Of all patients who developed NAS, retransplantation for NAS was necessary in 22.6 % of DBD and 33.3 % of DCD liver recipients. Conclusion. DCD liver transplantation is not only associated with a higher rate of NAS, compared to DBD transplantation, but also with a radiologically more severe and widespread presentation of NAS.

Oxygenated hypothermic machine perfusion after static cold storage improves endothelial function of extended criteria donor livers

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Background: Lack of oxygen and biomechanical stimulation during static cold storage (SCS) of donor livers compromises endothelial cell function. This study investigated the effect of 2 hours of end-ischemic oxygenated hypothermic machine perfusion (HMP) on endothelial cell function of extended criteria donor (ECD) livers. Method: Sixteen human livers that were declined for transplantation were transported to our center using conventional static cold storage (SCS; 4oC) and subjected to normothermic machine perfusion (NMP) to assess viability and function. Six livers underwent 2 hours oxygenated HMP (12°C) after SCS and prior to NMP. Ten control livers underwent NMP immediately after SCS. Endothelial cell function was assessed by quantification of mRNA expression encoding for transcription factor Krüppel-like-factor-2 (KLF-2), endothelial nitric oxide synthase (eNOS), and thrombomodulin (TM) using real-time PCR. Nitric oxide (NO) production (nitrite/nitrate levels) and release of thrombomodulin (TM) into the perfusion fluid were determined during NMP. Results: In livers that underwent end-ischemic HMP, mRNA expression of KLF-2 ($p=0.04$), eNOS ($p=0.03$) and TM ($p=0.03$) increased significantly during NMP. This response was not observed in the control livers. In parallel, NO levels in the perfusate increased during NMP of livers that first underwent HMP, but not in control livers. Moreover, at the end of NMP cumulative TM release into the perfusate was significantly higher in control livers compared to livers first subjected to HMP ($p=0.03$). Conclusion: A short period of 2 hours oxygenated HMP restores endothelial cell function and integrity after conventional static cold preservation and subsequent reoxygenation of ECD livers.

Normothermic Machine Perfusion of Donor Livers Using a Novel Hemoglobin Based Oxygen Carrier Solution, Eliminating the Need for Human Blood Products

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Introduction: Normothermic machine perfusion (NMP) enables viability assessment of donor livers prior to transplantation. Up until now, NMP has been conducted using human blood products including red blood cells (RBC). Aim of this study was to examine the efficacy of a new machine perfusion solution based on polymerized bovine hemoglobin (Hemopure). Methods: Twenty-four livers declined for transplantation were included. After a median static cold preservation period of 8.1 hours, livers underwent NMP for 6 hours using pressure-controlled portal and arterial perfusion. Group 1 (n=12) underwent NMP using a solution based on RBC and fresh frozen plasma (FFP), group 2 (n=6) was perfused with Hemopure and FFP, and group 3 (n=6) with Hemopure and Gelofusine, a gelatin-based colloid solution. Graft function and viability was compared. Results: Portal flow was significantly higher in livers perfused with Hemopure (median at 6 hr NMP in group 1: 848 ml/min [IQR: 663 - 1392], group 2: 1890 ml/min [1530 - 2173], group 3: 1830 ml/min [1713 - 2030]; $p<0.05$). Cumulative bile production was significantly higher in livers perfused with Hemopure (group 1: 8.2 ml/kg liver [6.0 - 23.6]; group 2: 27.0 ml/kg liver [15.5 - 71.7], group 3: 29.0 ml/kg liver [22.4 - 44.9]; $p<0.05$). Intrahepatic adenosine triphosphate (ATP) concentration after NMP was higher in livers perfused with Hemopure (group 1: 24.0 μmol/g protein [14.0 - 51.3], group 2: 49.6 μmol/g protein [34.8 - 59.2], group 3: 79.2 μmol/g protein [50.5 - 102.6]; $p<0.05$ between group 1 and 3). Conclusion: Ex situ NMP of human donor livers can be performed effectively using a novel acellular perfusion solution based on Hemopure, eliminating the need for human blood products. Normothermic liver perfusion using this Hemopure-based solution results in higher ATP concentration and more bile production, compared to an RBC-based solution.

Highly sensitized patients transplanted via the Eurotransplant Acceptable Mismatch program have excellent long-term graft survival

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The Eurotransplant Acceptable Mismatch (AM) program has been initiated 25 years ago in order to enhance transplantation of highly sensitized renal transplant candidates. Instead of avoiding unacceptable antigens, this program makes use of acceptable antigens, defined as antigens to which the patient has never formed antibodies, to predict a negative CDC crossmatch. Through addition of these acceptable antigens to the patient's own HLA phenotype, and mandatory shipment of a compatible organ to AM recipients, increased rates of transplantation of highly sensitized patients have been achieved. Here, we present long-term graft survival data on patients transplanted through the AM program. We analyzed 10-year death censored graft survival of patients transplanted through regular allocation (Eurotransplant Kidney Allocation System: ET-KAS) and through the AM program. ET-KAS patients were subdivided according to the level of sensitization (0-5% PRA: non-sensitized, 6-85% PRA: sensitized, and >85% PRA: highly sensitized). Graft survival was compared to (highly sensitized) patients transplanted through the AM program. AM patients had better 10-year graft survival compared to their highly sensitized counterparts transplanted through ET-KAS ($P<0.001$), whereas no statistically significant difference between AM patients and sensitized ET-KAS patients was observed. Non-sensitized patients had the best graft survival ($P= 0.03$). As the majority of AM patients received a re-transplant (71.2%) compared to a minority (14.9%) of ET-KAS patients ($P<0.000001$), we subsequently analyzed the 10-year graft survival of all re-transplant recipients. In this analysis, we found that AM patients had far superior graft survival compared to highly-sensitized ET-KAS patients ($P= 0.000003$), and similar graft survival compared to sensitized ($P= 0.05$) and non-sensitized patients ($P= 1.00$). Multivariate analysis on all highly sensitized patients showed that the following parameters were independently affecting long-term graft survival: the number of HLA-A, -B, -DR mismatches, transplant period, donor sex and age, recipient age, as well as receiving a transplant through the AM program. The AM program allows for increased rates of transplantation for highly sensitized patients while long-term graft survival of patients transplanted through the AM program is at least similar to that of patients transplanted through regular allocation.

BK polyomavirus seroreactivity of kidney donors predicts viremia and nephropathy in recipients

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Background Kidney transplant (KTx) donors are not implicated in predicting BK polyomavirus (BKV) infection in the immunocompromised recipient. It has been suggested, however, that BKV-infection originates from the kidney allograft. Since BKV-seroreactivity correlates with BKV-replication and, therefore, may mirror the infectious potential, we investigated whether baseline BKV-seroreactivity of KTx-donors predicts viremia and BKV-associated nephropathy (BKVAN) in recipients. Methods In a retrospective cohort of 407 living kidney allograft donor-recipient pairs, transplanted between 2003-2013, pre-KTx donor and recipient sera were tested for BKV IgG-levels. Baseline IgG-levels were correlated with the occurrence of BKV-viremia and BKVAN during the first year after transplantation. Results Baseline BKV-seroprevalence of both donors and recipients was high, ≥ 95%. A strong, statistically significant association was observed between donor BKV-IgG level and occurrence of viremia and BKVAN. This resulted in a sevenfold increased hazard ratio for BKV-viremia, which increased even further in case of a low BKV-seroreactive recipient. Baseline recipient BKV-seroreactivity as such was not associated with viremia or BKVAN. Multivariate analysis showed donor BKV-seroreactivity to be the strongest baseline factor associated with BKV-viremia and BKVAN. Conclusion Donor level of BKV-IgG is a strong predictor of BKV-infection in KTx-recipients. The proportional relation between donor BKV-seroreactivity and recipient infection suggests that donor BKV-seroreactivity reflects the infectious load of the kidney allograft. This finding promotes the use of BKV-serological testing pre-KTx, in order to assess the risk of BKVAN and to personalize BKV-plasma load-monitoring. Furthermore, it emphasizes the relevance of strategies aimed to increase BKV-immunity in kidney allograft-recipients.

Increasing Donor Age on the Risk of Permanent Pacing After Orthotopic Heart Transplantation

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Background: Due to scarcity of donor hearts, older and marginal donors are accepted for orthotopic heart transplantation (HTx). We evaluated the relationship between donor age and need for pacemaker (PM) implantation after HTx. Methods: Patients transplanted between 1984 until 2014 were analysed (n=612, 74% male; median follow up of 99 months [IQR 40-166]). Three groups were created based on donor age: Group I (0–35 y, n=345), Group II (35–50 y, n=190) and Group III (>50 y, n=77). The primary outcome was PM implantation after HTx for sinus node dysfunction (SND) or AV block (AVB). The need for early (<90 days after HTx) or late PM (>90 days) was evaluated. Results: The mean recipient age at HTx was 46.4±14.3 years [range 2-72 y]. Significant older donor hearts were transplanted during the last 10 years compared to the first 10 years (40.1±15.9 y vs. 25.7±8.3 y, p<0.001) and more early PM's were implanted (10.2% vs. 1.7%, p<0.001). Ischemic time (176±45 min vs. 181±48 min vs. 186±48 min, p=ns, respectively) was comparable for group I, II and III. Overall 11.6% (SND, n=26; AVB, n=45) received a PM after a median period of 13 months [IQR 1.3–97 months]. In group III a higher amount of early PM were implanted (11.7%, n=9) compared to group I (2.0%, n=7; p=0.001). For late PM implant equal rates were observed (6.5% vs. 7.2%, p=ns, respectively). Conclusion: Increasing donor age, particularly >50 years, is a major risk factor for the need of permanent pacing post-HTx.

Pretransplant donor specific HLA antibodies in 4770 renal transplant recipients: A preliminary analysis of the PROCARE cohort

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The clinical significance of Luminex-detected donor-specific HLA antibodies (DSA) that do not cause a positive complement-dependent crossmatch is unclear. Currently there is no consensus on how DSA should be included in clinical decision making. As part of the national PROCARE consortium study, all kidney transplantations performed in the Netherlands between 1995-2005, are investigated. From the more than 6000 transplantations we were able to collect 4770 pretransplant sera. In this cohort, 60% of the recipients was male, mean age was 46 (±14) years, 731 (15%) patients received a re-transplant, and the mean follow-up time was 9.3 years (±5.3; range 0-20 years). 1494 patients received a kidney from a living donor, 828 from a donor after circulatory death (DCD), and 2448 from a brain dead donor (DBD). Of 2072 recorded graft losses, 818 were due to death with functioning graft. Historical pretransplant panel-reactive antibodies value (hPRA)≥5% was observed in 1553 (33%) patients. By Luminex-analysis, we determined that 501 (10%) sera contained antibodies against HLA class-I only, 398 (8%) against HLA class-II only and 609 (13%) against both HLA class-I and -II (positivity defined according to manufacturer's instructions). Ten-year death-censored graft survival was 78% for patients without HLA antibodies. The presence of anti-HLA antibodies was associated with lower graft survival: 73% for anti-HLA class-I (p=0.018), 74% for anti-HLA class-II (p=0.087), and 64% for both anti-HLA class-I and -II (p<0.0001). Using donor HLA typing results, we will determine which sera contain pretransplant DSA. The relation between the effects of different levels and combinations of DSA with key clinical endpoints such as graft survival and function will be analysed.

Kidney transplantation from deceased donors for recipients over the age of 75 compared with recipients between 65 and 74 of age – A Dutch Cohort Study

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Objective: The age of candidates awaiting kidney transplantation has been increasing in the Netherlands. This impact on graft survival and mortality is not yet clear. The aim was twofold. 1) To compare graft survival from deceased donors for recipients ≥75 years and younger recipient age groups (≥70 and <75; ≥65 and <70). 2) To compare the effect of experiencing graft failure on mortality with increasing recipient age. Methods: In this retrospective cohort study, we used the Dutch Organ Transplantation Registry (NOTR) to include recipients (≥65y) from all Dutch centers, transplanted from 2002 to 2012 with a first DBD or DCD kidney (Maastricht category III). Graft failure and death were treated as competing events. Mortality was uncensored for the event of graft failure, treated as an time-dependent variable in Cox regression. Significant levels were set at 5%, for interaction analyses at 10%. Results: We identified 42 recipients aged 75+, 203 recipients aged 70-74, and 467 recipients aged 65-69. The probability of graft failure as a first event within 5 years was higher for recipients aged 75+ compared to recipients aged 70-74 and 65-69 (32.1% vs 12.4% vs 17.9%, p=.027), however, the probability of death as a first event within 5 years was lower for recipients aged 75+ (16.0% vs 34.2% vs 26.7%, p=.016). Mortality (uncensored for graft failure) within five years was comparable between recipients aged 75+ (39.9%), 70-74 (41.7%), and 65-69 (34.9%), p=.132. Recipients experiencing graft failure within five years were at higher risk of death (unadjusted HR 4.6, CI 3.3-6.3, p<.001). Compared with recipients 65-69, recipients 75+ were 3.1 times (CI 0.8-11.9, p=.095) at higher risk of death when experiencing graft failure. Incidence of primary non-function, delayed graft function, acute rejection treatments within 1 year after transplantation, and estimated glomerular filtration rate after three months one year were comparable between recipients age groups. Baseline risk factors for graft survival were also comparable between recipient age groups. Conclusion: Our findings should be interpreted with care, because recipients over 75 years probably represent a selected group. Although (uncensored) mortality was comparable, recipients 75+ are more likely to experience graft failure as the first event, and not patient death. If older aged recipients experience the event of graft failure, these recipients have higher risk of death compared with younger aged recipients.

Evaluating the waiting policy in patients with malignancies prior to renal transplantation: acceptable risks of recurrence after transplantation

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Introduction: A history of malignancy is considered a relative contraindication for transplantation and a tumor-free period of 3-5 years is usually advised before patients are considered eligible for transplantation. However, little is known about the risk of recurrence of malignancies after transplantation using this policy. The Dutch Organ Transplant Registry (NOTR) database only registers malignancies after transplantation. We investigated whether linking the national cancer database with the NOTR can provide us with adequate information needed to make a statement about this risk. Methods: The NOTR is operational since 2001 and includes the clinical data from recipients with a functioning organ transplant as reported yearly by the transplant centres. From 1989 onwards, the IKNL (Integraal Kanker Centrum Nederland) collects nationwide pathology results documenting malignancy in a database. All renal transplant recipients (RTR), transplanted between 1966 and 2013, were connected with the IKNL database using surname, sex, date of birth, ZIP code and treatment hospital. Data reporting malignancies of both databases were compared. Results: The NOTR contained 16717 RTR of which 3690 (22%) were diagnosed with a non-melanoma skin(NMS) and/or a solid tumor in the IKNL database. 593 (16%) RTR had a tumor before transplantation (RT);85 patients had only NMS tumor(s),508 had at least one solid tumor before RT. Of this 508 patients with at least one solid tumor before RT the median time before transplantation of the first tumor was 6 years (range 1-32 yrs). 53 RTR had more than one (max 5) solid tumor before transplantation. Only 21 (4%) of the 508 patients had a recurrence of their solid tumor at a median time of 3 (range 0-13) yrs after RT, 8,5 (range 3-24) yrs after the original tumor. The median tumor-free time before RT in RTR with recurrence was 5 (1-17) yrs. The primary tumors and recurrence rate were: 4 out of 69 bladder, 1 out of 44 colon, 5 out of 127 kidney, 1 out of 18 lung, 1 out of 15 non-Hodgkin lymphoma, 8 out of 66 breast and 1 out of 53 prostate tumors showed a recurrence after RT. There was no significant difference in tumor-free period before RT in RTR with or without recurrence. Conclusion: The current policy of using a tumor-free before transplantation leads to an acceptable recurrence rate of malignancy after RT, which is in general below 5% and ranges between 1.8% and 12.2 %.

Levels of VEGF-C, PLGF and Follistatin at 12 months post transplantation are associated with increased risk for long term progressive renal dysfunction

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Introduction The integrity of the microvasculature is critical for long term survival following solid organ transplantation. We hypothesize that biomarkers of endothelial injury and repair are early predictors of chronic rejection, and preliminary evidence suggests that angiogenic biomarkers are associated with chronic cardiac allograft vasculopathy. Here we investigate if angiogenic markers measured 12 months after renal transplantation can predict late allograft dysfunction. Methods Levels of 17 angiogenic proteins and anti-HLA donor specific antibodies (DSA) were measured by mulitanalyte profiling 12 months after renal transplantation in sera of 152 recipients. Forty-five patients had progressive renal dysfunction, defined as at least 20 ml/min/1.73m^2 eGFR loss between year 1 and 5 (mean baseline eGFR 54±22 ml/min/1.73m^2), and 107 control patients had stable renal function (mean baseline eGFR 48±15 ml/min/1.73m^2). All patients had low to standard immunological risk and started on triple therapy with calcineurin inhibitors. Six months after transplantation 33 patients switched to dual therapy, including 13 with mTOR inhibitors. Results The 5-year death-censored graft survival was 100% in the control group and 79.2% in the progressor group. Follistatin, a promoter of tubular regeneration, was significantly increased (median(IQR) = 1146(1060) vs. 826 (1341) in controls, p=0.033) 12 months after transplantation in recipients with progressive renal dysfunction. Also, the angiogenic and pro-inflammatory factors PLGF (median(IQR) = 16(37) vs. 10(26) in controls, p=0.019) and VEGF-C (median(IQR) = 276(372) vs. 183(274) in controls, p=0.029) were increased in the progressors, independent of treatment regimen. The remaining biomarkers including endothelin1, FGF1/2 and VEGF-A showed no associations with loss of renal function. In total, 46 patients had allograft rejection. Late, but not early rejection, was associated with progressive renal decline at 5 years (OR 3.15, 95%CI 1.27–7.81, p 0.013). *De novo* DSAs were found in 22 patients (14.5%), however no association with biomarkers was found.
Conclusion Increased levels of VEGF-C, PLGF and Follistatin at 12 months post-transplant were associated with progressive renal dysfunction at 5 years. These specific biomarkers have been reported to play important roles in (lymph)angiogenesis and inflammation. These markers have potential to identify patients with progressive renal dysfunction at early times post-transplant.

Pubertal maturation and T cells in renal transplant recipients

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Introduction: The risk of graft loss in renal transplant recipients increases during ages 17-24 years compared to adjacent ages, which can not be fully explained by non-adherence to immunosuppressive medication. In the Adolesce-NT study, we hypothesise that pubertal maturation is associated with increased immuno reactivity and related to the increased graft loss in this high-risk group. Research question: do the characteristics and absolute numbers of $CD4^+$ and $CD8^+$ T cells, B and NK cells differ for pubertal status in end-stage renal disease (ESRD) patients awaiting renal transplantation (RT), RT recipients and healthy controls?
Methods: We included 42 patients with ESRD (57% male), 54 patients >1 year after RT (67% male) and 53 healthy controls (40% male) aged 10-30 years in our prospective, ongoing study. Puberty was based on age: 10–16 years for healthy females and 11–17 years for healthy males. Given that pubertal maturation is delayed for an average of 1.7 years at RT, puberty in ESRD patients and RT recipients was defined as: ages 12–18 years for females and 13–19 years for males. Three subgroups of pubertal status were defined: before, during and after puberty. Flow cytometric analysis was performed on peripheral blood using a Trucount tube for absolute T, B and NK cell counts and two 8-color labelling to define $CD4^+$/$CD8^+$ T cell subsets: naive, central memory (CM), effector memory $CD45RO^+$ T cells (Temro) and $CD45RA^+$ T cells (Temra). In each study group, differences in lymphocyte counts were compared among pubertal status subgroups using analysis of variance (ANOVA) models and the Mann–Whitney *U* test (α level, 0.05). Results: In ESRD, the number of $CD4^+$ Temro was higher after puberty (median, 336; IQR, 235–378) than during puberty (206; 177–300; P=0.02) and before puberty (142; 84–213 cells/μL; P=0.002). Also in healthy controls, the number of $CD4^+$ Temro was higher after puberty (median, 355; IQR, 275–465) than during puberty (243; 182–270 cells/μL; P<0.001). In RT recipients, the $CD8^+$ CM T cell count was higher during puberty (median, 3.8; IQR, 1.8–14.5) than after puberty (1.4; 0.6–2.5 cells/μL; P=0.03). Cell counts among other subgroups of pubertal status within the study groups did not significantly differ.
Conclusion: As memory T cells are key players in allograft rejection, the higher number of $CD8^+$ peripheral CM T cells during puberty in RT recipients may play a role in the higher rate of graft loss in relation to pubertal maturation.

Good Functionality But Lower Yield After Islet Isolation From Donation After Circulatory Death Pancreata

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Donation after circulatory death (DCD) is increasingly performed due to a shortage of donation after brain death (DBD) organs. However, for islet isolation and transplantation there are concerns about islet yield and islet graft function. We investigated the use of DCD pancreata for islet isolation and transplantation. Islet isolation procedures from 192 DBD and 93 DCD donor pancreata between 2008-2014 were studied. Donor and procurement characteristics were compared between DBD and DCD groups and were corrected for mismatched covariates (UNIANOVA). The number of isolated islets expressed as islet equivalents (IEQ), purity, and tissue volume were quantified after every isolation, and were repeated on day 1 and day 3 during culture. Dynamic glucose-stimulated insulin secretion was performed if clinical transplantation was considered. Since 2011 DCD islets were used in human transplantation procedures in combination with DBD islets. Three months after transplantation mixed meal tests were performed. Islet yield differed significantly after isolation (day 0) (437,603 IEQ (DBD) and 343,418 (DCD, $p<0.001$). DBD islet isolations yielded a larger final volume (+26.8±4.38 µL, $p= 0.014$) and maximum purity (+5.00±2.01%, $p=0.013$). After medium changes IEQ was 378,470 (day 1) and 294,715 (day 3) for DBD islets and 291,279 (day 1) and 218,444 (day 3) for DCD islets ($p<0.05$ for DBD vs. DCD IEQs and $p<0.001$ for IEQ change per day). Importantly, the percentage decrease in IEQ from day 0 to 1 and day 0 to 3 did not differ between DBD and DCD groups ($p=0.478$ and $p=0.732$, respectively). DCD related ischemia times were not related to islet yield. Insulin secretion was not different between DBD and DCD islets (peak SI: 4.6±0.3 (DBD, n=82) and 5.4±1.3 (DCD, n=13), p=NS). Transplantations using DBD single grafts or double grafts (DBD+DBD or DBD+DCD), showed no difference in AUC C-peptide/(IEQ/kg recipient) in mixed meal tests ($p=0.077$). In conclusion, isolations from DCD pancreata generated a lower islet yield compared to DBD pancreata but DCD and DBD islets showed similar islet functionality. DCD islets should strongly be considered in clinical islet transplantation.

Increasing the number of potential organ donors with 37%: a prospective observational multicenter study on unrecognized potential organ donors outside the intensive care unit

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Background: Data from the Dutch Transplant Foundation show that potential organ donors are effectively never missed on the Intensive Care Unit (ICU). However, there are a few studies suggesting that there might be unrecognized potential organ donors outside the ICU environment. The aim of this study is to assess how many potential organ donors exist outside the ICU, and identify factors related to non-recognition of these potential organ donors. Methods: We performed a prospective observational study in 7 hospitals in the Netherlands during a 15 months period in 2013-2014. All hospital deceased patient forms were screened by an in house transplantation coordinator according to the following inclusion criteria: died within 72 hours after hospital admission due to devastating brain injury, aged <86 years, fulfilled criteria for organ donation and had not been admitted to the ICU during the entire hospital stay. An intensivist specialized in organ donation interviewed the physicians of these patients according to a standardized questionnaire. The focus of the questionnaire was on different steps in logistics and medical decision taking from hospital admission till death of the patient. Results: In total there were 1226 deceased patients aged <86 years. We found 77 unrecognized potential organ donors outside the ICU with a mean age of 74.7±10.3 years and mean Glasgow Coma Scale of 5.2±2.6. Thirteen patients (16.9%) were intubated. Although the Donor registry of 64.9% of the patients was consulted, in only 42.0% of these patients this happened when the patient was still alive. Organ donation was discussed with the relatives of 16 patients (20.8%). Post mortal tissue donation was discussed with relatives of 37 patients (48.1%). Donation was not discussed in 24 patients (31.2%). We found several factors indicating lack of knowledge and experience in donation practices. In addition, several logistical factors were noted to negatively influence donation practices in patients on the emergency department. Extrapolation of our data to a national level suggests that the current pool of potential organ donors could be increased with 37%.

Conclusion: Non-intubated patients with devastating brain injury outside the ICU are often not recognized as potential donors. Educating emergency and neurology physicians to recognize potential organ donors and collaborating closely with ICUs and organ donation teams could increase the number of potential organ donors with 37%.

Anonymity in Live Kidney Donation Reconsidered: Patients' and Donors' Experiences, Preferences and Attitudes

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Background In recent years the numbers of unspecified kidney donation and (domino)paired exchange procedures have increased significantly. In the Netherlands and Sweden anonymity is perpetual in such procedures. Anonymity protects donors and recipients against potential risks. Though, imposed anonymity could be experienced as paternalistic. Little is known about the experiences, preferences and attitudes of donors and recipients towards ano¬nymity. Method Participants who received/donated a kidney anonymously (directly or via (domino)paired kidney exchange) between 2009-2014 (NL) and between 2004-2014 (SW) were invited for an explorative retrospective survey on experiences, attitudes and preferences regarding anonymity. The survey was completed by 258 donors (D) and 157 recipients (R) (response-rates: D:72% and R:48%). Chi-squared and t-tests were conducted to identify differences between D and R. Results Our results suggest that the majority was satisfied with anonymity before (87%) and after the operation (80%). The desire to meet the other party before (D:7%, R:15%) and after the operation was low (D:22%, R:31%). Recipients were more open for a meeting than donors $p<0.05$. If the other party expresses the desire to meet, 58% of the donors and 60% of the recipients would be open for a meeting. Most agreed with maintenance of anonymity before (73%) and after the donation (56%). Donors agreed more with anonymity before and after donation than recipients, $p<0.05$. However, the majority was of the opinion that it should be possible to meet before (61%) or after the operation (73%) if both parties agreed. Swedish participants were more conservative about meetings prior to transplantation compared to Dutch participants. Conclusion Although donors and recipients prefer anonymity, a strict policy on anonymity is viewed as unnecessary if both parties agreed to meet. We might reconsider the anonymity-policy. Revoking anonymity generates practical and ethical challenges. We should carefully consider the pros and cons of the removal of anonymity and experiences of other countries.

Hypothermic machine perfusion is also beneficial for deceased donor kidneys when cold ischemic time is short and a short cold ischemic time is also beneficial when kidneys are machine perfused

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Introduction Hypothermic machine perfusion (HMP) of deceased donor kidneys is associated with better outcome when compared to static cold storage (SCS). However, it is generally assumed that HMP will only improve post-transplant results for kidneys with a substantial degree of ischemic injury. Many transplant clinicians believe that renal grafts with a short cold ischemic time (CIT) will benefit little from HMP. Also, it is often presumed that kidneys are "safe" during HMP and the duration of cold ischemia is less relevant while renal grafts are on the machine. Aim of the current study was to investigate whether HMP also results in a lower incidence of delayed graft function (DGF) compared to SCS for kidneys that are transplanted with a maximum of 10 hours of cold ischemia and to test whether CIT remains an independent risk factor for DGF when kidneys are machine perfused. *Methods* We analysed data that has been prospectively collected in the Machine Preservation Trial. In this international RCT, HMP was compared to SCS of deceased donor kidneys. A total of 376 consecutive kidney donors were included, of whom one kidney was machine perfused and the contralateral organ was preserved by SCS. A post hoc multivariable data analysis was performed to investigate the effect of HMP versus SCS on renal grafts with a short (up to 10 hrs) CIT and to quantify the influence that CIT has on the risk of DGF when kidneys are machine perfused. *Results* Of these 752 transplanted kidneys the mean CIT was 15 hrs and 5 min (SD 4 hrs 58 min). DGF incidence was 27.9% in the whole cohort. DGF incidence in the sub group with up to 10 hrs CIT was 6.0% (N=3/50) in the HMP arm and 28.1% (N=18/64) in the CS arm (univariable P=0.002, multivariable OR 0.02, P=0.007). Three year graft survival in the < 10 hrs CIT group did not differ significantly between study arms (88.0% for HMP and 81.2% for SCS, P=0.308). CIT remained an independent risk factor for DGF for all machine perfused kidneys recovered from DBD donors (OR =1.07, P=0.008), DCD donors (OR = 1.13, P=0.006) and ECD donors (OR = 1.14, P=0.001).
Conclusion HMP results in lower rates of DGF than SCS in kidney transplantation. The current analysis shows that, contrary to popular belief, this is also true for renal grafts that are transplanted after a short CIT. In addition, our data suggests that CIT remains a relevant and independent risk factor for DGF in HMP-preserved kidneys.

The use of human liver scaffolds for stem cell-driven graft engineering

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Background: As age and obesity of the donor population increases, the number of acceptable donor organs is declining at alarming speed and alternatives are urgently needed. Over the past decade, tissue engineering has offered new strategies for the generation of transplantable organs. One strategy is to use extracellular matrix (ECM) derived from untransplantable organs by the effective removal of all cells. These scaffolds can potentially be reseeded with parenchymal and vascular cells. The aim of this study is to develop transplantable human liver matrices, constructed by recellularization of human liver scaffolds with endothelial cells and stem cell-derived hepatic organoids. Methods: 104 human umbilical vein endothelial cells (HUVEC) were seeded in uniform sections (Ø8 mm, 250 µm thick) of human liver ECM for five days at 37˚C in a 48-well plate in HUVEC culture medium. Every day, for 5 days, sections were harvested, fixed in 4% paraformaldehyde and embedded in paraffin. Immunohistochemistry was done using the endothelial markers vimentin and Factor 8/von Willebrand Factor (vWF). Results: Previously we have developed an effective method for decellularization of human liver grafts, completely removing all cellular and nuclear material. Extensive analysis revealed that the ECM is perfectly preserved during this process and basal membranes remain intact. Only traces of remnant DNA and no proteins related to HLA molecules were detected, ensuring absence of allo-reactivity when used for transplantation. The first step in the recellularization process is re-paving the vascular walls of the matrix with endothelial cells. Uniform endothelial cell coverage of the vascular tree permits blood flow in the scaffold and prevents thrombosis when transplanted. Immunohistochemistry revealed vimentins and F8/vWF positive cells from day 1 onwards, demonstrating the settlement of HUVECS and re-endothelialization of the vascular walls in the ECM. In an upscaling experiment, a decellularized segment 2/3 human liver graft was recellularized with 4x108 human HUVEC using continuous oxygenated perfusion. After 3 days, a re-establishment of the endothelial lining was demonstrated, providing proof of concept for perfusion re-endothelialization of decellularized liver matrices. Conclusion: This study shows that recellularization of human liver scaffolds with endothelial cells is feasible and can be applied for graft engineering.

POSTERS

Intima Media Thickness (IMT) and Major Adverse Cardiac Events (MACE) in patients after kidney transplantation

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Background The MECANO trial, a prospective, randomized, multicenter trial in the Netherlands, was aiming to optimize immunosuppression (IS) and to reduce side effects. IMT was measured as a cardiovascular (c.v.) marker after kidney transplantation. Seven years survival and MACE-free survival probability were calculated by the Cardiovascular Risk Calculator for Renal Transplant Recipients. This sub study aimed to investigate IMT and MACE as predictors of survival and/or c.v. events. Methods IMT of the arteria carotis communis was measured at week 2, month 6 and m. 24. Patients were treated with induction therapy (basiliximab) and triple IS (CsA(C), Myfortic(M), prednisolone(P)). At M6 patients were randomized to group 1 (C, P, N=81), 2(M, P, N=32) and 3 (Everolimus, P, N=81). MACE can be predicted using a 7-variable model including age, previous coronary heart disease (CHD), diabetes, low-density lipoprotein, creatinine, number of transplants, and smoking (pMACE). Mortality can be predicted by a 6-variable model, including age, CHD, diabetes, creatinine, total time on renal replacement therapy and smoking (pMort).
Results Mean IMT at baseline, N=192, for all patients was 0.64±0.14 mm. At M6, N=175, IMT was 0.65±0.15 and at M24 (N=111) IMT was 0.67±0.16. IMT of group 2 was significantly lower than the IMT of group 1 and 3 (ANOVA p=0.023 for baseline IMT, p=0.032 for IMT at M24). pMACE and pMort did not show a group difference. Both pMACE and pMort increased significantly with IMT quartile (ANOVA p<0.001). After correction for age, this increase was still present (p<=0.005).We predicted events and mortality after 7 years using pMACE, pMort, age and IMT. Best predictor is pMort with 79% classified correctly, including adding age in the regression, 81 % is classified correctly (n.s.).
Conclusion: Higher IMT correlated with higher pMACE and pMort scores. However, prediction of events and mortality could not be improved by including IMT in the logistic regression model.

Incidence, risk factors and treatment of incisional hernia after kidney transplantation; an analysis of 1564 consecutive patients.

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Background: The objective was to evaluate the incidence and treatment of incisional hernia following kidney transplantation, and to identify potential risk factors. Methods: A retrospective cohort study was performed. All kidney transplant recipients between 2002 and 2012 were included. Two groups were identified: patients with incisional hernia and patients without. Risk factor analysis for development of incisional hernia was performed. Results: A total of 1564 kidney recipients were included. Fifty patients (3.2%) developed incisional hernia. On univariate analysis, female gender (54% vs. 35% p = 0.006), BMI>30 kg/m2 (38 % vs. 17%, p< 0.001), concurrent abdominal wall hernia (30% vs. 16%, p=0.007), multiple explorations of the ipsilateral iliac fossa (38% vs. 19%, p=0.001), left iliac fossa implantation (36% vs 24%, p=0.046), history of smoking (72% vs 57%,p=0.032) and duration of surgery (210 minutes vs. 188 minutes, p=0.020) were associated with the development of incisional hernia. In multivariate analyses female gender (HR 2.6), history of smoking (HR 2.2), obesity (BMI >30) (HR 2.9), multiple explorations of the ipsilateral iliac fossa (HR 2.0), duration of surgery (HR 1.007), and concurrent abdominal wall hernia (HR 2.3) were independent risk factors. Twenty-six of 50 patients (52%) underwent surgical repair, of which nine (35%) required emergency repair.
Conclusions: The incidence of incisional hernia following kidney transplantation is 3.2%. We found obesity (BMI>30), female gender, concurrent abdominal wall hernias, history of smoking, duration of surgery, and multiple explorations to be independent risk factors for the development of incisional hernia after kidney transplantation. These risk factors should be taken into account to prevent incisional hernia.

Suprapubic ureteric stenting in kidney transplantation; does the type of stent matter?

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Background: The aim of this study was to evaluate the effect of two types of suprapubic ureteric stents on the number of urological complications after kidney transplantation. Methods: Data were retrospectively collected from 366 consecutive kidney transplantations performed between January 2013 and January 2015 in our hospital, in which a suprapubic externalized ureteral stent was placed during surgery. Urological complications were defined as urinary leakage or ureteral stenosis requiring PCN placement. Results: A total of 197 patients received a straight stent with two larger side holes, introduced without a guidewire (type A ;8 Fr 'Covidien' tube) and 169 patients received a single J stent with 7 smaller side holes introduced with a guidewire '(type B;7 Fr 'Teleflex' single J stent). We found a significant higher incidence of PCN placements in type A stenting: 34 (17%) PCN interventions versus 16 (9%) in type B stenting (p= 0.030). No significant difference was found between the indications for PCN placement in both groups (p= 0.423). Stent dysfunction and early removal (< 8 days) was equally distributed in both groups (p= 0.397) while incidence of rejection and urinary tract infection (UTI) were higher in type B stenting. Patient and graft survival did not differ between the groups.
Conclusions: In conclusion, 'stent type B' is associated with less urological complications compared to 'stent type A'. The type of stent does not affect patient and graft survival.

One year post-VZV booster: still equal response in renal transplant recipients compared to healthy persons

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Introduction: Herpes zoster occurs more frequently and with more complications in solid organ transplant recipients than in age matched healthy persons. Vaccination could prevent herpes zoster. However, patients with end stage renal disease (ESRD) are known to respond much poorer to vaccinations against hepatitis B and influenza than healthy individuals do. Therefore, we studied the effect of a VZV booster vaccine on B-cell response in patients with ESRD and healthy controls. Methods: In a prospective study, 26 patients, aged at least 50 years and awaiting renal transplantation were vaccinated with Zostavax®. Gender and age-matched living kidney donors were included as controls (n=27). Varicella Zoster Virus (VZV) specific IgG titres were measured before, at 1, 3 and 12 months post vaccination. Results: All patients and donors have reached 3 months after vaccination, 23 patients and 25 donors also reached month 12 after vaccination. Both in patients and controls VZV-specific IgG titers were significantly higher at all time points post compared to before vaccination (M1: $p<0.0001$, $p<0.0001$; M3: $p=0.0002$, $p<0.0001$; M12: $p=0.006$, $p=0.0008$; patients and controls, respectively). The patients' IgG titers were comparable to the donors' titers at all time points (pre: $p=0.64$, M1: $p=0.94$, M3: $p=0.90$, M12: $p=0.84$). No difference was found between patients transplanted within one year after vaccination and the not transplanted patients. Discussion: VZV booster vaccination equally increases VZV-specific IgG titers in ESRD patients compared to healthy individuals. Prophylactic VZV vaccination pre-transplantation could reduce herpes zoster incidence and severity post transplantation.

Treatment with tacrolimus versus cyclosporine A is a delicate balance between BK virus replication and rejection in renal transplant recipients

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Background: Triple immunosuppressive therapy with prednisolone, mycophenolic acid and tacrolimus is associated with a low incidence of allograft rejection, but is associated with a higher incidence of BK nephropathy (BKVAN). We studied the frequency of BK virus (BKV) complications in renal transplant recipients treated with mycophenolate mofetil (MMF) or mycophenolic acid (MPS) and either cyclosporine A (CsA) or tacrolimus (Tac). Material/methods: Retrospectively, 359 patients who received a renal transplant between 2010 and 2012, were treated with MPS or MMF in combination with CsA (CsA) or Tac (Tac) and mostly prednisolone, were studied . BKV DNA was measured in urine and EDTA-plasma samples. Protocolized renal biopsies were performed at 12 months and upon clinical indication. The incidence of BKVAN and course of BKV infection during 24 months follow-up was analysed. Other variables studied were estimated glomerular filtration rate (eGFR), occurrence of allograft rejection, loss of allograft and death. Results: Incidence of BKV viremia was not significantly different between the CsA (n=42/190) (22.1%) and the Tac (n=36/169) (31.3%) group. However, biopsy proven BKVAN occurred more often in the Tac group (6.4%) versus the CsA group (2.1%) (p=0.04). Longitudinal data analysis showed a significant earlier decline of viral load in urine and EDTA-plasma in the CsA group (t=3 months) compared to the Tac group (t=6 months) (viremia p=0.005). Graft loss, eGFR and mortality rate did not differ in both treatment groups, as well as between the BKV positive vs. BKV negative group. Incidence of rejection was significantly higher in the CsA (19.5%) compared to the Tac (11.2%) (p=0.03) group.
Conclusions: This study shows that immunosuppressive treatment with Tac is associated with a lower incidence of rejection, but possibly at the cost of an increased risk of developing BKVAN in the first two years post-transplant. Overall transplant survival was similar, but for patients at high risk of developing BKVAN a cyclosporine based regimen could be considered.

Is it Clinically Relevant to Perform a protocol MAG3 Scan Postoperative? : A Retrospective Monocentric Study

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Objective: A MAG3 scan can aid in renal transplant patient care if kidney dysfunction develops, but the value of a protocol MAG3 scan is unknown. We evaluated the clinical relevance of a protocol MAG3 scan one day after transplantation. Methods: We performed a retrospective, single-center, case study including all patients who underwent renal transplantation between January 2013 and January 2015. Results: In our cohort of 396 patients, 177 patients had an abnormal MAG3 scan. In 31 patients the result of the MAG3 scan led to a change in clinical care, including a change in medication in five patients, further diagnostic test in 17 patients and an intervention in six patients. In three patients the protocol MAG3 scan showed urinary leakage, but only in one was this clinically silent. Of the five patients that showed (partial) renal infarction on the protocol MAG3 scan, three had normal perfusion after additional testing. All detected perfusion defects were small. Patients with an abnormal MAG3 scan had significantly older donors (56.1 ± 14.3 yr vs 50.0 ± 15.1 yr; $p<0.01$) more often a postmortal donor (58.7% vs. 11.8%; $p<0.01$) and longer warm ischemia time (23.5 ± 7.8 min vs. 20.5 ± 6.7 min; $p<0.01$). Despite these significant differences, considerable overlap existed in these characteristics.
Conclusion: In 31 of 396 patients, the protocol MAG3 scan led to a change in renal transplant patient care. Despite significant differences in donor age, donor type and warm ischemia time between patients with a normal or abnormal MAG3 scan, no cut-off point in these characteristics could be found to limit this per protocol strategy. The value of a protocol MAG3 scan seems limited.

Predictors of postoperative cardiovascular complications until three months after kidney transplantation.

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Background: Previous studies focused on predictors for long-term cardiovascular complications after renal transplantation. Our aim was to identify factors involved in cardiac events within three months after transplantation. Methods: We conducted a chart review for all renal transplants performed in 2010 and 2011 in our center. Factors included are type and number of transplants, delayed graft function (DGF=need for dialysis after transplantation), previous cardiovascular events, cardiac evaluation on indication according to ESC guidelines: left ventricular ejection fraction (LVEF), cardiac stress test and risk estimation; and postoperative blood loss (decrease in hemoglobin level=ΔHb). A composite end point of any cardiovascular event (ischemia with positive enzymes, myocardial infarction, heart failure, and/or coronary intervention) was used. Results: 354 renal transplants were included, of which 71% were living donation and 83% were first transplants. 58 patients (16%) had had a cardiovascular event before transplantation (myocardial infarction, revascularization and/or heart failure). MIBI scan was performed in 130 patients (48 patients with persistent and/or reversible defects); stress ultrasound in 40 patients (1 with ischemia); exercise in 137 patients (6 with ischemia). In 4 patients, the screening led to cardiac revascularization before transplantation. In 38 transplant patients, a cardiac event occurred; reanimation in 4 patients; acute coronary syndrome in 9 patients (of whom 5 patients underwent intervention); and heart failure in 16 patients. Four patients died within three months after transplantation; 3 patients of cardiac cause. In univariate analysis, type of transplant (living or deceased donor), DGF, age, any cardiovascular event before transplantation, myocardial revascularization, myocardial infarct, MIBI scan, LVEF, and ΔHb were all significantly associated with cardiac events within three months after transplantation. In multivariate analysis, type of transplant (RR 2.9, p=0.006), Pretransplant myocardial infarction (RR 7.9, p<0.001) and abnormal MIBI scan (RR 2.8, p=0.043) remained associated with cardiovascular events within three months after transplantation.
Conclusion: The most vulnerable population for post-transplant cardiovascular events are recipients known with previous myocardial infarction and positive MIBI scan who receive a deceased donor kidney transplantation.

A successful approach to kidney transplantation in patients with secondary hyperoxaluria

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Introduction: Chronic oxalate nephropathy is observed secondary to enteric hyperoxaluria that is associated with malabsorption e.g. in short bowel syndrome. It may lead to end-stage renal disease. Kidney transplantation in patients with chronic oxalate nephropathy can be challenging given the risk of recurrent calcium-oxalate nephrolithiasis and crystal-induced kidney injury resulting in graft dysfunction in the peri-transplant setting. Therefore, we studied whether a strategy to decrease serum oxalic acid prior to transplantation may allow successful kidney transplantation. Patients and methods: We established a protocol to reduce serum oxalic acid levels prior to and shortly after kidney transplantation based on reduced intake and increased removal of oxalic acid via intensified hemodialysis (HD). Months before transplantation a low oxalic acid diet (40 mg/day), cholestyramine, potassium citrate, and calcium carbonate were started. One week before transplantation (living donor transplantation) or immediately after surgery (deceased donor transplantation), an oxalic-acid free drip-feed and daily 6h HD session were started. When a urine output>2L was reached HD was stopped and 40mg oxalic acid diet was re-started. Patients were instructed to maintain diuresis > 2L/day. Results: We report three patients with short bowel syndrome following surgery for Crohn's disease who presented as potential kidney transplant recipients. All three patients had elevated serum oxalic acid levels and biopsy-proven calcium oxalate depositions in their native or transplanted kidney. The protocol reduced serum oxalic acid levels from 102, 112, and 48 to 23, 13, and 11 μmol/l. Patients 1 and 2 received a living donor kidney and had immediate functioning grafts. Patient 3 received a deceased donor kidney and achieved urine output >2L/day after 3 weeks. The post-transplantation periods were complicated by sepsis in Patient 1 and symptomatic native kidney stones in Patient 2 requiring temporary re-institution of the protocol. The patients are currently 12, 11, and 7 months after transplantation with stable estimated glomerular filtration rates of 40, 46, and 50 ml/min/1.73 m2, respectively. Conclusions: We conclude that successful kidney transplantation in patients with secondary hyperoxaluria is feasible by implementing a strategy aimed at reducing serum oxalic acid levels in the peri-transplantation period.

Barriers and facilitators in regular gynaecological screening of female renal transplant recipients

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Background: Organ transplant recipients have an increased risk of Human Papillomavirus (HPV) related anogenital (pre)malignancies. Several guidelines recommend to perform annual cervical cancer screening in women who underwent renal transplantation. However, participation rate of female renal transplant recipients (RTRs) in gynaecological screening is low. The aim of this study is to identify barriers and facilitators for annual gynaecological screening in Dutch female RTRs from both patient and professional perspective and to present suggestions for increasing the participation rate. Methods: A qualitative study was performed with women who underwent a renal transplantation at the Radboud university medical center and nephrologists specialized in care for renal transplant patients, using explorative semi-structured interviews in focus groups. In total four focus groups were conducted: two with female RTRs and two with nephrologists. Results: In total 14 female RTRs and 13 nephrologists participated. The main barriers mentioned by both nephrologists and female RTRs were similar: examination by general practitioner and/or assistant is experienced as more uncomfortable and less reliable compared to the examination by a gynaecologist, limited knowledge of professionals and limited information supply to patients. However, female RTRs focused more on the impact of the examination. Total agreement was found on the facilitators: a reminder, a checklist, integration of gynaecological examination in yearly check-up, self-sampling, and information supply at the right moment.
Conclusions: Based on these findings we suggest that female RTRs receive a checklist one year after transplantation with the examinations they should undergo. Furthermore, HPV self-sampling in the yearly check-up by the nephrologist would obviate barriers and meet the main facilitators. Implementing these changes might improve the participation rate of female RTRs in gynaecological screening.

HPV prevalence before and after renal transplantation in females with end-stage renal disease

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Background: Organ transplant recipients have increased risk for developing human papillomavirus (HPV) related (pre)malignancies of the lower genital tract. The HPV prevalence is mainly assessed in females who underwent renal transplantation (RT) and ranges from 27-66%. The natural course of HPV infections during the period before and after RT is largely unknown. The aim of this study is to assess the genital prevalence of HPV in female renal transplant recipients before and after RT. Knowledge with respect to the biological behaviour might provide a scientific basis for rational prevention, such as HPV vaccination, screening and novel therapies with respect to immunosuppression.
Methods: All female patients who were referred to the outpatient clinic of the Radboudumc between the 28th of February 2012 and the 1st of April 2015 to judge whether they were suitable for RT, were invited to participate in the study. Full gynaecological examination with HPV self-sampling and cervical smear, was performed at first visit, after 1 and after 2 years. Furthermore, HPV self-sampling was performed every 3 months. All patients were asked to fill out questionnaires on relationships/sexual behaviour. Results: In total 123 patients were included and 65 patients underwent a transplantation. The median age of the graft recipients was 54 years. HPV prevalence before transplantation was 24% (95% CI 13-35) and after transplantation 31% (95% CI 19-43), p-value 0.20. The hrHPV prevalence before transplantation was 17% (95% CI 8-27) and after 26% (95% CI 15-37), p-value 0.08. Eight patients (12.3%) had cytological abnormalities of which 3 patients had high-grade lesions. No relevant changes in sexual behaviour after RT were reported.
Conclusions: In this cohort of patients with end-stage renal disease, the HPV prevalence was higher than in the general population, before as well as after the transplantation. The increase in prevalence after transplantation, mainly of hrHPV types, suggests activation of latent HPV infections during immunosuppression. Our data support regular HPV testing after transplantation, with gynaecological examination in case of hrHPV positivity.

Donor Comprehension of Provided Information During Informed Consent Process in Live Donor Nephrectomy; Does It Matter What We Tell Donors? A Pilot study

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Background Safety and informed consent are even more important in live kidney donation than in other surgical procedures, since donors undergo a surgical procedure for the benefit of others. Current literature demonstrates great variations in informed consent practices. Donors report varying degrees of satisfaction with the information and preparation for live donor nephrectomy. Whether this is due to lack of education or comprehension remains unclear. It has been suggested that donors do not actually hear everything we tell them, but only use the information to confirm their decision, instead of weighing risks and benefits. It is still vital that these donors receive all necessary details. Aim To assess the informed consent procedure in live donor nephrectomy, test donors on their comprehension of the provided information, and assess donor satisfaction with the informed consent procedure Methods The preoperative surgical outpatient clinic visits of 46 potential living kidney donors were observed. Provided information was scored using standardized checklists, team members (N=9) received an "informer score" for each visit, one point was awarded for each mentioned item. Immediately after giving consent for donor nephrectomy, and again on the day of admission for donation, donors received a questionnaire testing their knowledge of the upcoming operation. Informers as well as donors could score a maximum of 20 points. Scores were compared between donors and informers. Outpatient scores were compared with admission scores. Demographic data and baseline donor characteristics were documented for correlation purposes. Results Median informer score was 12 out of 20 points (range 2-20). Median donor score was 6 out of 20 (range 2-11). Donors scored best on duration of admission and convalescence, and worst on long-term complications. Risk of mortality was disclosed by 91% of informers, but only reproduced by 22% of donors at the outpatient clinic and 14% on admission. Donors living with children under 18, a higher educational level and registered (post-mortem) donors scored significantly better. Median donor satisfaction was 9 out of 10 (range 4-10).
Conclusion There were marked variations between the information provided by different informers, important complications were not always disclosed. Overall donor scores were low, although satisfaction was high. Whether donors are actually well enough informed at the time of giving consent merits further investigation.

Towards a standardized informed consent procedure for live donor nephrectomy: What do surgeons tell potential donors?

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Background A recent systematic review demonstrated that there is no consensus on how the informed consent procedure in live donor nephrectomy should be arranged and practices vary. The aim of this survey study was to evaluate the surgical informed consent procedure for live donor nephrectomy, with special regards to disclosed complications. Methods A web-based survey was sent to all surgeons in the Netherlands who were believed to be, or had been in the past, involved in live kidney donation (n=50). Surgeons were asked if, and how often they mentioned 23 items regarding short- and long-term complications. In addition, questions were included regarding the informed consent practices in each transplant center. Center- and surgeon characteristics (e.g. center volume, surgeons' gender, specialization, experience) were compared to assess whether information disclosure was related to any of these features. Results The response rate was 98% (N=49), and responses were obtained from all eight kidney transplant centers. Of these 49 respondents, 32 were still involved in living kidney donor education. Surgeons had the following subspecializations: transplant surgery (50%), vascular surgery (31%), abdominal surgery (13%), and urology (6%). Informed consent procedures vary between centers, ranging from assumed to signed consent. Some respondents from the same center report different procedures. Bleeding was the only complication every surgeon mentioned. Risk of death was always mentioned by 16 surgeons (50%), sometimes by 12 (37.5%), four surgeons (12.5%) never disclosed this disastrous complication. Reported mortality rates ranged from 0.003% to 0.1%. Mentioning frequencies for all other complications varied per individual surgeon, but also per center. High volume surgeons reported more complications than low volume surgeons. The risk of postoperative pain was more often disclosed by consultant surgeons than fellows, and the risk of death was more often disclosed by surgeons with a differentiation in transplant surgery.
Conclusion Important complications are not always disclosed during the surgical informed consent process for live donor nephrectomy. Informed consent procedures vary. To optimally prepare living kidney donors for the procedure, a standardized informed consent procedure for live donor nephrectomy is highly recommended.

Peri-operative Events and Complications in Minimally-Invasive Live Donor Nephrectomy: What Should We Tell Potential Donors? A Systematic Review and Meta-Analysis

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Background: There are many different techniques for live donor nephrectomy, preferences vary per center. A small number of randomized controlled trials have been performed comparing these different techniques with regard to complications and adverse events. Donors have to be educated about all risks and details during the informed consent process. For this to be successful, more information regarding short-term outcome is necessary. PURPOSE: To systematically assess short term complications after minimally-invasive live donor nephrectomy and to compare different techniques currently employed for this procedure. Methods: A literature search was performed, all studies discussing short-term complications after minimally-invasive live donor nephrectomy were included. Outcomes evaluated were intra- and postoperative complications, conversions, operative and warm ischemia times, blood loss, length of hospital stay, pain score, convalescence, quality of life and costs. RESULTS: 174 Articles were included in the systematic review, 37 in the meta-analysis. Conversion rate was 1.3%. Intraoperative complication rate was 2.4%, bleeding being the most frequent (1.6%). Postoperative complications occurred in 6.8% of donors. Ileus (6.3%) infectious complications (2.6%), wound infection (1.6%) and bleeding (1.1%) were encountered most. Mortality was reported in 128 articles, three fatalities were described (0.02%). None of the minimally-invasive techniques stood out from the rest with regard to complication- or conversion rate. A few minor differences were identified: intra-operative bleeding was more often encountered after hand-assisted procedures (3.9 vs 3.7%, p=0.04), as was postoperative ileus (1.7 vs 0.3%, p=0.06). When compared to mini-open procedures, intra-operative events occurred more often after laparoscopic procedures: 10.2 vs 4.2%, p=0.02, but postoperative infections were more often seen after mini-open procedures; 18% versus 7.9%, p=0.03. This was mainly attributed to an increased incidence of pneumonia after mini-open procedures: 7.9 versus 4.3%, p=0.04.
Conclusions: Minimally-invasive live donor nephrectomy is safe, and associated with low complication rates and an even lower risk of mortality. These data, combined with further analysis of donor comprehension and satisfaction will assist us in developing a standardized, donor-tailored informed consent procedure for live donor nephrectomy.

Which way to stent the ureter? – comparison of 2 ways of urinary drainage in pediatric kidney transplantation

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Purpose. Ureteral stenting in kidney transplantation serves to limit the development of obstruction and urinary leakage, but forms a source of complications as well. A JJ catheter is most frequently used as ureteral stent. External stenting (pyelovesicostomy or splint) on the other hand allows separate analysis of the urine from the transplanted kidney, and avoids a reoperation to remove the JJ catheter. In this study we compared the complication rate of external stenting with that of a JJ catheter in pediatric renal transplant recipients. Methods. Children who received a kidney transplant at Erasmus MC Sophia, Rotterdam between 2006 and 2014 were compared to children transplanted at The Hospital for Sick Children, Toronto, Canada between 2010 and 2014. Patients in Rotterdam received a splint for initial urinary drainage (splint group), and in Toronto a JJ stent (JJ group). Surgical procedures and immunosuppressive therapy were similar. Outcome measures included the need of additional urological interventions and the incidence of urinary tract infections (UTI) during 3 months after transplantation.The data were retrospectively collected. Results. The splint group (n=62) and the JJ group (n=50) did not differ significantly in age, sex, primary diagnosis, method of ureteral implantation, but differed in donor source (LD 55% vs. 36% respectively), and induction therapy (ATG or basiliximab in JJ group, only basiliximab in splint group). The splint was removed after a median of 9 days (IQR 8-12), the JJ catheter after 42 days (IQR 38-50). In the splint group 7 (11.3%) children needed 9 urological reinterventions (6 a JJ catheter and 3 a percutaneous nephrostomy), in the JJ group 2 (1 renewal of JJ catheter, and 1 a percutaneous nephrostomy (log rank p 0.157)). In the splint group 20 children (32%) developed 28 UTIs, 9 during presence of the external drain; in the JJ group 25 children (50%, p 0.057) had 66 UTI (p 0.024), 42 during presence of the JJ catheter (p 0.001).
Conclusion. Children with a JJ stent developed more UTIs than children with a splint, however, there was a, not significantly, larger number requiring reinterventions in the splint group. Both options for urinary drainage have complications suggesting the need for modification of current methods.

Circulatory support and the immediate graft function in pediatric kidney transplantation

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Introduction: During transplantation of an adult donor kidney in a pediatric recipient a supra-pediatric blood pressure is targeted for at the time of revascularization (RV) to facilitate an optimal perfusion of the graft. Aim of this study was to investigate the effect of fluid and inotropic management on 1) the blood pressure at RV and 2) the speed of graft recovery after RV. Methods: In this prospective, multicentre, ongoing study, data of 30 consecutive children who underwent a kidney transplantation (KT) at one centre are presented. A blood pressure of 100-115/60-75 mmHg at revascularization, dependent on recipient age, was aimed at, using crystalline and colloidal fluid therapy (in mL/kg), with or without inotropic support by dopamine and/or noradrenaline. The primary outcome measure was the half-life of the serum creatinine immediately before revascularization (T1/2[SCr_{RV}]). Secondary outcome measures were the blood pressure at revascularization and the estimated glomerular filtration rate at 3 months after KT ($eGFR_{M3}$). Results: The median T1/2[SCr_{RV}] was 11.6 hours (IQR, 6.4-15.8). In univariate Cox regression analyses a shorter T1/2[SCr_{RV}] was associated with pre-emptive KT (P=0.03) and grafts of living donors (P=0.04), but not with recipient age, the relative amount of fluid administered and vasopressor score (dopamine dose [μg/kg/min] × 1) + (noradrenaline [μg/kg/min] × 100) at RV. In the multivariate model a shorter T1/2[SCr_{RV}] was associated with a lower vasopressor score at RV (hazard ratio, 0.94; 95% CI, 0.90-0.97; P<0.001), adjusted for recipient age, living donor graft, pre-emptive KT and the amount of administered fluid. The median $eGFR_{M3}$ was 59.5 (IQR, 45.0-80.3) mL/min/1.73m^2. Using univariate linear regression analyses, a higher $eGFR_{M3}$ was associated with younger recipient age (P=0.001), a larger amount of administered fluid during surgery (P<0.001) and a higher vasopressor score at RV (P=0.02). In a multivariate model these relations were not significant anymore. The blood pressure increased; in children < 10 years from median 79/37 mmHg 2 hr before RV to 106/54 mmHg at the time of RV, in those ≥ 10 years from 97/50mmHg to 124/58 mmHg.
Conclusion: Circulatory support during surgery resulted in an increase of the blood pressure. Contrary to our expectations, inotropic support impaired immediate graft recovery, whereas fluid administration did not affect it significantly. The $eGFR_{M3}$ was not affected by inotropic support or fluid management.

Systematic review and meta-analysis of the impact of computed tomography assessed skeletal muscle mass on outcome in patients awaiting or undergoing liver transplantation

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Background and aims: Although liver transplant outcome has improved significantly, the shortage of human organs remains prevalent. Therefore, strict patient selection is of paramount importance. Recently, low CT-assessed skeletal muscle mass was identified as a novel prognostic parameter to predict outcome in liver transplant candidates. Our aim was to perform a systematic review and meta-analysis on the association between CT-assessed muscle mass and outcome in liver transplant candidates. Methods: A systematic search was performed according to the PRISMA-guidelines. Eligibility and quality assessment, and data-extraction were performed in duplicate. Meta-analyses were performed using random effects models. Results: In total, 19 studies, including 3803 partly overlapping patients (65% male, mean age 52-62), fulfilled the inclusion criteria. Main indications for transplantation were viral infections, followed by alcoholic liver cirrhosis. Median MELD-score ranged from 9-21, albumin level 2.8-3.4 g/dl, and BMI 24.0-29.4 kg/m². Nine studies reported the cross-sectional muscle area (CSA, cm²) with corresponding skeletal muscle index (SMI; CSA corrected for height, cm²/m²), whereas the psoas area (PA) and dorsal muscle group area were reported in nine and one study, respectively. Sarcopenia prevalence ranged from 20-70% and various (gender-specific) cut-off values were used. The pooled hazard ratio of sarcopenia for waiting list mortality was 1.75 (95% CI 1.02-3.01, p=0.04). However, this finding is of limited value due to a small number of studies. The pooled hazard ratios of sarcopenia and cross-sectional skeletal muscle mass (per incremental cm²/m²) for post-transplant mortality were 1.84 (95% CI 1.11-3.05, p=0.02) and 0.98 (95% CI 0.96-1.00, p=0.05), respectively, independent of MELD score. Due to substantial heterogeneity between reported outcome measures, no meta-analyses could be performed for short-term outcomes. Conclusion: Sarcopenia impairs outcome in patients undergoing liver transplantation. Limited evidence also suggests that sarcopenia is associated with waiting list mortality. Therefore, skeletal muscle mass assessment may contribute to pre-transplant risk assessment.

Optimizing microRNA biomarker detection in liver graft preservation solution by counteracting heparin-mediated inhibition

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Introduction: Ischemia-type biliary lesions (ITBL) after liver transplantation strongly increase patient morbidity and impair graft survival. Our earlier study showed that release of hepatocyte- and cholangiocyte-derived miRNAs (HDmiRs and CDmiRs, respectively) into graft preservation solution are predictive for the development of ITBL following transplantation. Recently, concerns are raised that microRNA detection by PCR-analysis can be inhibited by the anti-coagulant heparin. Since graft procurement is performed in the presence of heparin, the PCR detection of HDmiRs and CDmiRs in perfusates might be hampered. The aim of this study was to determine whether heparin in graft perfusates influences miRNA biomarker detection. Methods: Total RNA was isolated from perfusate samples of grafts that developed ITBL (n=22) and non-ITBL (n=35). Specific cDNA for CDmiR-222, CDmiR-296, HDmiR-122, and HDmiR-148a was synthesized in the presence of 6 IU of heparinase I. A synthetic C. elegans miRNA (Cel miR-39) was added as an internal correction for sample variation during the RT step. Relative expression levels were calculated and normalized for Cel miR-39 levels. Results: Real time PCR results for Cel miR-39 shows a mean Ct level of 20.23+/-1.61, indicative for a strong abrogation of PCR impairment by heparin. Treatment of RNA samples with heparinase I resulted in a considerable increase in detection and, simultaneously, a reduction in standard deviation (3.52 to 1.62) and IQR (3.09 to 1.92) of the Ct levels for all measured miRNAs. Also after heparinase treatment HDmiR/CDmiR ratios were significant different between the ITBL and the non-ITBL group (P values ranging between 0.0011 and 0.013). Conclusion: This study demonstrates the usefulness of heparinase-treatment of graft perfusate containing traces of heparin in order to optimize miRNA detection. Furthermore, these results confirm that calculations with organ-derived miRNA ratios are useful for analysis. In other situations, the use of heparinase I is encouraged to obtain high enough levels of detection if contamination is suspected.

Pretransplant HRCT Characteristics are Associated with Worse Outcome of Lung Transplantation for Cystic Fibrosis Patients

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Objectives Peri- and postoperative complications diminish the outcome of lung transplantation (LTx) in patients with cystic fibrosis (CF). We hypothesized that the degree of pathological findings on pre-LTx high resolution computed tomography (HRCT) is associated with higher morbidity and mortality in CF.
Methods All our CF patients undergoing LTx between 2001 and 2011 were included. HRCT examinations were evaluated according to a scoring system for pulmonary disease in CF patients, the Severe Advanced Lung Disease (SALD) score and for pleural involvement.
Results Fifty-three patients were included. Dominant infectious/inflammatory disease according to the SALD score was observed in 10 patients (19%). Five (50%) of those patients died within one week after LTx, compared to 2 (5%) patients without dominant infectious/inflammatory disease ($p<0.001$). This difference in survival percentage remained also significant after multivariate analysis. Patients with infectious/inflammatory disease were transfused more packed red blood cells; 26 versus 8 in the first week ($p<0.001$). Pleural thickening was associated with higher requirement (10 units) for blood transfusion during LTx, compared to patients with normal pleura (4 units).
Conclusions The analysis of HRCT in CF patients according to the SALD score showed that dominant infectious/inflammatory disease is associated with a higher mortality after LTx. HRCT may be a tool for estimating the risk of mortality after LTx in patients with CF.

Effect of recipient length and type of diagnosis on waiting time for lung transplantation candidates

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Introduction Lung transplantation is used as a last option treatment for patients with an end-stage of their pulmonary disease such as cystic fibrosis (CF), pulmonary fibrosis (PF) or COPD. Previous studies suggest that lower recipient height causes increased waiting time and waiting list mortality. We hypothesized that lower recipient length increases waiting list time.
Methods In the period from 2000 up to 2014 288 patients underwent lung transplantation. Total waiting time and recipient length was retrieved from the ENIS database. Patients were divided in 3 length groups (<1,65cm, between 165-175 cm and >175cm). Kaplan Meier curves were used for statistical analysis.
Results The mean waiting time was 591days (SD±537days) and mean age was 51,4 years(SD 13,2). Male/female distribution was unequally distributed in the 3 length groups. Between the different diagnosis groups there was a significant longer waiting time for CF and PF patients ($p<0.004$). Comparison of the 3 length groups did not show differences in waiting time. Further analysis revealed that the CF male patients showed a prolonged waiting time (CF: CI 2180.764-2771.236).
Discussion We have found that there was no difference in waiting time for lung transplantation in the 3 different recipient length groups. However, diagnosis of CF and PF had a negative effect on the mean waiting time. Further analysis is warranted why the latter occurs.

High incidence of herpes zoster after kidney, liver, heart and lung transplantation

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Background: Primary varicella zoster virus (VZV) infection causes varicella and lifelong latent infection in neural ganglia from which it may reactivate leading to herpes zoster (HZ). Immunocompromised transplant recipients are at risk to develop HZ and severe clinical complications. Therefore, we investigated the incidence of HZ after the first organ transplant and analysed the severity of HZ. Methods: The records of 958 transplant recipients after the first kidney (KTx: n=420), first liver (LTx: n=224), heart (HTx: n=195) and lung (LuTx: n=119) transplantation were analysed for VZV-PCR DNA and clinical signs of HZ. Results: HZ infection was clinically diagnosed and confirmed by PCR in 107 patients: 38 KTx, 16 LTx, 36 HTx and 17 LuTx recipients. 9/38 patients post-KTx had complicated HZ: 6 had disseminated HZ (≥3 dermatomes) of whom one died due to encephalitis/meningitis 2 weeks later and 3 had cranial nerve involvement. 2/16 patients post-LTx had disseminated HZ. 14/36 patients had complicated HZ post-HTx: 2 had systemic dissemination, 5 had cranial nerve involvement and 7 had post herpetic neuralgia (PHN). 8/17 patients had complicated HZ post LuTx: 3 had PHN and in one patient the cranial nerves were involved and she died six days later. The overall incidence rate of HZ post-KTx (14.4 cases/1000 PY), LTx (24.5 cases/1000 PY), HTx (30.8 cases/1000 PY) and LuTx (38.2 cases/1000 PY) was significantly higher than in the general population of 50-70 years of age (7-8 cases/1000 PY). Conclusion: HZ is a frequent complication after kidney, liver, heart and lung transplantation. Boosting the VZV immune response by prophylactic VZV vaccination pre-transplantation may limit the incidence and severity of HZ post-transplantation.

Plasma alemtuzumab levels show great interpatient variability, but are not associated with late acute rejection in simultaneous pancreas-kidney recipients

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Introduction: Alemtuzumab induction followed by a steroid-free, tacrolimus (Tac) and mycophenolate mofetil (MMF) based regimen effectively prevented acute rejection after simultaneous pancreas-kidney transplantation (SPKT). Acute rejection was rare in the first three months with a second peak in the cumulative incidence between 3 to 6 months, despite comparable Tac and MMF exposure and similar reconstitution of immune cells in patients with and without rejection. Here, we investigated whether later acute rejections were associated with alemtuzumab plasma levels, since significant interpatient variability has been reported in non-solid organ transplant studies. Methods: This retrospective cohort study included 73 consecutive SPKT recipients, all receiving alemtuzumab induction (15 mg subcutaneously, day 0 & 1) and steroid-free maintenance with Tac and MMF. Alemtuzumab levels were measured with ELISA on 3 time points in 10 patients with acute rejection within 6 months and 10 control patients without rejection. Kaplan-Meier estimate (log rank) was used to compare time to undetectable plasma levels. Results: A total of 15 patients (20.5%) experienced acute rejection in the first year after SPKT: two patients <3 months, eight between 3 to 6 months, and five between month 6 to 12. Plasma alemtuzumab levels showed great interpatient variability, ranging from 0.04 to 0.30 µg/mL at month 1 and undetectable to 0.08 µg/mL at month 3. In 13 out of 20 patients (6 controls, 7 rejections) alemtuzumab levels were undetectable (<0.01µgl/mL) at 3 months. Plasma alemtuzumab levels were not associated with acute rejection (log rank 0.486). Despite comparable therapeutic drug monitoring results, 10 of 15 first acute rejection episodes were preceded by a standard (empiric) dose reduction at 3 months or an additional reduction due to intercurrent infections or leukopenia. Conclusion: Alemtuzumab levels in SPKT recipients showed great interpatient variability, there was however no association between therapeutic drug monitoring parameters and acute rejection episodes beyond 3 months. The observation that late acute rejections were associated intercurrent infections and additional dose reductions, suggests that these empiric reductions in Tac or MMF, in the absence of steroids, constitute an increased risk for late acute rejection in SPKT.

Development of donor specific antibodies after islet-after-kidney transplantation

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Islet transplantation is performed in a small group of patients with complicated type 1 diabetes mellitus. Often, multiple donor pancreata are used to achieve a satisfying clinical result, thereby exposing recipients to a large pool of HLA antigens and potential risk of allo-immunization. We studied the development of donor specific HLA antibodies (DSA) in islet-after-kidney (IAK) transplantation recipients and furthermore aimed to assess the relation with the amount of donor pancreata utilized. Methods: Patients receiving an IAK transplantation with alemtuzumab induction therapy for a first transplant, basiliximab for subsequent transplants, and tacrolimus/MMF/prednisolone maintenance therapy were followed. Recipients were screened after 3 months and then yearly for donor specific HLA antibodies using a Luminex assay. Patients were also assessed for islet function using insulin independence and beta score (from 0 to 8 points): a combined measure of insulin secretion and clinical outcome. Results: 18 IAK patients were assessed (13M/5F, age 50.8±9.3 years). Previous solitary kidney transplantation was present in 12/18 recipients (one patient had received 3 kidney transplantations) and simultaneous pancreas-kidney transplantation in 6/18 recipients (two patients had received two pancreas transplantations). DSA were present in 10/18 (67%) recipients before islet transplantation. Follow up after IAK was 47.4±23.5 (range 22–97) months. Patients underwent 1.9±0.5 (range 1–3) islet transplantation procedures using 2.8 ±1.1 (range 1–5) pancreata. Insulin independence was achieved by 72%. At the last follow up 6/15 (40%) recipients were insulin independent and the median beta score was 5 (range 0–8). HbA1c decreased from 63.6±16.5 to 50.5±11.9 mmol/mol (-21%, p=0.009). One patient had graft failure. Four patients (22%) developed DSA against islet donor HLA antigens (both type I and type II). The number of donor pancreata used was similar for both groups (2.8±1.7 pancreata (DSA+) versus 2.8±0.9 pancreata (DSA-); p=0.96). Development of DSA was not associated with a lower beta score (median 3.5 (DSA+) versus 5 (DSA-), p=0.44). Conclusion: 22% of IAK recipients developed DSA, as compared to 67% after previous solid organ transplantation. There was no association between the number of pancreata used for islet transplantation and development of DSA against donor islet HLA antigens. Development of DSA was not associated with a decline in islet transplant function.

The role of methylprednisolone in the rescue of functional graft loss after islet rejection

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There are currently no accurate tools for the early detection of acute islet graft rejection. The diagnosis is generally made after severe functional loss has already occurred. Methylprednisolone, rituximab and immunoglobulin have been reported as treatment, but there is a scarcity of data on the efficacy of these treatment options on islet graft outcome. Therefore we compared the outcome in recipients with acute rejection that received methylprednisolone to those who did not. Methods: 7 patients with type 1 diabetes who had received an islet transplantation and had acute allograft rejection were studied. Signs of allograft rejection included sudden hyperglycemia, lower C-peptide concentrations, increased immunological markers and precipitating events. All patients received supportive care, including optimization of medical therapy. Methylprednisolone treatment consisted of 1000mg i.v. daily for three days. Clinical data before, during and 3 months after the episode of acute rejection were obtained. Patients were also assessed for islet function using insulin independence and beta score (from 0 to 8 points): a combined measure of insulin secretion and clinical outcome. Results: Rejection was indicated by hyperglycemia (7/7), 74.1% lower C-peptide concentrations (7/7), preceding low exposure to immunosuppressants (4/7), preceding infection (3/7), and presence of donor-specific antibodies (3/7). No change in anti-GAD titer or PRA was present in the acute phase of rejection. Two patients received i.v. steroids within one week after their first hyperglycemia; five others did not. Patient and transplantation characteristics in both groups were similar. Before the rejection, the two patients in the treated group had a beta score of 6 and 7, with the second being insulin independent; the untreated group had a median beta score of 6 with 2 of 5 patients being insulin independent. Stimulated C-peptide levels were 1.79 ±0.87 nmol/L for the treated group and 1.50±0.74 for the untreated group. Rejection occurred 7.1 (range 2.5–16) months after transplantation. No patients retained insulin independence. Beta score dropped to a median of 1 in both groups and stimulated C-peptide decreased to 0.19±0.2 and 0.28±0.46 nmol/L in the treated and untreated group, respectively. Conclusion: Methylprednisolone treatment in 2 patients with acute islet allograft rejection did not restore allograft function nor did it lead to better outcomes as compared to untreated patients.

Islet Donor Risk Score: An Evidence-Based IEQ Prediction Model

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Introduction: In order to better identify suitable donors for islet transplantation programs, it is imperative to find a model of islet isolation yield prediction based on donor characteristics. Current prediction models are either not evidence based or pertain to whole organ transplantation. Our aim is to generate an islet donor risk score (iDRI) that predicts islet isolation yield. Methods: Clinical islet isolation outcome in IEQ was analyzed in relation to donor characteristics at the Leiden University Medical Center from 2008-2014 (n=289). Factors with a p-value <0.20 and <25% missingness in univariate analysis were entered into a multivariate backward elimination model. The least significant factor predicting IEQ was eliminated each round until only values with p<0.05 remained. Results: 37 Factors were entered into the multivariate analysis and five remained: BMI, DBD/DCD, sex, amylase and CIT, making up the iDRI. The iDRI accounts for 28% of the variability in IEQ (correlation iDRI with IEQ p<0.0001, r2=0.279). The mean iDRI of isolations used for single organ transplantation was significantly higher than the mean of all other isolations (632,022±44,821 vs 415,407±8,243, p<0.0001).
Conclusion: The iDRi could be a useful tool to predict islet isolation outcome. Validation of the iDRI will be performed in islet isolation datasets from other centers.

Identification of non-HLA antibody targets in kidney transplantation for a new diagnostic assay

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Introduction: HLA antibodies are an established risk factor for antibody-mediated rejection and impaired graft survival. Evidence originating from HLA identical sibling transplants indicates that non-HLA antibodies play a role as well. Numerous non-HLA antibodies directed against a heterogeneous subset of both allow- and autoantigens have been identified in renal transplantation. Standardized assays for the measurement of non-HLA antibodies are lacking. We performed a literature study to determine which non-HLA antibody targets should be implemented in a new assay. Results: In 106 studies over 3000 potential non-HLA antigens were described in renal transplant patients, and antibodies against 21 of these were found to be associated with a poor prognosis such as autoantibodies directed against recently discovered targets including agrin and endorepellin. The most extensively studied non-HLA antibodies were MHC class I related chain A antibodies, anti-endothelial cell antibodies and anti-angiotensin II type I receptor antibodies. In addition, multiple groups also studied endothelin-1 type A receptor and vimentin anti-bodies.
Several studies have indicated that the presence of non-HLA antibodies is a risk indicator for rejection and decreased graft survival. However, assembling of these results in order to determine the exact clinical relevance is limited by heterogenic study populations and outcome measures, and also by different testing methods and large variations in reported incidences of antibodies even with the same assay.
Conclusion: The exact clinical relevance of non-HLA antibodies has yet to be determined because of highly heterogenic study designs and inconclusive results in a number of studies. However, it is hypothesized that non-HLA antibodies are associated with impaired graft outcome and that non-HLA and HLA-antibodies have a synergistic effect. HLA antibodies can evoke endothelial damage and subsequent exposure to selfantigens, amplifies inflammation caused by binding of non-HLA antibodies activating complement. Considering the number of newly identified non-HLA antibodies and technical difficulties with current assays, the development of a new diagnostic assay is warranted. Preferentially, this assay would measure multiple antibodies at once as this will provide valuable information regarding the role of non-HLA antibodies in rejection and could eventually help identifying different risk profiles for rejection and impaired graft survival.

IVIG and high dose steroid treatment of transplant glomerulopathy effectively slows progression of loss of renal allograft function

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Introduction; Transplant glomerulopathy (TG) is commonly associated with chronic antibody mediated rejection and is a major cause of kidney allograft loss with no established effective therapy. At our centre, patients with TG within the context of chronic antibody mediated rejection are treated with intravenous immunoglobulins (IVIG) and pulse methylprednisolone (MP). In this study we analysed the efficacy of this treatment. Patients, materials and methods; From 2007 until 2015, 40 patients with biopsy proven TG were treated with IVIG/MP. All patients underwent a renal biopsy because of progressive decline in renal function (eGFR) at least 1 year post transplantation. Biopsies were scored according to the Banff classification. After TG was confirmed by biopsy, patients were administered three doses of 1 g intravenous MP combined with a single dose of IVIG (1 g/kg body weight). The efficacy of the treatment was analysed by comparing the slope of eGFR 12 months prior to treatment to the course of eGFR in the 12 months after treatment by linear multilevel analysis. Clinical and histomorphological parameters were analysed for association with outcome. Results; Treatment with IVIG/MP resulted in a significant decrease in eGFR gradient from -10.0 ml/min/1.73m2/year pre-treatment to -4.9 ml/min/1.73m2/year post-treatment (P<0.001). Three patients were non-responders returning to dialysis within the first year after treatment. No parameter associated with non-responsiveness could be identified. 29 out of 40 patients reached a 2-year follow up end-point. Data extrapolation showed that in 69% of these patients a beneficial effect is still present. Additionally, prior to IVIG/MP, proteinuria increased with an average of 0.61 g/L/year and thereafter decreased with 0.11 g/L/year (P=0.0069). Conclusions; IVIG/MP treatment for TG is associated with an average 50% reduction in eGFR loss within the first year after treatment and reduces proteinuria significantly. However, more efficient therapeutic options are needed.

Discontinuation of mycophenolate mofetil does not significantly change blood pressure in renal transplant patients: results of the TacMono study

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Introduction: Mycophenolate mofetil (MMF) markedly decreases blood pressure in rats1. Human data on renal immune cell infiltration in hypertension are scarce and observational but indicate that similar mechanisms may be operative 2. Discontinuation of MMF in a randomized fashion in stable kidney transplant patients provides an excellent opportunity to study the effects of MMF on blood pressure. Methods: In 2014 the TacMono study was started with the objective to randomize 80 low-risk kidney transplant recipients (≤3 HLA mismatches and ≤4% panel reactive antibodies) to either continue tacrolimus/ MMF or half their MMF dose at month 6 followed by MMF discontinuation at month 9. Hence, after nine months the latter group of patients are treated with once daily slow release tacrolimus (Advagraf) as the only immunosuppressive drug. Blood pressure is measured 6, 9 and 12 months after transplantation. The mean arterial pressure (MAP) of the last 6 out of 7 30-minute-Datascoop recordings were analyzed. Per patient the percentage change in blood pressure compared to baseline MAP was calculated. The change in MAP over time was corrected for the use of antihypertensive drugs using the WHO daily defined dose (DDD). Mann-Whitney U testing was used to analyze differences between the two groups. Results: Till November 2015, 17 patients have been randomized of which 11 have completed nine months and 7 patients twelve months follow-up. Median MMF dose at randomization was 1000 mg daily. Median MAP at randomization was 98 mmHg (range 87-124,5). Decreasing MMF did not alter blood pressure levels: the MAP decreased 4% after dividing the MMF dose in half (controls 5% increase) and returned to baseline randomization levels after discontinuation of MMF (controls 7% increase), both p >0,1. In 7 patients the antihypertensive regimen was changed during the study period: in TacMono patients no net change in cumulative DDD was observed after nine and twelve months (median use 2,83 DDD at baseline), while in standard dual therapy no net change was observed after nine months and 50% increase after twelve months (median use 2,50 DDD at baseline). Conclusion: Our preliminary results indicate that MMF in clinically relevant dosages does not influence blood pressure in kidney transplant patients. 1 Boesen, Clin Exp Pharmacol Physiol 2010. 2 Herrera, J Am Soc Nephrol 2006.

Pregnancy in patients with a renal transplant: role of immune-suppressive drugs in pregnancy outcome

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Pregnancy in women with a renal transplant (RTX) is associated with an increased risk of maternal and fetal complications, such as preeclampsia (PE) and preterm birth (PTB). In these patients, azathioprine (AZA) and calcineurin inhibitors (CNI) are the preferred immunosuppressive drugs (ISD) during pregnancy. Previous research has shown that ISD influence the composition and function of peripheral immune cells. Since uterine immune cells play an essential role in embryonic implantation, placentation and fetal tolerance, we hypothesize that the use of ISD in RTX patients influences the pathogenesis of pregnancy related complications. We performed a retrospective study between 1997 and 2013 of 26 RTX patients (mean age 31 ± 4 years) who carried a total of 40 pregnancies. We investigated the maternal and fetal outcomes according to ISD use. Furthermore, we initiated a prospective study to characterize lymphocytes isolated from peripheral blood (PBMC) and placental tissue by flowcytometry, obtained at the time of delivery from RTX patients compared to healthy pregnant controls. Results of the retrospective study showed that 40% of pregnancies were complicated by PE , 47% by PTB and 43% by low birth weight. Patients using CNI developed PE earlier as compared to patients using AZA (gestational age at onset respectively 32 wks and 37 wks, p=0.009). Mean protein levels rose during pregnancy for our total study population (AZA 0.50 g/L, p=0.008; CNI 0.84 g/L, p=0.002). No statistical differences were found in the course of renal function with respect to immunosuppressive regimens. Patients using CNI showed a higher diastolic blood pressure within 6 months post-delivery (p=0.005). Fetal outcomes were similar, although newborns of patients using CNI tended to have a lower birth weight. Preliminary results from the immunological study of 5 RTX pregnant patients showed an increased percentage of $CD4^{+}FoxP3^{+}CD25^{high}$ regulatory T cells (Treg) in placental derived lymphocytes from RTX patients compared to controls (n=9), while the percentage of Treg in PBMC was significantly lower in RTX patients as compared to controls.

Our data pertaining to maternal and fetal outcome to pregnancy favors the use of AZA above CNI as a preferred immunosuppressive choice for pregnant RTX patients. Our preliminary data from immunological assays showed an altered lymphocyte phenotype and suggests a role for Treg in the pathogenesis of pregnancy related complications in pregnant RTX recipients.

Influence of donor factors and operative technique on surgical outcome in a cohort comprising 18 years of mini-incision and laparoscopic kidney donation

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Background While laparoscopic live kidney donation (LDN) has been increasingly performed in recent years, mini incision donor nephrectomy (MDN) remains a known safe and feasible option for live kidney donation. Aim of the present study was to describe the outcome of both techniques as practiced in our center, and to identify possible factors that may influence these outcomes.
Methods A cohort of 836 live kidney donors (702 MDN, 134 LDN) undergoing live kidney donation between May 1997 and May 2015 was retrospectively analyzed. Primary outcome was occurrence of any major or minor complication during initial hospitalization, secondary measures included peri-operative blood loss, operating time and hospital stay. Factors included in the analysis were donor age, BMI, kidney side and operative technique.
Results In our cohort, the overall incidence of any complication was 10.3%, with 5 patients (0.6%) needing reintervention. No mortality was observed. In univariate analysis, there was no significant difference in complication rate between MDN and LDN (10.8% vs 7.5%). Surprisingly, patients aged <60 tended to have more complications (11.9% vs 8.2%, p=0.09). The subgroup of patients with high BMI showed a significantly higher complication rate in left kidney donation (13.1% vs 3.9%, p=0.019). In multivariate logistic regression analysis, left kidney donation and age <60 were significantly associated with a higher complication rate (OR 2.6 and 1.6, respectively). Secondary outcomes included significantly less blood loss (109 vs 307 ml), longer operating time (221 vs 198 min) and shorter hospital stay (4 vs 5 days) in LDN when compared to MDN. BMI, age and kidney side were not of significant influence.
Conclusion MDN and LDN are both safe options for live kidney donation, with limited complication rate. The data in our cohort show an association between kidney side and age on complications. Although retrospectively analyzed, these results may help in clinical decision making when selecting kidney side and operative technique in living donor retrieval surgery.

Whole blood phospho-specific flowcytometry reveals the influence of immunosuppressive drugs on monocyte activation after kidney transplantation

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Introduction Monocytes have been identified as key players driving rejection processes. Surprisingly, little is known about the effects of immunosuppressive drugs on activation cascades of monocytes during these responses. Here, single-cell phospho-specific flow cytometry was used to explore the effects of immunosuppression on signaling pathways in monocytes of kidney transplant patients. Patients, materials and methods We measured the phosphorylation of the divers signaling pathways including NFκB, MAPK and AKT(mTOR) in peripheral blood CD14+ monocytes of kidney transplant patients (n=14) in the first month after transplantation. Patients received maintenance therapy of tacrolimus, mycophenolate mofetil and prednisone in combination with basiliximab induction therapy. Results Before transplantation ex vivo phosphorylation levels of p38MAPK, ERK and AKT, but not of NFκB, were highly expressed by monocytes (MFI: 1863, 635, 1108 and 279 respectively) compared to isotype controls (MFI: 636, 199, 630 and 277, respectively; $p<0.001$ for p38MAPK, ERK and AKT). After transplantation these phosphorylated signaling molecules were significantly inhibited, 33%, 35% and 19% for p38MAPK, ERK and AKT, $p<0.05$, respectively. These levels of p38MAPK and AKT, but not of ERK, inversely correlated with tacrolimus pre-dose concentrations ($p=0.03$ and $p=0.01$, respectively). No correlation was found between phosphorylated p38MAPK, ERK and AKT levels and kidney function, i.e. serum creatinine or eGFR levels. Remarkably, p38MAPK phosphorylation levels before transplantation were significantly higher in patients suffering from a rejection episode than in patients without a rejection ($p=0.03$). Conclusion The decreased phosphorylation levels of p38MAPK, ERK and AKT after transplantation demonstrate that currently prescribed immunosuppressive drugs also inhibit early monocyte activation.

TNFR2-agonist facilitates high purity expansion of human Treg starting from low purity isolated Treg

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Due to the central role of T cell mediated regulation in the maintenance of allograft tolerance, Foxp3+ Treg are thought to be the most promising cell type for use as a tolerance inducing therapy. However, naturally occurring FOXP3+ Treg represent only a small fraction (<5%) of human peripheral blood CD4+ T cell. Thus, Treg must be isolated and expanded *ex vivo* for obtaining sufficient cells for therapeutic application in solid organ transplant patients. Although therapeutic Treg flow-sorting is feasible, most clinic centers aiming at Treg-based therapy focus on magnetic bead isolation of CD4+CD25+ Treg using a good manufacturing practice compliant closed system that achieves lower levels of cell purity. Polyclonal Treg expansion protocols commonly use anti-CD3 plus anti-CD28 monoclonal antibody (mAb) stimulation in the presence of rhIL-2, with or without rapamycin. However, the resultant Treg population is often heterogeneous and pro-inflammatory cytokines like IFNg and IL-17A can be produced. Hence, it is crucial to search for expansion protocols that not only maximize *ex vivo* Treg proliferative rates, but also maintain Treg stability and preserve their suppressive function. Here, we show that *ex vivo* expansion of low purity magnetic bead isolated Treg in the presence of a TNFR2 agonist mAb (TNFR2-agonist) together with rapamycin, results in a homogenous stable suppressive Treg population that expresses FOXP3 and Helios, shows low expression of CD127 and hypo-methylation of the *FOXP3* gene. These cells reveal a low IL-17A and IFNg producing potential and hardly express the chemokine receptors CCR6, CCR7 and CXCR3. Re-stimulation of cells in a pro-inflammatory environment did not break the stability of this Treg population. In a preclinical humanized mouse model, the TNFR2-agonist plus rapamycin expanded Treg suppressed inflammation *in vivo*. Importantly, this Treg expansion protocol enables the use of less pure, but more easily obtainable cell fractions, as similar outcomes were observed using either high purity FACS-sorted or low purity MACS-isolated Treg. Therefore, this protocol is of great interest for the *ex vivo* expansion of Treg for clinical immunotherapy.

CD86-expression on monocytes and B cells as a tool for therapeutic drug monitoring of belatacept

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Belatacept blocks CD28-mediated T-cell activation by binding CD86 on antigen presenting cells. No therapeutic drug monitoring of serum levels is recommended for belatacept, because of low inter-patient variability in pharmacokinetic parameters. We questioned whether the CD86 competition flow cytometry assay on monocytes and on donor-antigen stimulated B cells could be useful as a tool for pharmacodynamic monitoring of belatacept therapy. CD86-expression was assessed on monocytes and donor-antigen activated B cells of patients treated with tacrolimus or the Less-Intensive regimen of belatacept, in the stable situation and during rejection. Before transplantation, flow cytometric analysis of whole blood samples showed that CD86 was expressed on monocytes: median 2029 molecules/cell [1179-4102]. After one dose of belatacept the numbers of free CD86-molecules per monocyte dropped by >85% in all patients (n=17), p=0.0003. In tacrolimus-treated patients (n=19) the expression levels of this co-stimulatory molecule decreased by 33% (p=0.003), significantly less than in belatacept treated patients (p<0.0001). For the entire one year study period the numbers of free CD86-molecules per monocyte remained stable in patients without rejection treated with either belatacept or tacrolimus. Also during rejection the CD86-expression on monocytes was still blocked for >85% in belatacept-treated patients. CD86 was not detectable on circulating B cells and was subsequently studied in vitro after stimulation with donor antigen in the presence and absence of added belatacept. After stimulation, the CD86-expression on B cells increased to ~40%, and was 55% lower in the presence of therapeutic concentrations of belatacept (10 µg/mL) vs. 38% lower with tacrolimus (10 ng/mL), p=0.02. No significant differences were found between CD86-expression on B cells obtained from rejectors or non-rejectors. The fully effective blockade of CD86 on blood monocytes did not prevent the occurrence of rejection, which makes this assay less suitable for TDM to prevent rejection. Belatacept only partly blocked CD86-expression on in vitro donor-antigen re-activated B cells. Since the magnitude of blockade by belatacept was not different between rejectors and non-rejectors, this assay will not be instrumental in improving efficacy of belatacept treatment.

High numbers of pre-transplant donor-specific IL-21 producing cells predicts acute rejection after kidney transplantation

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Background: IL-21 is a master regulator of function and homeostasis of the immune system. The major sources of IL-21 are CD4+ T-cells, including memory follicular T-helper cells and Th17 cells, as well as NKT cells and CD8+ T-cells. IL-21 can act in an autocrine fashion on these cell populations and on other cells (NK cells, B-cells, Tregs, DC and macrophages). Overproduction of IL-21 occurs in many inflammatory diseases such as rheumatoid arthritis, psoriasis and SLE. Because IL-21 supports the induction and expansion of the aggressive cytotoxic CD8+ T-cells, we questioned whether pre transplant IL-21 production can predict acute rejection after transplantation. Methods: The frequency of circulating IL-21 producing cells to donor cells was determined by Elispot assay in 17 patients before kidney transplantation: 10 patient with biopsy proven rejection (acute cellular rejection types 1 and 2), treated with high dose methylprednisolone, and 7 patients without rejection after transplantation. Stimulation with staphylococcal enterotoxin B (SEB) and a cocktail of peptides to influenza, CMV and EBV (ICE) served as positive control for the HLA class II and HLA I response, respectively. Results: Higher numbers of donor-specific IL-21 producing cells were found in the rejectors compared to non-rejectors (median 34/3x10E5 PBMC, range 16-70 vs. 6/3x10E5 PBMC, range 3-105; p=0.04). The frequency of IL-21 producing cells was significantly higher after SEB than after ICE stimulation (median 89/5x10E4 PBMC, range 11-504 vs. 2/3x10E5 PBMC, range 0-50; p=0.0002). No difference was found in frequency of IL-21 producing cells after SEB and ICE stimulation between the patient groups. Conclusion: IL-21 is mainly produced via an HLA class II restricted response. The production of pre transplant donor-specific IL-21 producing cells is linked to a high risk of acute rejection. Therefore, blocking IL-21 production may provide prevention of acute rejection.

Characterization of Polyomavirus BK-specific CD8+ T cells in Renal Transplant Recipients Suffering from viral reactivation

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Introduction: Polyomavirus BK (BKV) causes severe interstitial nephritis (BKVN) in up to 10% of renal transplant recipients (RTRs), causing graft loss in a substantial number of them. Because T cell responses are important to viral control, we investigated the role of BKV-specific CD8+ T cell differentiation in the emergence of BKV reactivation and BKVN. Methods: Using HLA A02-restricted tetramers loaded with immunodominant BKV VP1- and large T antigen (LTAG)-specific epitopes, we isolated BKV-specific CD8+ T cell populations from the blood of sixty-six HLA A02-positive individuals suffering to varying degrees from BKV reactivation and/or histologically proven BKVN. We investigated the differentiation of these BKV-specific CD8+ T cells in relation to disease severity, longitudinally in time after transplantation. For that, we measured the expression of differentiation markers like CD45RA and CD27, chemokine receptors, such as CCR7 and CXCR6, the serine proteases granzyme K and B, and the transcription factors, T-bet and eomesodermin. Results: As judged by these markers, BKV-specific CD8+ T cells from patients with strong reactivation (BKV-PCR >1*10e4 copies/ml) displayed a block in differentiation in comparison to patients who better succeeded in controlling the virus. Conclusion: These findings indicate diminished differentiation of BKV-specific CD8+ T cells as a possible mechanism involved in the pathogenesis of severe BKV reactivation and BKVN.

The role of syndecan-1 in the interaction between dendritic cells and T cells

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Introduction: Syndecan-1 is a heparan sulphate proteoglycan capable of binding chemokines and growth factors by its heparan sulphate side chains. Both dendritic cells (DCs) and T cells express syndecan-1. We previously demonstrated an immunomodulatory role of syndecan-1 in an experimental model of glomerulonephritis. A possible role of syndecan-1 in the interaction between DC and T cells, of paramount importance in the initiation of allograft rejection, has not been studied yet. In this study we aimed to investigate the role of syndecan-1 in DC - T cell interaction, as well as DC and T cell functioning.
Materials and methods: The role of syndecan-1 on DC cell maturation was studied *in vitro* by incubation of mouse syndecan-1$^{-/-}$ or wild type (WT; C57Bl6) bone marrow derived DCs with different TLR ligands (PAM3CysSer, LPS, ODN1826). Maturation was analyzed by measuring the expression of co-stimulatory molecules (CD40, CD86) using flow cytometry. The role of syndecan-1 on T cells was studied *in vitro* by stimulating mouse syndecan-1$^{-/-}$ or wild type (WT; C57Bl6) CFSE labeled splenocytes either with concanavalin A or bone marrow derived Balb/c DCs. Proliferation was evaluated by dilution of CFSE signal. Co-culture supernatants were analyzed for cytokine levels to evaluate T cell differentiation. Results: Syndecan-1 deficient DCs stimulated with a TLR4 or TLR9 ligand showed a decreased co-stimulatory molecule expression compared to WT DCs. Syndecan-1 deficient T cells showed a diminished proliferative response upon low dose (0.25 µg/ml) concanavalin A and immature DC stimulation. Although the proliferative response upon mature DC and 0.5 µg/ml concanavalin A was comparable between groups, IL17 production was significantly reduced. Levels of IL2, IL4, IL10 and IFNγ in culture supernatant did not differ.
Conclusion: Syndecan-1 deficient DCs have a lower expression of co-stimulatory molecules after incubation with a TLR4 or TLR9 ligand, suggesting a role for syndecan-1 in DC maturation. Syndecan-1 seems also involved in T cell functioning, illustrated by diminished proliferative response upon stimulation by (immature) DC or (low dose) concanavalin A, and decreased IL17 production.

Endogenous Interleukin-37 diminishes CXCL1 release by dendritic cells upon stimulation with TLR ligands

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*O*bjective: Renal ischemia and subsequent reperfusion (IR) is an inevitable process upon transplantation procedures. Damage-associated molecular patterns (DAMPs) released upon IR induce innate immune responses by activating Toll-like receptors (TLRs) which subsequently exaggerate tubular damage and kidney dysfunction. Dendritic cells (DCs) are key players in innate immune responses and moreover drive the onset of adaptive immunity. The human cytokine Interleukin (IL)-37 is a potent inhibitor of innate immunity that can reduce the degree of DC activation and consequent adaptive immune responses, including lymphocyte proliferation. In this study we evaluated the effects of endogenous IL37 on the functional response of DCs by stimulation with different TLR ligands. Methods: Bone marrow cells were isolated from femurs obtained from wild type (WT) and transgenic mice expressing human IL37 (hIL37tg) and subsequently differentiated towards bone marrow-derived dendritic cells (BMDCs) by culturing in the presence of granulocyte-macrophage colony-stimulating factor (GM-CSF) for 8 days. BMDCs were stimulated with proinflammatory TLR agonists (lipopolysaccharide (LPS), Pam3Cys, CpG oligonucleotides (ODNs)) for 24hrs. The subsequent inflammatory response was determined by measuring cytokine release in the supernatant (ELISA) and gene expression profiles (quantitative RT-PCR), whereas the degree of DC maturation was determined using flow cytometry by quantifying cell surface marker expression (CD40 and CD86) on CD11c+ cells. Results: mRNA expression and protein secretion of the neutrophil attracting chemokine CXCL1 were strongly reduced upon stimulation of hIL37tg BMDCs as compared to WT BMDCs. In contrast, IL37 expression did not affect TNFα and IL6 mRNA and protein levels, nor the degree of IL10 mRNA levels. Of note, no differences were found in basal levels between unstimulated immature DCs of WT and hIL37tg origin. Various concentrations of LPS, and to a lesser extent Pam3Cys or CpG ODNs, clearly induced maturation of CD11c+ BMDCs, as reflected by elevated expression of co-stimulatory molecules CD40 and CD86. However, endogenous IL37 did not affect the degree of maturation. Conclusion: Our preliminary data indicate that endogenous IL37 selectively reduces CXCL1 production by DCs upon stimulation with TLR agonists. However, production of other proinflammatory cytokines and costimulatory molecules was not affected by endogenous IL37.

End stage renal disease patients have a skewed T cell receptor Vbeta repertoire

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Introduction: End stage renal disease (ESRD) is associated with a defective T-cell mediated immunity, resembling premature T-cell ageing. A diverse T-cell receptor Vbeta (TCR Vβ) repertoire is central to effective T-cell mediated immune responses to foreign antigens. In this study, the effect of ESRD on TCR Vβ repertoire diversity was assessed and associated with T-cell ageing parameters. Patients, materials and methods: Forty-five stable ESRD patients on the waiting list for their first kidney transplantation and 51 healthy individuals (HI) were included, matched for age and cytomegalovirus (CMV) serostatus. Twenty-one patients were within the young group (age 19 – 45 years) and 24 patients belonged to the elderly group (age 65 – 77 years). Patients with any clinical or laboratory evidence of acute bacterial or viral infection, malignancy, immunosuppressive drugs treatment within 28 days prior to transplantation (expect glucocorticoids) were excluded. Blood was drawn prior to transplantation of ESRD patients. The TCR Vβ repertoire was measured by a qualitative DNA-based multiplex TCR Vβ gene PCR. In addition, T cell ageing parameters like thymic output, evaluated by CD31-expressing naive T cells, differentiation status and relative telomere length (RTL) of T cells were assessed by flow cytometry. Results: A higher proportion of, in particular, elderly ESRD patients (87.5%) had a skewed TCR Vβ repertoire compared to age- and CMV serostatus-matched HI (32.0%, P<0.001). Age (odds ratio, OR, =2.3, P<0.05), CMV-serostatus (OR=6.7, P<0.05) and ESRD (OR=4.8, P<0.05) were independently associated with skewing of the TCR Vβrepertoire. Skewing of the TCR Vβ repertoire significantly occurred in CD8+, but not CD4+, memory T cells subsets in the elderly ESRD patients. More differentiated CD8+ T cells, i.e. highly differentiated effector memory T cells (EMRA) and CD28null T cells, were observed in young ESRD patients with a shifted TCR Vβ repertoire compared with those without a shifted TCR Vβ repertoire. Thymic output and relative telomere length of T cells were not significantly related to TCR Vβ skewing. Conclusions: ESRD significantly skewed the TCR Vβ repertoire, which may contribute to the uremia-associated defect in T-cell mediated immunity.

The impact of allograft rejection on DNA methylation after kidney transplantation

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Introduction DNA methylation is a well-known epigenetic mechanism which plays a critical role in cell function by regulating gene expression. Variations in DNA methylation profiles are increasingly associated with diseases, including immune-mediated diseases. However, the role of DNA methylation in organ transplantation is unknown. Here, we studied the methylation of regulatory cytosine phosphate guanine sites (CpGs) in genes involved in alloreactivity; the pro-inflammatory cytokine interferon γ (IFNγ) and the co-inhibitor molecule programmed death 1 (PD1) in kidney transplantation patients. Materials and methods The DNA methylation of regulatory CpGs (2 for IFNγ and 8 for PD1) was determined with pyrosequencing in FACS sorted naïve, central memory (CM), effector memory (EM) and EMRA CD8+ T cells of kidney transplantation patients before, 3 months and 12 months after transplantation. Both patients who developed a biopsy proven acute rejection within the first three months after transplantation (rejectors; n=5) and patients who remained free from rejection (non-rejectors; n=5) were included. As infection with cyto-megalovirus (CMV) may significantly alter the methylation of IFNγ, only CMV seronegative kidney transplantation patients and healthy donors (n=5) were studied. Results Both IFNγ and PD1 were significantly ($p<0.001$) higher methylated in the naïve CD8 T cells compared to the memory subsets (IFNγ: 55% in naïve versus 16% in CM, 12% in EM and 6% in EMRA; PD1: 43% versus 17%, 11% and 12%, respectively). Before transplantation the methylation status of both IFNγ and PD1 was comparable to healthy donors in the studied CD8+ T cell subsets. Remarkably, the methylation status of the different CpGs of both IFNγ and PD1 did not significantly change during the immunologically challenging first year after transplantation. Additionally, comparing rejectors with non-rejectors did not demonstrate significant differences for either the methylation of IFNγ or PD1. Conclusion Patients with chronic kidney disease with subsequent 1 year follow-up after kidney transplantation did not demon-strate significant alterations in DNA methylation of either IFNγ, or PD1 in CD8+ T cells compared to healthy individuals. Based on these findings we conclude that variations in DNA methylation of either IFNγ or PD1 is not associated with allograft rejection after kidney transplantation.

Immunosuppressive Medication and DNA Methylation of the Interferon-gamma Promoter in T cells

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Introduction DNA methylation is responsible for the control of cell function by regulation of gene expression, high methylation in the promoter region is associated with gene silencing. Methylation changes in immune-related genes can influence the immune response after transplantation. In this study, we first investigated the changes in DNA methylation of the pro-inflammatory cytokine interferon-gamma (IFN-γ) during immune activation and second analyzed the effect of the commonly used immunosuppressant tacrolimus. Patients, materials and methods Pure CD3+ T cells were isolated from total PBMCs by MACS negative selection. These T cells were stimulated for 7 days with anti-CD3/CD28, in combination with 10-6 M 5'-aza-2'-deoxycytidine, a demethylating agent, or with 10 ng/mL tacrolimus. Cells were harvested at day 0, 1, 3, 4, 7 and after bisulfite conversion and subsequent PCR, DNA methylation was quantified on two CpG sites (CpG-54 and CpG-186) in the IFN-γ promoter region using pyrosequencing analysis. Flow cytometry was used to analyze IFN-γ protein production. Results Stimulation significantly increased the percentage DNA methylation of the IFN-γ promoter from day 0 to day 4 (CpG-54; median: 52% range: (39%-66%) to 64% (54%-75%) with p=0.003, CpG-186: 42% (31%-52%) to 51% (35%-56%) with p=0.04). Addition of tacrolimus did not significantly change the DNA methylation. 5'-Aza-2'-deoxycytidine, which served as a positive control, lead to a significant decrease in DNA methylation from day 0 to day 4 (CpG-54: 52% (41%-66%) to 31% (23%-36%) with p=0.002, CpG-186: 46% (31%-52%) to 22% (18%-32%) with p=0.0006). As expected IFN-γ protein production was completely blocked in the presence of tacrolimus. Conclusions Based on these data we conclude that following immune activation the DNA methylation of IFN-γ significantly increased and that this change occurs within 4 days after stimulation. Suppression of IFN-γ protein production in the presence of tacrolimus is not due to a change in DNA methylation after immune activation. Therapeutic concentrations of the immunosuppressant tacrolimus do not alter the methylation status of IFN-γ during immune activation.

Is the Kidney Donor Risk Index a predictor of graft failure in the Dutch Kidney transplantation population?

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Assessment of the Kidney Donor Risk Index (KDRI) to predict graft failure in a Dutch deceased donor kidney transplant cohort. The Kidney Donor Risk Index (KDRI) was introduced in 2010 by the OPTN network in the United States to optimize the number of life years lived with a donor kidney. This index is calculated from a formula including 10 factors: donor age, height, weight, ethnicity, hypertension, diabetes, cause of death, serum creatinine, Hepatitis C status and type of donation (DBD or DCD). Since differences exist between the US and Europe regarding donor population and organ allocation protocols, we decided to evaluate the predictive value of the KDRI for graft failure in a recent European cohort of kidney transplant recipients. A retrospective analysis was performed on the association of KDRI donor risk factors with graft failure in 515 deceased donor kidney transplants, performed at our center between 2007 and 2015. Primary outcome measure was graft failure, defined as return to dialysis or death. All risk factors, except ethnicity and HCV status were available for analysis to compute the KDRI. The KDRI as a whole significantly predicted graft failure in our patient cohort (p=0,004). When analyzing the relative contribution of each KDRI parameter by multivariate analysis, only donor age proved to be a significant contributor to graft failure (p<0,001; HR=1,033; 95% CI 1,016-1,051) as well as patient survival (p<0,001; HR=1,042; 95% CI 1,022-1,062).A trend was observed towards poorer patient survival after DCD kidney donation (p=0.15). In this analysis ,donor age was the only significant KDRI factor contributing to graft loss in the investigated Leiden kidney transplant cohort. This may be related to the number of patients included. Larger study populations are now investigated to identify additional significant parameters. These studies may also aid in developing a risk index to predict outcome in a European kidney transplant recipient population that should include not just donor, but also recipient and transplant-related factors.

Mesenchymal stromal cells undergo major changes during therapeutic application

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Mesenchymal stromal cells (MSC) are increasingly used as an investigative therapeutic product for immune disorders and degenerative disease. Typically, MSC are isolated from human tissue, expanded in culture and cryopreserved until usage. The safety and efficacy of MSC therapy will depend on the phenotypical and functional characteristics of MSC. The freeze-thawing procedure may change these characteristics. Furthermore, the cells encounter a microenvironment after administration that may impact their properties. It has been demonstrated that the majority of MSC localize to the lungs after intravenous infusion, making this the site to study the effects of the in vivo milieu on administered MSC. In the present study we investigated the effect of freeze-thawing and the mouse lung microenvironment on human adipose tissue-derived MSC. There were effects of freeze-thawing on the whole genome expression profile of MSC, although the effects did not exceed inter-donor differences. There were no major changes in the expression of hemostatic regulators on transcriptional level, but significantly increased expression of procoagulant tissue factor on the surface of thawed adipose MSC, correlating with increased procoagulant activity of thawed cells. Exposure for 2h to the lung microenvironment had a major effect on MSC gene expression and affected several immunological pathways. This indicates that MSC undergo functional changes shortly after infusion and this may influence the efficacy of MSC to modulate inflammatory responses. The results of this study demonstrate that MSC rapidly alter in response to the local milieu and that disease specific conditions may shape MSC after administration.

Optimizing the immunogenicity and immunomodulatory properties of MSC

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Mesenchymal stromal cells (MSC) are attractive candidates for cellular immunotherapy after organ transplantation and for diseases characterized by immune system alteration. MSC have shown to be low immunogenic and contain promising immunomodulatory capacities. These properties are favorable for the applicability of MSC for cellular therapy, however there is evidence that MSC are more immunogenic than previously thought. Furthermore, improving their immunomodulation would be advantageous. This study aims to optimize MSC by making them better immunomodulators and less immunogenic. During in vitro experiments, umbilical cord-derived MSC were treated for 3 days under various conditions, i.e. in the presence of pro-/anti-inflammatory cytokines, vitamins and serum-deprivation. Their immunogenicity and immunosuppressive capacity were examined by gene expression analysis, surface marker expressions, IDO activity and inhibition of CD4 and CD8 T-cell proliferation. Subsequently, susceptibility to NK cell lysis was investigated via CD107a expression on NK cells. Furthermore, treatment of liver inflammation and MSC survival was examined in a CCL4-induced liver disease mouse model. In vitro results showed significantly increased expression by MSC of the immunomodulatory factor PD-L1 after treatment with IFNγ, IFNβ and TGFβ, while culture under serum-deprivation conditions (Starv) decreased PD-L1 expression. IFNγ treated MSC were the most potent inhibitors of CD4 and CD8 T-cell proliferation as well as their IFNγ production. In addition, stimulation with IFNγ increased IDO activity. Furthermore, increased HLA type-I and -II levels were observed in IFNγ, IFNβ, vitamin B6 (VitB6) and Starv+VitB6 treated MSC. These MSC were significantly protected against NK lysis, which may correlate to the increased HLA type-I levels. In addition, TGFβ-MSC were significantly protected against NK cell lysis, even though HLA levels remained unchanged. In vivo, TGFβ-MSC had improved persistence after infusion compared to the other MSC while clearance of Starv-, VitB6- and Starv+VitB6-MSC was accelerated compared to untreated MSC. Nonetheless, liver function showed a trend of improvement after administration of TGFβ and Starv treated MSC. These data show the versatility of MSC to culture conditions and the possibility of optimizing MSC into less immunogenic cells with improved immunomodulatory properties, which is important for further development of MSC for cellular immunotherapy.

The delicate balance between fraud and patient care

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Integer behavior is a general prerequisite for all persons involved in patient care and recent incidents in Germany have demonstrated the disastrous consequences for the complete transplantation society if these requirements are not met. Taking this into account it is hard to conceive that for the sake of the patient we deliberately manipulated laboratory results. A patient was listed for a second renal transplant and the result of the HLA antibody screening indicated the presence of multispecific HLA antibodies, including HLA antibodies specific for the HLA mismatches of the first transplant and antibodies specific for a self-HLA antigen of the patient (DR51). High resolution typing of the patient revealed that the patients DRB5 allele was a variant without protein expression (DRB5*01:08N; so-called null-allele) explaining the immunization against the non-expressed apparent self antigen DR51. Although this allele is listed as "common" (see cwd.immunogenomics.org), it is not encountered frequently and almost all DR15 matched kidney offers would result in a positive B cell cross match due to the DR15 linked expression of DR51. Therefore, the HLA matching phenotype of the patient was changed in ENIS by removing DR15 and DR51 and designating these antigens as unacceptable. The patient was listed for the Acceptable Mismatch Program and, within a few months, received a DR15-DR51 negative renal offer with only a single HLA-B locus mismatch and a split mismatch for HLA-DR, which tested negative in the prospective cross match. The transplantation was uneventful with stable excellent renal function 6 months after transplantation. Without this manipulation this patient would probably never have received an acceptable kidney offer. There was no personal gain for any of the professionals involved; the manipulation was not performed secretly and was communicated with the Eurotransplant Reference Laboratory. In our opinion this example and similar cases with allele specific HLA antibodies are exceptional examples of justified manipulation of laboratory results. For transparency reasons we suggest to include this option in the Eurotransplant manual.

A Novel, Rapid, Efficient, Automated, Pancreatic Islet Isolation Technique

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Currently, islet isolations are expensive, lengthy and require a high expertise level from its operators. Our aim is to increase the efficiency of islet isolation. We present a new, single pass, closed method of tissue collection, washing, buffer change and islet purification. Briefly, digested pancreatic tissue is mixed with human serum (1:22) and pumped (200 ml/min) through a Medtronic Biotherm II heat exchanger, cooling the tissue to 4°C. The tissue is then continuously concentrated and washed in a 225 ml Latham centrifugation bowl at 1400 RPM. After increasing centrifugation speed to 1500 RPM, tissue is retained in the bowl and UW solution is pumped in to change buffer. Next, the contents of the bowl are emptied into a bag. For density separation in the centrifuge bowl , two speed controlled Masterflex pumps are used to mix the digest in UW with an incremental amount of Iopromide (1.32 g/ml). For most of the process only one operator is required. Three research pancreata were used to optimize system parameters and settings (centrifuge speeds, solution amounts, density gradient profile). One human islet isolation was performed in which the digested tissue was equally split between the novel method and the current method. One complete isolation was performed using optimized parameters. Dynamic GSIS was performed one day after culture. During optimization IEQ were promising (104,674, 227,174 and 206,522) despite technical difficulties. Comparing the novel and current method by dividing the digest, only a 13% difference in IEQ was obtained in favour of the current method. Using the optimized parameters, 728,261 IEQ (6089 IEQ/g) was isolated in 1 full isolation according to the novel method. High islet purities and almost islet-free exocrine tissue was obtained. No difference in GSIS stimulation index was found between the two methods. Markedly, total isolation time (after set-up) was under 3 hours. This novel technique, while still being optimized, represents a significant improvement in islet isolation efficiency.

Preliminary results of isolated islets after hypothermic machine perfusion of human donor pancreata

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Background Islet transplantation is an effective treatment option for patients with type I diabetes mellitus. Due to the persistent shortage of good quality donor organs, pancreata from marginal donors are more frequently used for islet transplantation. The standard preservation method cold storage (CS) inadequately prevents ischemia prior to islet isolation. In kidneys and livers, hypothermic machine perfusion (HMP) is demonstrated to be superior to CS in experimental models and clinical settings. It is hypothesized that HMP improves the quality of pancreata for islet isolation. Methods Human donor pancreata unsuitable for clinical transplantation were connected to our modified dual arterial machine perfusion system, after an initial period of cold ischemia during transport. Islets were isolated after 6 hours of oxygenated HMP. The islet equivalent (IEQ) was analyzed at day 0 and day 3. In vitro islet function was analyzed by performing a dynamic glucose stimulated insulin secretion (GSIS) test. After 3 or 4 days of culture, islets were transplanted under the kidney capsule in STZ-induced diabetic mice (3000 IEQ/mouse). Blood glucose levels were monitored every other day for 28 days. The results were compared with a control group consisting of CS preserved pancreata which were initially accepted for clinical transplantation. Results So far, 6 pancreata have been included in this study: 3 pancreata from donation after circulatory death (DCD) donors have been subjected to HMP and 3 pancreata from donation after brain death (DBD) donors were included in the CS control group. In the HMP group, islet IEQ after isolation was 336.956 ± 91.019 and declined to 281.521 ± 116.745 after three days of culturing. In the CS group, IEQ declined from 381.340 ± 369.845 to 209.239 ± 154.580 at day 3. Dynamic GSIS showed no difference of in vitro islet function between the groups. After transplantation in mice, HMP preserved islets were able to achieve normoglycemia in more mice than the CS preserved islets. Because of high variability, no significant differences between groups were seen. Conclusion The preliminary data suggests that functional, viable islets can be readily isolated from pancreata after HMP. Inclusion of additional pancreata in both HMP group and the CS control group is ongoing.

Tacrolimus (Tac), rather than cyclosporine (CsA), interacts with insulin resistance (IR) to alter key transcription factors for β-cell identity & function without altering NFAT localization

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Inhibiting the calcineurin(CN)/NFAT-pathway in β-cells may contribute to posttransplant diabetes. The presumed higher diabetogenicity of Tac is thought to owe to an IC50 for CN that is 10-15x lower than CsA. However, CsA trough levels are 10-20x higher than Tac. Other pathways may explain the presumed diabetogenicity of Tac. Clinical observations and experimental studies suggest that the diabetogenicity of Tac, rather than CsA, depends on an IR milieu, similar to T2DM. Thus, we hypothesized that Tac more than CsA alters nuclear factors necessary for β-cell identity & function, like MafA, PDX-1, and FoxO1, that is dependent on IR but independent of NFAT. We cultured INS-1 cells with palmitate and glucose for 5 days to emulate IR, and Tac or CsA was added for last 48h. We also studied the effect of Tac vs CsA in obese (OZR) vs lean Zucker rats (LZR) for 12 days. Tac withdrawal and conversion to CsA were evaluated in both models. Nuclear presence of transcription factors for β-cell identity & function was determined by immunolocalization, and insulin was measured in medium or plasma after glucose challenge. Glucose and palmitate increased nuclear FoxO1 but decreased nuclear MafA and insulin secretion in INS-1 cells; all these changes were magnified by Tac but not CsA. The addition of Tac on top of palmitate/glucose was the only treatment that reduced nuclear PDX-1 compared to control. Importantly, FoxO1 and MafA localization, as well as glucose-stimulated insulin secretion, recovered after Tac withdrawal or conversion to CsA. In OZR, Tac induced diabetes in all animals compared to only 40% for CsA. Neither Tac nor CsA caused diabetes in LZR. The onset of diabetes in Tac-treated OZR was accompanied by an increase in nuclear FoxO1 and decrease in nuclear MafA in β-cells, as well as a lower insulinogenic index compared to CsA-treated OZR, non-treated OZR, and LZR. Tac withdrawal/conversion to CsA improved diabetes similarly. Notably, nuclear NFAT localization was similar between Tac and CsA in all experiments. We conclude that Tac, rather than CsA, interacts with an insulin resistant milieu to accelerate the change in nuclear localization of key transcription factors for β-cell identity & function that is reminiscent of T2DM, without altering NFAT localization.

Immunosuppressive drugs do not interfere with direct-acting antivirals for treatment of HCV recurrence

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Background. Liver disease caused by chronic hepatitis C (HCV) infection is currently the major indication for liver transplantation. Recently, new direct acting antivirals (DAAs) have been developed for the treatment of patients with chronic HCV, including patients who underwent liver transplantation. Although a few reports have investigated the efficacy of DAAs after liver transplantation, the exact effects of specific immunosuppressive medication on the antiviral efficacy is largely unknown. The aim of this study is to investigate the antiviral activity of the NS5A inhibitor daclatasvir (DAC) and the NS3 inhibitor asunaprevir (ASU) combined with immunosuppressants in a cell culture model for HCV. Method. As a model for HCV replication we used Huh7 cells, stably transfected with the non-structural coding sequence of HCV coupled to luciferase (Huh7-ET). Cells were treated with three different doses of DAAs, in combination with cyclosporin A (CSA), tacrolimus (TAC), mycophenolic acid (MPA) or rapamycin (RAPA). Huh7 cells stably transfected with a luciferase gene controlled by an Interferon-Stimulated Response Element (ISRE-luc cells) were used to investigate effects on interferon-stimulated gene expression. Results. TAC and RAPA had no effect on antiviral activity of DAC or ASU. Also CSA did not significantly inhibit the antiviral action of DAAs. MPA, a potent inhibitor of the nucleotide synthesizing enzyme IMPDH, has antiviral effect itself, but also further enhanced the antiviral action of both DAC and ASU. Previously we have shown that the antiviral action of MPA is related to the induction of antiviral effector genes, the so called interferon-stimulated genes. In Huh7-ISRE-luc cells, DAAs did not induce gene expression and no additional effect of DAAs on the MPA stimulated gene expression was found. This suggests that the combined antiviral effect of MPA and DAAs is mediated via independent mechanisms. Conclusion: The immune suppressants TAC, RAPA and CSA did not affect the antiviral activity of DAAs. MPA enhanced the antiviral activity of both DAC and ASU. This implies that there is no contra-indication to combine antiviral therapies with these immunosuppressants in the post-transplantation management of HCV recurrence.

Characterisation of peribiliary glands in a new model: precision-cut bile duct slices

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Non-anastomotic strictures (NAS) are a major cause of morbidity and graft failure after orthotopic liver transplantation. NAS is considered to be the most problematic biliary complication as it is the most frequent indication for retransplantation. Recent research suggests that the regenerative capacity of peribiliary glands (PBGs), which are niches of progenitor cells lining the bile ducts, plays a role in de development of NAS. Precision-cut tissue slices (PCTS) are a widely used *in vitro* technique, in which thin slices of fresh human tissue are cut, incubated and cultured and thereby kept viable for up to several days. In PCTS, all the cell types of the tissue remain in their natural environment, with intercellular and cell-matrix interactions remaining intact. Our aim was to establish Precision-cut Bile Duct Slices (PCBDS) as a model to study the regenerative capacity of PBGs in human extra–hepatic bile duct. Extra-hepatic bile ducts (EHBD) of livers declined for transplantation were used (n=5) and sliced using a Krumdieck tissue slicer. Thereafter, they were incubated in plates filled with Williams' medium E (supplemented with glutamax, glucose and antibiotics; incubator with 80%O_2/20%CO_2 shaking at 90 rpm at 37°C). Medium was refreshed and slices were harvested every 24 hours for up to 144 hours. HE, PDX1, and CK19- stainings were performed on paraffin-embedded samples for histomorphological assessment. Histomorphological assessment showed cell loss gradually over time, conversely, PBGs and neural tissue survived for up to 144 hours. In addition, preliminary data show that these PBGs express PDX1, a progenitor marker, and CK19, a cholangiocyte marker.

In conclusion, PCBDS allow for PBGs to remain viable up to 144 hours and express characteristic progenitor and cholangiocyte traits. These preliminary data suggest that PCBDS can be used to study PBGs and their regenerative capacity. Future research will focus on agents to stimulate regeneration of PBGs in this model, in the search of a potential intervention for NAS.

Quality of donor lung grafts: A comparative study between fast and slow brain death induction models in rats

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Despite the fact that brain death (BD) negatively affects graft quality and transplantation outcome, brain-dead donors remain the major source for transplantation. This study is designed to test if fast or gradual increase in intracranial pressure, ultimately leading to brain death, differentially affects quality of donor lungs. Fisher rats were randomly assigned into three donor groups: 1) ventilated animals, no other interventions and immediately sacrificed, 2) fast - and 3) gradual BD induction. For the latter two modalities animals were sacrificed at 30 minutes, 1 hour, 2 hrs. and 4 hrs. after BD induction. BD animals were hemodynamically stabilized (MAP > 80 mmHg) by HAES/noradrenaline and ventilated with a VT = 6.5 ml/kg of body weight and a PEEP of 3 cmH2O. Hemodynamics and pulmonary inspiratory pressure were monitored. Lungs (n = 8/ group; excluding lost animals n = 6) were analyzed with a histological scoring system and for pro-inflammatory changes in gene expression with RTD-PCR. During slow induction severe hypotension occurred in contrast to severe hypertension during fast BD induction. After BD induction MAP was maintained above the target value however in the fast model higher inotropic support was required. In both groups patho-histological changes were found, albeit that parenchyma injury was more pronounced in the fast model. No difference in the expression of proinflammatory genes was observed between both models. The results of this study suggest that the time course of intracranial pressure increase leading to BD is critical for the quality of the potential donor lungs.

Association between a donor TARC/CCL17 promotor polymorphism and impaired clinical outcome after lung transplantation

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Lung transplantation (LTx) outcome is hampered by development of chronic rejection, presented as the bronchiolitis obliterans syndrome (BOS). TARC/CCL17 is a chemo-attractant of which serum levels measured during the first month post-LTx are predictive for BOS development. Since *TARC/CCL17* promotor polymorphisms correlate with serum TARC/CCL17 levels, we investigated seven selected single nucleotide polymorphisms (SNPs) present in this region and their potential association with LTx outcome. We analyzed donor and patient SNP configurations and haplotypes and identified a single SNP (rs223899) in the donor correlating with patient TARC/CCL17 serum levels (p=0.066) post-transplantation. Interestingly, this SNP configuration in patients did not show any correlation with pre-LTx TARC/CCL17 serum levels (p=0.776). Survival analysis showed that receiving a graft from a donor heterozygous for rs223899 has a disadvantageous impact on transplantation outcome. When stratified per donor SNP genotype, patients receiving a transplant from a heterozygous donor showed a significant lower BOS-free survival (50% vs. 75%, p=0.023) and lower survival rate (50% vs 80%, p=0.0079). Since rs223899 is located within a NFκB binding site, heterozygosity at this position could result in a reduced expression of TARC/CCL17. Our data indicate that a single SNP in the promotor region of *TARC/CCL17* correlates with lower serum TARC/CCL17 levels and affects clinical outcome after LTx.

Inadequate upregulation of anti-oxidative mechanisms in brain-dead rat kidneys

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Introduction: Delayed graft function (DGF) remains a complication in renal transplant recipients. Brain death-related lipid peroxidation, an oxidative stress marker, is correlated with DGF. BD pathophysiology comprises ischemic, inflammatory, and metabolic changes which can all lead to oxidative stress. Furthermore, BD pathophysiology is influenced by the speed at which intracranial pressure (ICP) increases and therefore, oxidative and anti-oxidative processes could be influenced as well. Clinically, the speed at which ICP increases varies greatly among donors. To determine underlying causes of lipid peroxidation, we investigated oxidative and anti-oxidative processes in brain-dead rat kidneys after fast and slow BD induction. Methods: BD was induced in male Fisher rats by inflating a 4.0F Fogarty catheter in the epidural space. Slow induction was achieved by inflating the catheter at a rate of 0.015ml/min and fast induction at a rate of 0.45ml/min. Rats were observed for 0.5h, 1h, 2h, or 4h. Kidneys were collected for analysis. Results: Both fast and slow induction led to increased superoxide levels, decreased glutathione peroxidase (GPx) activity, decreased GSH levels and increased iNOS, piGST, and HO-1 mRNA expression. These effects were more pronounced and persistent after slow induction. Additionally, the GSSG:GSH ratio was significantly increased after slow induction. After fast induction, GPx activity decreased but returned to baseline values. Conclusion: BD leads to increased oxidant production and decreased anti-oxidative defenses which was more pronounced after slow induction. Modulation of superoxide, GPx activity, and GSH levels could decrease lipid peroxidation and lead to improved transplantation outcomes.

Systematic review of current clinical DCD heart transplantation practice and its implications for the Dutch DCD protocol

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In diverse centra in de wereld worden DCD harten succesvol gebruikt voor transplantatie. Bij het schrijven van dit abstract staat de teller op ongeveer 18 DCD harttransplantaties. Absolute voorwaarde voor het succes is een korte eerste warme ischemietijd die ingaat nadat de circulatie is gestopt. Gestreefd wordt naar 10 minuten met als maximum 20 minuten warme ischemie. Een andere voorwaarde is enige vorm van machine perfusie om het hart te kunnen resusciteren. Aan de hand van een sytematische review van de methoden en resultaten van de reeds lopende DCD harttransplantatie programma's in de wereld wil ik met het publiek bespreken en bediscussiëren hoe we DCD hartdonatie in het Nederlandse systeem zouden kunnen in passen.

Unexpected donation after circulatory death (uDCD) – A great potential for new organs?

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The number of patients waiting for a transplant exceeds the number of donor organs suitable for transplantation. Therefore, the search for new organ sources continues. uDCD donors are patients that died as result of an out of hospital cardiac arrest (OHCA). They are scarcely used in the Netherlands as a source of organ grafts. A possible reason for the minimal use of this donor type is the complexity of the protocol in terms of logistics. Three transplant centres in the Netherlands started a pilot with the aim to assess the uDCD donor potential. The innovative part of the pilot was the use of normothermic regional perfusion for resuscitation of the kidneys before procurement and ex vivo lung perfusion after retrieval to assess lung functioning. All patients deceased on the emergency department (ED) between October 2014 and October 2015 within the age range of 18 – 50 were potential donors for kidneys and lungs, and in the age range of 51 – 65 potential lung donors. Donors could only be included when fulfilling all of the following inclusion criteria: a witnessed arrest, basic life support which started within 10 minutes, advanced life support within 20 minutes and resuscitation time within an organ-specific time span. Furthermore, the donors were excluded if there were any medical contraindications and permission for donation was not given. In total, 208 OHCA patients died on the ER from whom 32 were potential kidney donor and 68 lung donor. From the 32 potential kidney donors, 15 did not meet the inclusion criteria (47%), in 7 cases, there was no consent (22%), 9 showed medical contra-indications (28%), and once logistical problems occurred (3%). From the 68 potential lung donors, 22 did not meet the inclusion criteria (33%).18 did not consent (27%), 24 had medical contra-indications (35%) and 3 were cancelled due to logistical problems (5%). One donor satisfied all the criteria and was taken to the operating theatre for lung retrieval. However, during procurement the lungs were not suitable for transplantation.

This pilot shows there is definitely a group of potential uDCD donors in the Netherlands. Nevertheless, due to a wide variety of reasons, up till now no uDCD donor resulted in organ retrieval. Although there were a wide variety of reasons why donation in this pilot was not successful, combining new techniques with new organ sources remains at least part of the solution for the organ shortage. We are obliged to explore these organ sources furthermore.

Afname van weefseldonoren door daling aantal overledenen in ziekenhuizen?

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Introductie De landelijke ziekenhuissterfte is met 15% gedaald in 2010 t.o.v. 2008. Daarnaast is bekend dat deze ziekenhuissterfte onderhevig is aan verschillende invloeden. Door de daling van de ziekenhuissterfte is het mogelijk dat er een tekort aan weefseldonoren zal ontstaan. In 2011 is de leeftijd voor weefseldonatie opgehoogd van 80 naar 85 jaar om aan de toenemende vraag naar cornea 's te voorzien. Niettemin werd in 2012 landelijk een afname geconstateerd van 6% aan weefseldonoren. Gezien deze landelijke daling van het aantal weefseldonoren en de daling van het aantal overledenen is onduidelijk of dit ook geldt voor de regio Leiden. Wij hebben onderzocht of de daling van het aantal overleden patiënten de reden is voor de afname van het aantal weefseldonaties in de ziekenhuizen binnen de regio Leiden. Methode Van 2006 t/m 2014 is in de ziekenhuizen van de regio Leiden gekeken hoeveel patiënten zijn geregistreerd in de Nederlandse Overledenen Registratie Donoren van de Nederlandse Transplantatie Stichting. Een onderverdeling is gemaakt in periode I - 2006 t/m 2010 en periode II -2011 t/m 2014. Het donorwervingsproces van weefseldonatie is in kaart gebracht; vanaf het herkennen van de potentiele weefseldonor tot het effectueren van de donor. Resultaten Het totaal aantal overledenen is met 21% gedaald in 2014 (n=4415) t.o.v. 2006 (n=5588). Door de leeftijdsverhoging in 2011 naar 85 jaar is het aantal overledenen geschikt voor weefseldonatie 76% in periode II t.o.v. 58% in periode I. Het aantal door de behandeld arts als medisch geschikt geachte weefseldonoren is echter gelijk gebleven (34%). Het raadplegen van het donorregister is 78% in periode II t.o.v. 79% in periode I. Het benaderen van de nabestaanden is gestegen in periode II naar 93% t.o.v. 84% in periode I. Het weigeringspercentage nabestaanden is nagenoeg gelijk gebleven (65%). Het aantal aangemelde weefseldonoren is gedaald naar 24% in periode II t.o.v. 27% in periode I. Het aantal geëffectueerde weefseldonoren t.o.v. het potentieel (conversion rate) is 19% in periode II t.o.v. 20% in periode I. Conclusie Door de daling van het aantal overledenen in de regio Leiden is er een lichte afname te zien in het aantal weefseldonoren. De ophoging van de leeftijd t.b.v. corneadonatie heeft niet geleidt tot een verhoging van de door de arts geschikte donoren. Winst kan nog behaald worden in het raadplegen van het donorregister, het benaderen van de nabestaanden en in het voeren van het donatiegesprek met hen.

Significant more consent for organ donation for doctors trained in 'Communication about Donation'

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The training 'Communication about Donation' (CaD), developed by the Dutch Transplant Foundation in 2007, facilitates medical professionals in approaching families of potential organ and tissue donors. According to the Masterplan Organ Donation the CaD training is mandatory for intensivists since 2012, therefore many CaD trainings were organized in the Dutch hospitals. The main part in the practical training includes role-playing with actors. In the period November 2012 - October 2015 family approaches, for only organ donation, are evaluated by a questionnaire. Evaluations took place by 'donation intensivists' in a face to face setting, by telephone or by email. Items about the consent process were evaluated for example; if the doctor was trained in CaD, what was the outcome of consulting the Donor Registry, if donation was requested decoupled from breaking the bad news and, how many family members were present during the request. In total 1723 questionnaires were retrieved. The number of doctors trained in CaD was 1094, 531 are not (yet) trained and in 98 cases this information is missing. In 1533 cases the family reached a decision about donation. The consent rate for organ donation in the CaD trained group was significant higher ($p<0.029$); 56.3% (579/1028) compared to the non-CaD trained group 50.9% (257/505). After excluding potential donors with 'consent' in the Donor Registry, the family consent rate was 42% for CaD trained doctors and 36.2% for the group not trained in CaD ($p=0.069$).

Conclusion. These figures show that it is important that family of a potential organ donor is approached by a doctor trained in CaD. Although the results are promising the consent rate is still low and we expect there is room for improvement, compared to other countries. A complete analysis will be shown at the congress.

Towards a Standardized Informed Consent Procedure for Live Donor Nephrectomy: the PRINCE (Process of Informed Consent Evaluation) Project: Study Protocol for a Nationwide Prospective Cohort Study

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Background Informed consent is mandatory for every (surgical) procedure, but is even more important in living kidney donors, undergoing surgery for the benefit of others. Informed consent procedures for live donor nephrectomy vary per center and even per individual healthcare professional. By assessing what information donors need to prepare them for the operation and convalescence, the basis for a standardized, uniform surgical informed consent procedure for live donor nephrectomy can be created to ensure full informed consent. Aim To assess: -donor comprehension of all aspects of the donation procedure at different stages of information provision; -whether the information provided in the Dutch kidney transplant centers is sufficient; -which elements have to be included in the donor education program, and finally to create a uniform, standardized informed consent procedure for live donor nephrectomy. Methods The PRINCE project is a prospective, multicenter cohort study, carried out in all eight Dutch kidney transplant centers. Donors' understanding of the live donor nephrectomy procedure and postoperative course will be evaluated using pop quizzes (i=5). A baseline cohort (prior to receiving any information from a member of the transplant team in one of the transplant centers ("cohort 1"; n=400)) will be compared to a control group ("cohort 3"; n=200), who receive the pop quiz on the day of admission for donor nephrectomy. Donor satisfaction will be evaluated for the last group. A third group of donors ("cohort 2"; n=80) will be selected from cohort 1, and followed more closely throughout their whole screening- and donation process. The primary endpoint is donors' understanding of the given information. In addition, those elements that have to be included in the standardized format informed consent procedure will be identified. Secondary endpoints are donor satisfaction, current informed consent practices, and correlation of donor understanding with surgeons' estimation thereof. Results The study has been approved by the local ethics committees in seven centers. Inclusion is ongoing in these centers. Inclusion has reached 50% in both cohorts 1 and 3. For cohort 2, inclusion rate (currently 15%) is expected to increase later on in the study. Conclusion This national collaboration will provide us with answers regarding live kidney donation informed consent procedures in the Netherlands.

Raising awareness of unspecified live kidney donation: an ELPAT view

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Living donor kidney transplantation (LDKT) is the preferred treatment for patients with end-stage renal disease (ESRD), and unspecified live kidney donation (UKD) is morally justified. However, despite the excellent results of LDKT, UKD is limited to a minority of countries in Europe due to both legal and moral reasons. Consequently, there are significant variations in practice and approach between countries and the potential contribution of UKD is under-valued. Where UKD is accepted as a routine part of living organ donation (LOD), an increasing number of patients in the domino paired exchange programme are successfully transplanted when a 'chain' of transplants is triggered by a single UKD. Our Working Group has examined the limitations on UKD in Europe and recommend strategies to increase transplant opportunities by raising awareness and engaging with key audiences across nations, recognising that the maturity and characteristics of individual (LDKT) programmes will impact on levels of engagement. Key audiences include the public, healthcare professionals, policy makers and society or religious leaders. Their roles and responsibilities are defined and discussed in the context of the following recommendations: 1. Countries wishing to undertake UKD must have a legal framework to support LOD and be committed to LDKT and UKD. 2. UKD offers the best opportunity to maximise transplant opportunities for patients with end stage kidney disease through the domino paired exchange (donor chains) programme. 3. Raising awareness by providing stratified information that is country specific, culturally sensitive and relevant across all sectors of society offers a sustainable option for increasing UKD activity. 4. The content and context of raising awareness initiatives must be appropriate for both mature and emerging programmes and relevant to all target audiences. 5. Collaboration between dedicated groups: previous UKDs, healthcare professionals, and procurement organisations, is the most effective model for engaging with target audiences. 6. Competent authorities with support of dedicated groups are best placed to achieve legislative change in individual countries. Increasing UKD by raising awareness contributes more kidneys to the shared living donor pool, extending the benefit of LDKT to more patients, even if they do not have a suitable living donor of their own.

Inclusion of compatible donor-recipient pairs in the Dutch kidney exchange programme: a new challenge

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Background: Since 2004 incompatible donor-recipients pairs have participated in the Dutch kidney exchange program. However, also compatible couples could be enrolled in this programme. One kidney donation can then result in multiple transplant procedures. However, such a programme is not widely implemented and the willingness to participate is unknown. Initial results from our own center showed that five compatible couples participated successfully in the Dutch kidney exchange programme, which resulted in fourteen transplant procedures. Further development of such a programme necessitates a structured process and identification of possible barriers, including an understanding of the motivation and willingness of both recipients and donors. Methods: A literature search was performed for relevant data regarding logistical issues and ethical concerns. Discussion meetings with our transplant team were held and the commission of medical ethical issues of our hospital was consulted for their opinion on the protocol of this programme. Results: The most important topics mentioned within the literature are: 1.undue influence, 2.organisational issues as wait time, who should travel and the item on anonymity, 3.equivalence of organs, 4.empathy or altruism and 5.financial compensation. These issues were discussed and the importance of avoiding undue influence and maintaining anonymity were recognized. In addition, no financial compensation should be offered. The organisational issues will always be discussed with the compatible pairs and their wishes should be facilitated as much as possible. The possibility of equivalence of the quality of the kidneys will be discussed within the committee of the Dutch kidney exchange programme. These conclusions formed the basis of the development of a structured enrolment procedure and a neutral information leaflet for compatible donor-recipient pairs. This protocol was discussed and approved by the commission of medical ethical issues of our hospital. In addition, different research instruments are under development to gain more insight in motivation and possible barriers, covering important subjects such as emotional and rational considerations and moral obligations. In conclusion, a protocol has been developed at the Erasmus MC to include compatible pairs in the Dutch kidney exchange programme. The motivations and possible barriers for the pairs that were important for their decision to participate or not will be studied.

Transplantatieverpleegkundigen in een perifeer dialysecentrum geven een aantoonbare kwaliteitsverbetering van de transplantatievoorbereiding

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Achtergrond: In 2013 werd in het kader van de opleiding tot transplantatieverpleegkundige een kwaliteitsonderzoek gedaan naar de transplantatievoorbereiding in een perifeer dialysecentrum. Op basis van de conclusies en aanbevelingen werd een transplantatiepoli opgezet met een centrale rol voor geschoolde transplantatieverpleegkundigen. Belangrijke doelstellingen waren het verbeteren van de voorlichting en het bewaken en het in duur verkorten van het voorbereidingstraject op niertransplantatie.
Resultaten: Er is een gestage groei van het aantal voorlichtingsgesprekken in de afgelopen jaren. De duur van het voorbereidingstraject is duidelijk verkort (van gemiddeld langer dan 1 jaar naar ruim 4 maanden). Er zijn diverse bijkomende voordelen. Zo zijn er ruimere gesprekstijden voor voorlichting en is er een vast aanspreekpunt voor alle betrokkenen (patiënten, zorgverleners, transplantatiecentrum) wat de communicatie bevordert. De transplantatieverpleegkundige documenteert en bewaakt het proces zorgvuldig en ontlast hiermee de betrokken nefrologen.
Conclusies: Een transplantatiepoli, met geschoolde transplantatieverpleegkundige, biedt in een perifeer dialysecentrum een duidelijke kwaliteitsverbetering van de transplantatievoorbereiding.

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