NEDERLANDSE **TRANSPLANTATIE** VERENIGING

Bootcongres 2017

Wetenschappelijke voorjaarsvergadering

Nederlandse Transplantatie Vereniging

8 en 9 maart 2017

Theaterhotel Figi te Zeist

georganiseerd in samenwerking met

UMC Utrecht

UMC Utrecht

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Welkom op het Bootcongres in Zeist!

Namens de organisatiecommissie van het UMC Utrecht nodig ik u van harte uit om deel te nemen aan het 29ste Bootcongres van de Nederlandse Transplantatie Vereniging in Zeist.

Dit jaar hebben wij in het programma aandacht voor een aantal thema's:
Wij willen stil staan bij de nieuwe technieken die (re-)generatie van organen dichterbij brengen. Ook is er gekozen om stil te staan bij betekenis van een orgaantransplantatie voor de psyche en voortplanting. Als derde thema willen wij stil staan bij de kracht van de aantallen en de rol van big data in orgaantransplantatie. 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. Het geeft een goed overzicht van het hoge niveau van de Nederlandse transplantatie geneeskunde. Naast de orale presentaties zullen er wederom gemodereerde postersessies zijn waarin professionals hun expertise kunnen delen.

Vanzelfsprekend is er dit jaar weer een aparte onderwijssessie. Ook is er na het grote succes van het afgelopen jaar een sessie voor de 'Young Investigators' waarbij het programma geheel door een aantal jonge onderzoekers zelf is ingevuld.

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

Arjan D. van Zuilen
Voorzitter organisatiecommissie UMC Utrecht

Organisatiecommissie Bootcongres 2017

Vanuit het UMC Utrecht
Ed A. van de Graaf, mede namens bestuur NTV
Henny G. Otten
Nicolaas de Jonge
Maaike J.J. Sperber
Judith M. Wierdsma
Arjan D. van Zuilen
en vele anderen

Bestuursleden Nederlandse Transplantatie Vereniging
Marlies E.J. Reinders
Martin Hoogduijn
Jeroen de Jonge
Henri G.D. Leuvenink
Dave L. Roelen
Marion J.C. Wessels

Vanuit het secretariaat NTV te Haarlem
Tineke L. Flietstra
Jeanine G. Gies
Marie José van Gijtenbeek
Melanie IJzelenberg

Participerende patiëntenverenigingen
Harten Twee
Nederlandse Leverpatiënten Vereniging
Nierpatiënten Vereniging Nederland
Nederlandse Cystic Fibrosis Stichting

Accreditatie is verleend door de volgende verenigingen:

Nederlandse Vereniging voor Heelkunde	14
Nederlandse Vereniging voor Immunologie	12
Nederlandse Internisten Vereniging	10
Nederlandse Vereniging voor Kindergeneeskunde	12
Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose	12
Nederlandse Vereniging van Maag-Darm-Leverartsen	10
Nederlandse vereniging voor Thoraxchirurgie	10

V&VN, kwaliteitsregister algemeen	12
V&VN, kwaliteitsregister, deskundigheidsgebied Dialyse	12
V&VN, verpleegkundig specialisten register	12

Hotel Theater Figi Zeist

Het Rond 2
3701 HS Zeist
Telefoon: 030 692 74 00
Website: http://figi.nl/hotel/

Bereikbaarheid met openbaar vervoer

Hotel Theater Figi is per openbaar vervoer uitstekend bereikbaar.
Bij het NS-station 'Driebergen-Zeist' (op ca. 3 kilometer van Figi) staan zowel taxi's, als bussen die vlak voor Hotel Theater Figi stoppen (lijn 50 richting Utrecht, halte 'Het Rond'). www.9292.nl / www.ns.nl. De Utrechtse Taxi Centrale (UTC) biedt een speciaal taxi tarief vanaf het station van € 11,00 p.p.
Zie verder ook http://figi.nl/contact/routebeschrijving/

Bereikbaarheid met de auto

Zie voor informatie: http://figi.nl/contact/routebeschrijving/

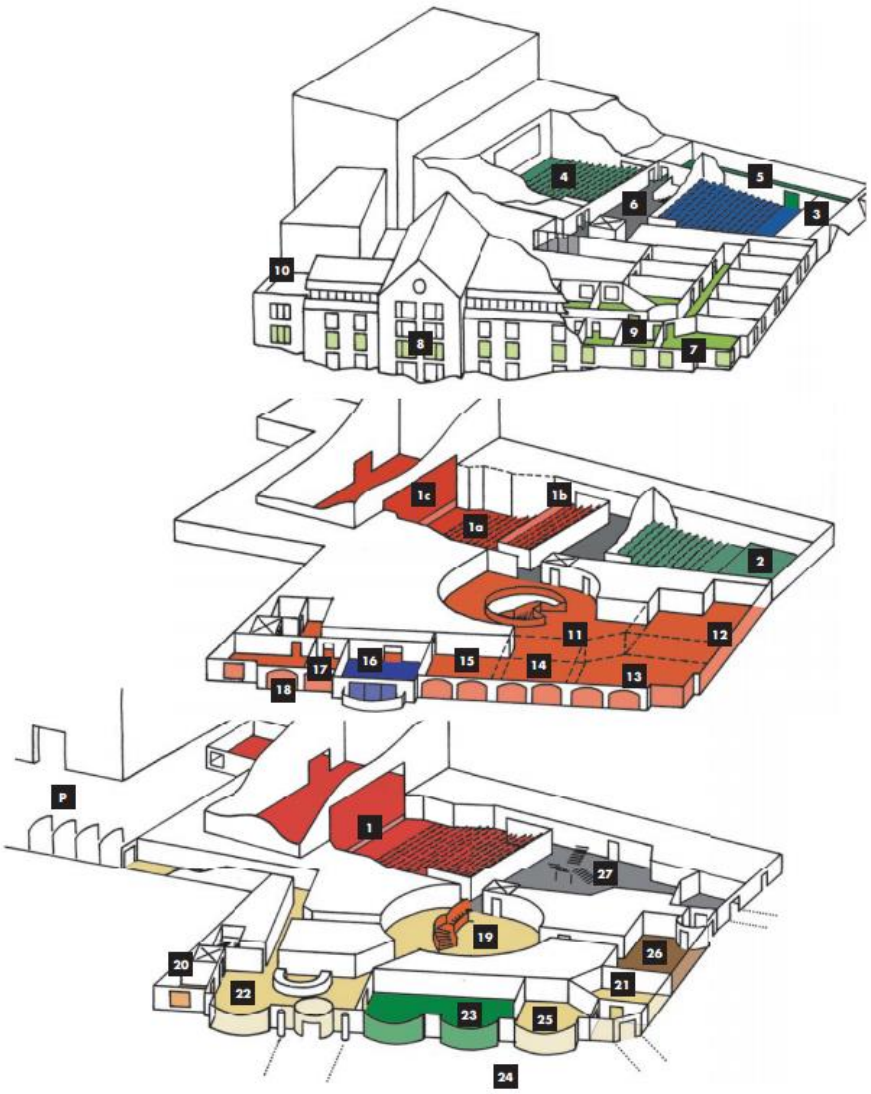
Parkeermogelijkheden

De parkeergarage is direct naast Hotel Theater Figi gelegen en is kosteloos voor hotelgasten. Uitrijkaarten kunt u verkrijgen bij de receptie van Figi.
Voor de uitrijkaarten gelden de volgende tarieven: 1 dagdeel € 4,00 -
2 dagdelen € 8,00 en 3 dagdelen €12,00.

Wifi

In Hotel Theater Figi is een openbaar Wifi-netwerk beschikbaar waarop u kunt inloggen, een gebruikersnaam/wachtwoord heeft u niet nodig.

Plattegrond zalen



THEATER- EN CONGRESZALEN

1 Hendrik Marsmanzaal
1a Zaal
1b Balkon
1c Podium
2 Willem Pijperzaal
3 Johan de Meesterzaal
4 Anne de Vrieszaal
5 Lumière Foyer
6 Theaterfoyer 3e verdieping

BANQUET- EN VERGADERZALEN

7 Suites
8 Boardrooms
9 Hotelkamers
10 Dakterras
11 Atrium 1e verdieping
12 Copijnzaal
13 Springerzaal
14 Zocherzaal
15 Tersteegzaal
Tersteeg-/Zocherzaal
Atrium 1 met omliggende banquetzaler

16 Daniël Marotzaal
17 De Boschzaal
18 Stoopendaalzaal
De Bosch-/Stoopendaalzaal

19 Atrium begane grond
20 George Figi Salon
21 Stuivinga Salon

P PARKEERGARAGE

ALGEMEEN

22 Hotellobby
23 Restaurant
24 Terras
25 Espressobar
26 Theatercafé
27 Theaterfoyer begane grond

Voor het Bootcongres zijn de volgende congreszalen in gebruik:

1: Hendrik Marsmanzaal, begane grond (het balkon op de 1e etage is *niet* in gebruik)
2: Willem de Pijperzaal 1e etage
3: Johan de Meesterzaal 2e etage

Inleveren presentaties

Wij verzoeken sprekers zo spoedig mogelijk na aankomst de presentatie in te leveren in de Bosch en Stoopendaalzaal op de eerste etage (bereikbaar met de lift vanuit de hotellobby).

Ophangen posters

De posters graag direct na aankomst ophangen op de gereed staande (en genummerde) posterborden. Deelnemers worden verzocht de posters pas te verwijderen na de laatste pauze op donderdag 9 maart.

Tijdstip en locatie van de maaltijden

Woensdag
Lunch: 13.00 – 14.00 uur Atrium begane grond
(deelnemers aan de onderwijssessie ontvangen bij de zaal een lunchpakket)
Diner: 19.00 – 21.30 uur Copijn-Zocher-Springerzaal

Donderdag
Lunch en moderated postersessies: 12.15 – 13.30 uur
Atrium begane grond en Theaterfoyer

Bijeenkomsten voorafgaand en tijdens Bootcongres

Dinsdag 7 maart 2017

Landelijk Overleg Nier Transplantatie *Locatie: Springerzaal - Figi*	16.00 – 19.00
Landelijk Overleg Regionale Uitname Teams *Locatie: Copijnzaal - Figi*	15.30 – 17.30
Landelijk Overleg Transplantatie Thoracale Organen *Locatie: Zocherzaal - Figi*	17.00 – 19.30
Landelijke Werkgroep Transplantatie Verpleegkunde *Locatie: Copijnzaal - Figi*	18.00 – 19.00

Donderdag 9 maart 2017

Ledenvergadering Nederlandse Transplantatie Vereniging *Locatie: Hendrik Marsmanzaal*	17.00 – 18.00

Schematisch overzicht programma
Woensdagochtend 8 maart 2017

Woensdag		**Hendrik Marsmanzaal**
10.00 –10.30 10.30 –10.40 10.40 –11.45		Ontvangst en registratie Theaterfoyer begane grond - koffie Atrium en Theaterfoyer Opening congres door voorzitter NTV Marlies E.J. Reinders en voorzitter LOC Arjan D. van Zuilen *Plenaire sessie I:* Thema: Innovation in Organ replacement - Marianne C. Verhaar (Utrecht): Organ (Re-)generation, the next step - Jos Malda (Utrecht): Ctrl-P Organ
11.45 – 12.45		*Plenaire sessie II:* - Sessie verzorgd door Eurotransplant, i.v.m. 50-jarig bestaan
12.50 – 13.50	Lunch/onderwijssessie	

Schematisch overzicht programma
Woensdagmiddag 8 maart 2017

Woensdag		**Hendrik Marsmanzaal**	**Willem Pijperzaal**	**Johan de Meesterzaal**
12.50 – 13.50	Lunch Theaterfoyer		*Onderwijssessie + lunchpakket* - Ed A. van de Graaf (UMCU) Schimmelinfectie in transplantatie - Rutger J. Ploeg Welke mechanismes liggen ten grondslag aan machine preservatie?	
14.00 – 15.30		*Plenaire sessie III* Thema: Non immunological issues after transplantation - Heike Spaderna (Trier, Germany): Psychosocial issues before and after solid organ transplantation - Robin Vos (Leuven, België): Fertiliteit en zwangerschap - Maaike A. Sikma (UMC Utrecht) Inzichten in tacrolimus kinetiek		
15.30 – 16.00	Thee Theaterfoyer			
		Hendrik Marsmanzaal	**Willem Pijperzaal**	**Johan de Meesterzaal**
16.00 – 17.15		*Plenaire sessie IV* 20-jarig bestaan van Nederlandse Transplantatie Stichting, gevolgd door feestelijke toast op NTS		

17.30 – 19.00		*Parallelsessie V* – basaal 1	*Parallelsessie VI* – klinisch 1	*Parallelsessie VII* – klinisch 2
19.00		Diner		

Schematisch overzicht programma
Donderdagochtend 9 maart 2017

Donderdag		**Hendrik Marsmanzaal**	**Willem Pijperzaal**	**Johan de Meesterzaal**
08.00 – 09.00		*Early Bird Sessie* *Parallelsessie VIII – Early Bird sessie* Richtlijnen in niertransplantatie georganiseerd door LONT		*Early Bird Sessie* *Parallelsessie XI* – klinisch 3
09.00 – 10.30		*Parallelsessie IX* - basaal	*Parallelsessie X* - verpleegkunde	*Parallelsessie XII* - klinisch 4
10.30 – 11.00	Koffie Theaterfoyer	**Na koffiepauze vervolg plenaire sessie in de Hendrik Marsmanzaal**		
11.00 – 12.15		*Plenaire sessie XIII* Thema: Patiëntenparticipatie - Keuzes in de orgaantransplantaties: kwantiteit of Kwaliteit - Kwaliteit Hanneke M. Kwakkel-van Erp - Kwantiteit Herold J. Metselaar - Harten spreker voorgedragen door HartenTwee - Nieren spreker voorgedragen door Nierpatiënten Vereniging Nederland - Lever spreker voorgedragen door Nederlandse Leverpatiëntenvereniging - Longen spreker voorgedragen door Nederlandse Cystic Fibrosis Stichting - Wrap-up Bernadette J.J.M. Haase-Kromwijk		
12.15 – 13.30	Lunch Theaterfoyer	*Moderated Postersessie (*Klinisch, Basaal, Donatie/Verpleegkundig/paramedisch)		
13.30 – 14.30		*Plenaire sessie XIV* *Thema: Big Data* - Henny G. Otten (Utrecht): PROCARE - Folkert W. Asselbergs (Utrecht): iGene TRAiN		

Schematisch overzicht programma
Donderdagmiddag 9 maart 2017

Donderdag		**Willem Marsmanzaal**	**Willem Pijperzaal**	**Copijnzaal**
14.30 – 16.00		*Parallelsessie XV* - Basaal	*Parallelsessie XVI* Young investigators sessie Aan deze sessie zullen diverse sprekers een bijdrage leveren	*Parallelsessie XVII* Bijeenkomst Transplantatie coördinatoren
16.00 – 16.15	Thee Theaterfoyer			
		Theaterzaal		
16.15 – 16.55		*Plenaire sessie XVIII* Thema: Prijsuitreikingen - Uitreiking van de ATRP prijs 2017 - Lezing winnaar van de Astellas Trans(p)la(n)t(at)ionele Research Prijs 2016 - Uitreiking Novartis Transplantation Awards 2017 - Uitreiking LWTV Innovatie-kwaliteitsprijs 2017 - Lezing LWTV Innovatie-kwaliteitsprijs 2015 - Uitreiking Distinguished Research Award 2017 - Uitreiking Gauke Kootstraprijs 2017, gevolgd door lezing van de prijswinnaar		
16.55 – 17.00	Sluiting congres door Arjan D. van Zuilen, voorzitter lokaal organisatiecomité			
17.00 – 18.00	Algemene ledenvergadering Nederlandse Transplantatie Vereniging			

Woensdag 8 maart 2017

Sessie I – Plenair — Hendrik Marsmanzaal

10.00 Ontvangst en registratie

10.30 Opening

Voorzitters: *Dr. Marlies E.J. Reinders, voorzitter NTV, internist-nefroloog LUMC*
Dr. Arjan D. van Zuilen, voorzitter LOC, internist-nefroloog UMCU

Thema: **Innovation in Organ replacement**

10.40 **Organ (Re-)generation, the next step**
Prof. dr. Marianne C. Verhaar, hoogleraar experimentele nefrologie
Afdeling nefrologie, UMC Utrecht

11.15 **Ctrl-P Organ?**
Dr. ir. Jos Malda,
Afdeling orthopaedie UMC Utrecht
Gezondheidszorg Paard Universiteit Utrecht

11.45 Einde Sessie I

Sessie II – Plenair — Hendrik Marsmanzaal

Voorzitters:

Thema: **50 jaar Eurotransplant**

11.50 In het kader van het 50-jarig bestaan zal stil gestaan worden bij de ontstaansgeschiedenis van Eurotransplant en de ontwikkelingen in de diensten die Eurotransplant leverde en levert.

12.50 Lunchpauze
Deelnemers aan de onderwijssessie kunnen zich begeven naar de Willem Pijperzaal op de eerste etage. Bij de ingang van de zaal wordt een lunchpakket uitgereikt.

Woensdag 8 maart 2017

Onderwijssessie **Willem Pijperzaal**

Voorzitters: *Dr. Martin J. Hoogduijn, wetenschappelijk medewerker, Erasmus MC*
Prof. dr. Henri G.D. Leuvenink, onderzoeker UMC Groningen

12.50 **Schimmelinfectie in transplantatie**
Dr. Ed A. van de Graaf, longtransplantatiearts UMC Utrecht

13.20 **Welke mechanismes liggen ten grondslag aan machine preservatie?**
Prof. dr. Rutger J. Ploeg, chirurg, Oxford Transplant Centre, U.K.

13.50 Sluiting onderwijssessie

Sessie III – Plenair **Hendrik Marsmanzaal**

Voorzitters: *Dr. Ed A. van de Graaf, longtransplantatiearts, UMC Utrecht*
Marion J.C. Wessels, MA, Verpleegkundig specialist, UMC Utrecht

Thema: **Non immunological issues after transplantation**

14.00 **Psychosocial issues before and after solid organ transplantation**
Prof. dr. Heike Spaderna, Universität Trier, Germany

14.30 **Fertiliteit en zwangerschap**
Prof. dr. Robin Vos, Universiteit Leuven, België

15.00 **Inzichten in tacrolimus kinetiek**
Dr. Maaike A. Sikma, intensivist UMC Utrecht

15.30 Koffiepauze

Woensdag 8 maart 2017

Sessie IV – Plenair — Hendrik Marsmanzaal

Voorzitter: *Drs. Bernadette J.J.M Haase-Kromwijk, directeur NTS*

Thema: **Twintigjarig jubileum Nederlandse Transplantatie Stichting**

16.00 Presentatie mijlpalen 20 jaar NTS
Drs. Bernadette J.J.M Haase-Kromwijk, directeur NTS

16.20 In het kader van het 20-jarig bestaan zal Paul Smit (filosoof en cabaretier) een voordracht verzorgen en stil staan bij de rol van de NTS in een unieke mix van humor en inhoud.

17.05 Afsluiting jubileumprogramma
Prof. dr. Willem Weimar, voorzitter NTS

17.15 Einde jubileumprogramma

Parallelsessie V – Basaal 1 — Hendrik Marsmanzaal

Voorzitters: *Prof. dr. Carla C. Baan, Hoofd Transplantatie Laboratorium, Erasmus MC*
Dr. Maarten B. Rookmaaker, internist-nefroloog UMC Utrecht

Thema: **Analyse niet-hematopoietische cellen in orgaantransplantatie**

Voordrachten in het Engels, spreektijd 8 minuten, discussietijd 4 minuten.

17.30 The role of recipient epithelial cells in regeneration after liver transplantation: Different kinetics of chimerism for hepatocytes and bile duct epithelial cells (p. 52)
F.J.M. Roos[1], J.W. Selten[1], W.G. Polak[1], M.M. Verstegen[1], H.F.B.M. Sleddens[2], M. Doukas[2], H.J. Metselaar[3], J.N.M. IJzermans[1] and L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus Medical Center Rotterdam, Rotterdam, [2]Dept of Pathology, Erasmus Medical Center Rotterdam, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

Parallelsessie V – Basaal 1 **Hendrik Marsmanzaal**

17.42 Regeneration of kidney vasculature with human kidney-derived endothelial cells in decellularized rat and human kidneys (p. 53)
D. Leuning[1], A. de Graaf [1], C.W. van den Berg[1], E. Lievers[1], L. Wiersma[1], H. de Boer[1], C. Avramut[2], B. van den Berg[1], C. van Kooten[1], M. Reinders[1], M. Takasato[3], M. Little[4,5], M. Engelse[1] and T. Rabelink[1], [1]Nephrology, LUMC, Leiden, [2]Cell Biology, LUMC, Leiden, The Netherlands, [3]RIKEN Center for Developmental Biology, Kobe, Japan, [4]Murdoch Childrens Research Institute, Melbourne ,[5]Pediatrics, The University of Melbourne, Australia

17.54 Expansion and characterization of peribiliary gland-resident stem cells using organoid cultures (p. 54)
M.M.A. Verstegen[1], M. de Wolf[1], K. Burka[1], M.J.C. Bijvelds[2], H. Gehart[3], J.N.M. IJzermans[1], H.R. de Jonge[2] and L.J.W. van der Laan[1], [1]Dept of Surgery, [2]Gastroenterology & Hepatology, Erasmus Medical Center-University Medical Center, Rotterdam, [3]Hubrecht Institute, Utrecht, The Netherlands

18.06 Ageing of bone marrow and umbilical cord derived MSC during culture expansion (p. 55)
S.F.H. de Witte[1], E.E. Lambert[1], A.M. Merino[1], T. Strini[1], J.C.W. Douben[2], S.J. Elliman[3], P.N. Newsome[4], J.E.M.M. de Klein[2], C.C. Baan[1] and M.J. Hoogduijn[1], [1]Nephrology and Transplantation, Dept of Internal Medicine, [2]Dept of Clinical Genetics Medicine, Erasmus Medical Center, Rotterdam, The Netherlands, [3]Orbsen Therapeutics Ltd., Galway, Ireland, [4]Dept of NIHR Liver Biomedical Research Unit and Center for Liver Research, University of Birmingham, United Kingdom

18.18 Changes in Myocardial Microvascularisation After Heart Transplantation and During Cardiac Allograft Vasculopathy (p. 56)
M.M.H. Huibers[1], F. van Pijpen[1], H.J.H. Kirkels[2], N. de Jonge[2], A. Vink[1] and R.A. de Weger[1], [1]Dept of Pathology and [2]Cardiology, University Medical Center Utrecht, The Netherlands

Parallelsessie V – Basaal 1 — Hendrik Marsmanzaal

18.30 Inflammatory conditions dictate the effect of MSC on B cell function (p. 57)
F. Luk[1], L. Carreras-Planella[2], S.S. Korevaar[1], S.F.H. de Witte[1], F.E. Borràs[2], M.G.H. Betjes[1], C.C. Baan[1], M.J. Hoogduijn[1] and M. Franquesa[1, 2], [1]Nephrology and Transplantation, Dept of Internal Medicine, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands, [2]Nephrology and Transplantation, Institut d'Investigació Germans Trias i Pujol, Badalona, Spain

18.42 In vivo tracking of live and dead mesenchymal stromal cells (p. 58)
S.F.H. de Witte[1], M. Gargesha[4], A.M. Merino[1], S.J. Elliman[4], P.N. Newsome[3], D. Roy[4], C.C. Baan[1] and M.J. Hoogduijn[1], [1]Nephrology and Transplantation, Dept of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Orbsen Therapeutics Ltd., Galway, Ireland, [3]Dept of NIHR Liver Biomedical Research Unit and Center for Liver Research , University of Birmingham, United Kingdom, [4]BioInVision Inc., Mayfield Village, OH, United States of America

18.54 **Prijsuitreiking**

Parallelsessie VI – Klinisch 1 — Willem Pijperzaal

Voorzitters: Prof. dr. Luuk B. Hilbrands, internist-nefroloog, Radboudumc, Nijmegen
Dr. Hanneke M. Kwakkel-van Erp, longarts, UMC Utrecht

Thema: **HLA-antilichamen en immunomodulatie**

Voordrachten in het Nederlands, spreektijd 8 minuten, discussietijd 4 minuten.

17.30 Association of repeated HLA mismatches with graft survival in kidney transplantation: data from the Dutch transplant registry (p. 59)
J.W. van der Heijden[1], T. Hoekstra[1], C. Ranzijn[2], C. Konijn[3], N. Lardy[2], F.J. van Ittersum[1] and S.A. Nurmohamed[1], [1]VU University Medical Center, Dept of Nephrology, Amsterdam, [2]Sanquin Diagnostic Services, Dept of Immunogenetics, Amsterdam, [3]Dutch Transplant Foundation, Leiden, The Netherlands; on behalf of the LONT investigators

Parallelsessie VI – Klinisch I **Willem Pijperzaal**

17.42 Course of donor specific anti-HLA antibodies after induction therapy with rituximab in renal transplantation (p. 60)
M.C. Baas[1], W.A. Allebes[2], M. van den Hoogen[3], I. Joosten[2] and L.B. Hilbrands[1], [1]Dept of Nephrology, [2]Dept for Blood Transfusion and Transplantation Immunology, Radboud University Medical Center, Nijmegen, [3]Dept of Internal Medicine, Nephrology and Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands

17.54 Alemtuzumab is superior to ritxumab as induction therapy in ABO incompatible kidney transplantation (p. 61)
A.E. de Weerd, M. van Agteren, J.A. Kal-van Gestel, J. van de Wetering and M.G.H. Betjes, Dept of Nephrology and Kidney Transplantation, Erasmus Medical Center Rotterdam, The Netherlands

18.06 The value of repeat biopsies in kidney allograft recipients with delayed graft function (p. 62)
N. Sajadjan[1], M.C. van den Heuvel[2], T.M. Huijink[3], R.A. Pol[2], S.P. Berger[1], Dept of [1]Nephrology and [2]Pathology and [3]Surgery, University Medical Center Groningen, The Netherlands

18.18 The role of donor-specific anti-HLA antibodies in kidney transplant survival revisited! (p. 63)
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.E. van Reekum[4], A.D. van Zuilen[4], M. 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], C.E. Voorter[8], L. Wieten[8], E.M. van Duijnhoven[9], M. Gelens[9], M.H.L. Christiaans[9], F.J. van Ittersum[10], S.A. Nurmohamed[10], N.M. Lardy[11], W. Swelsen[11], K.A. van der Pant[12], N.C. van der Weerd[12], I.J.M. ten Berge[12], F.J. Bemelman[12], A. Hoitsma[13], P.J.M. van der Boog[14], J.W. de Fijter[14], M.G.H. Betjes[15], S. Heidt[16], D.L. Roelen[16], F.H. Claas[16] and H.G. Otten[1], [1]Laboratory of Translational Immunology, UMC Utrecht, Utrecht, [2]Laboratory Medicine, Lab. Medical Immunology, Radboud University Medical Center, Nijmegen, [3]Dept of Nephrology, Radboud University Medical Center,

Nijmegen, [4]Dept of Nephrology, UMC Utrecht, Utrecht, [5]Julius Center for Health Sciences and Primary Care, UMC Utrecht, Utrecht, [6]Dept of Nephrology, University of Groningen, UMC Groningen, Groningen, [7]Dept of Laboratory Medicine, University of Groningen, UMC Groningen, Groningen, [8]Dept of Transplantation Immunology, Tissue Typing Laboratory, Maastricht UMC, Maastricht, [9]Dept of Internal Medicine, Division of Nephrology, Maastricht UMC, 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]Dutch Organ Transplant Registry (NOTR), Dutch Transplant Foundation (NTS), Leiden, [14]Dept of Nephrology, Leiden University Medical Center, Leiden, [15]Dept of Internal Medicine, Nephrology, Erasmus Medical Center, Rotterdam, Dept of Nephrology, Rotterdam, [16]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands

18.30 Predicted Indirectly ReCognizable HLA epitopes presented by HLA-DRB1 (PIRCHE-II), a novel tool to identify permissible HLA mismatches in kidney transplantation (p. 64)

K. Geneugelijk[1], M. Niemann[2], J. Drylewicz[1], A.D. van Zuilen[3], I. Joosten[4], W.A. Allebes[4], A. van der Meer[4], L.B. Hilbrands[5], M.C. Baas[5], C.E. Hack[1], F.E. van Reekum[3], M. Verhaar[3], E.G. Kamburova[1], M.L. Bots[6], M.A.J. Seelen[7], J-S. Sanders[7], B.G. Hepkema[8], A.J. Lambeck[8], L.B. Bungener[8], C. Roozendaal[8], M.G.J. Tilanus[9], J. Vanderlocht[9], C.E. Voorter[9], L. Wieten[9], E.M. van Duijnhoven[10], M. Gelens[10], M.H.L. Christiaans[10], F.J. van Ittersum[11], S.A. Nurmohamed[11], N.M. Lardy[12], W. Swelsen[12], K.A. van der Pant[13], N.C. van der Weerd[13], I.J.M. ten Berge[13], F.J. Bemelman[13], A. Hoitsma[14], P.J.M. van der Boog[15], J.W. de Fijter[15], M.G.H. Betjes[16], S. Heidt[17], D.L. Roelen[17], F.H. Claas[17], H.G. Otten[1] and E. Spierings[1], [1]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands, [2]PIRCHE AG, Berlin, Germany, [3]Dept of Nephrology, University Medical Center Utrecht, Utrecht, [4]Laboratory Medicine, Lab. Medical Immunology, Radboud University Medical Center, Nijmegen, [5]Dept of Nephrology, Radboud University Medical Center, Nijmegen, [6]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, [7]Division of Nephrology, Dept of Internal Medicine, University of Groningen, University Medical Center Groningen, Groningen, [8]Dept of Laboratory Medicine, University

of Groningen, University Medical Center Groningen, Groningen, [9]Dept of Transplantation Immunology, Tissue Typing Laboratory, Maastricht University Medical Center, Maastricht, [10]Dept of Internal Medicine, Division of Nephrology, Maastricht University Medical Center, Maastricht, [11]Dept of Nephrology, VU Medical Center, Amsterdam, [12]Dept of Immunogenetics, Sanquin, Amsterdam, [13]Renal Transplant Unit, Dept of Internal Medicine, Academic Medical Center, Amsterdam, [14]Dutch Organ Transplant Registry (NOTR), Dutch Transplant Foundation (NTS), Leiden, [15]Dept of Nephrology, Leiden University Medical Center, Leiden, [16]Dept of Internal Medicine, Nephrology, Erasmus Medical Center, Rotterdam, Dept of Nephrology, Rotterdam, [17]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands

18.42 Two promoter polymorphisms in the genes encoding for complement regulating proteins CD46 and CD59 in kidney donors are associated with biopsy proven acute rejection (p. 65)

L.A. Michielsen[1], A.D. van Zuilen[1], T. Kardol-Hoefnagel[2], M.C. Verhaar[1] and H.G. Otten[2], [1]Dept of Nephrology and Hypertension, University Medical Center Utrecht, Utrecht, [2]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands

18.54 **Prijsuitreiking**

Parallelsessie VII – Klinisch 2 — Johan de Meesterzaal

Voorzitters: *Drs. Franka E. van Reekum, internist-nefroloog, UMC Utrecht*
Dr. Michiel C. Warlé, vaat- en transplantatie chirurg, Radboudumc Nijmegen

Thema: Nazorg na orgaantransplantatie

Voordrachten in het Nederlands, spreektijd 8 minuten, discussietijd 4 minuten.

17.30 Colorectal carcinoma after renal transplantation: Screening looks like a valuable option (p. 66)
C.A.J. Oudmaijer[1], J.I. Roodnat[1], J.A. Kal-van Gestel[1], I. Lansdorp-Vogelaar[2], A.J. Hoitsma[3], T. Luth[4], J. van de Wetering[1], [1]Dept of Nephrology & Transplantation, Erasmus University Medical Center Rotterdam, [2]Dept of Public Health, Erasmus University Medical Center Rotterdam, [3]Dutch Organ Transplant Registry, [4]Dutch Cancer Registration, The Netherlands

17.42 Actieve ziekte pre-transplantatie is een onafhankelijke risicofactor voor terugkeer van primaire scleroserende cholangitis (PSC) post-levertransplantatie (p. 67)
T. Visseren[1,2], L. van Kleef[1], J.N.M. IJzermans[2], W. Polak[2], H.J. Metselaar[1], S. Darwish Murad[1], Dept [1]Maag-, Darm- en Leverziekten, [2]Dept Heelkunde, Erasmus Medisch Centrum, Rotterdam, The Netherlands

17.54 Mycophenolate Mofetil trough levels and Chronic Lung Allograft Dysfunction in lung transplant recipients (p. 68)
C.L.A. Pladet[1], K.M. Vermeulen[2], W. van der Bij[1], G.N. Nossent[1], M.E. Erasmus[3] and E.A.M. Verschuuren[1], [1]Dept of pulmonary diseases and tuberculosis, [2]Dept of Epidemiology, [3]Dept of cardiothoracic Surgery, University Medical Center Groningen, University of Groningen, The Netherlands

18.06 A sudden increase in delayed graft function in living donor kidney transplantation and a changed peroperative fluid regimen (p. 69)
G.J. Nieuwenhuijs-Moeke[1], T.M. Huijnk[2], R.A. Pol[2], M. El Moumni[2], M.M.R.F. Struys[1,3] and S.P. Berger[4], [1]Dept of Anaesthesiology, University of Groningen, University Medical Center Groningen, Groningen, [2]Dept of Surgery, University

of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [3]Dept of Anaesthesiology, Ghent University, Ghent, Belgium, [4]Dept of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

18.18 Oxalate deposition in the renal allograft biopsy within 3 months after transplantation (p. 70)
M.L.H. Snijders[1], M.C. Clahsen-van Groningen[1], D.A. Hesselink[2] and J.I. Roodnat[2], [1]Dept of Pathology, Erasmus Medical Center, Rotterdam, [2]Dept of Nephrology and Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands

18.30 A lower mean exposure to tacrolimus, not intra-patient variability is associated with chronic active antibody mediated rejection (p. 71)
K.A. Sablik[1], M.C. Clahsen–van Groningen[2], T. van Gelder[1], M.G.H. Betjes[1], [1]Dept of Nephrology and Transplantation, Erasmus Medical Center, [2]Dept of Pathology, Erasmus Medical Center, Rotterdam, The Netherlands

18.42 The importance of Acute Kidney Injury in patients with Left Ventricular Assist Devices: A Multi-Center study addressing Incidence, Risk Factors and Impact on 1-year Mortality and Renal Function (p. 72)
R. Muslem[1], K. Caliskan[1], S. Akin[1], K. Sharma[2], N. Gilotra[2], A. Constantinescu[1], G. Whitman[2], R. Tedford[2], D.A. Hesselink[3], A. Bogers[4], S. Russell[2] and O.C. Manintveld[1], [1]Dept of Cardiology, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Johns Hopkins Heart and Vascular Institute, Baltimore, Maryland, [3]Dept of Internal Medicine, Div. of Nephrology and Renal Transplantation, Erasmus Medical Center, University Medical Center Rotterdam, [4]Dept of Cardiothoracic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

18.54 Einde abstractsessie

Avondprogramma

19.00 Ontvangst en dinerbuffet Copijn-Zocher-Springerzaal

Donderdag 9 maart 2017

Parallelsessie VIII – Early Bird sessie 1 — Hendrik Marsmanzaal

Voorzitter: *Dr. Stefan P. Berger, internist-nefroloog, UMC Groningen*

Thema: **Discussie en consensussessie: niertransplantatierichtlijnen in ontwikkeling**

08.00 Ontvanger keuring
Dr. Marije C. Baas, internist-nefroloog, Radboudumc Nijmegen

08.15 Donor keuring
Dr. Stefan P. Berger, internist-nefroloog, UMC Groningen

08.30 Post transplantatie diabetes,
Dr. Aiko P.J. de Vries, internist-nefroloog, Leids UMC

08.45 Transplantatie en bot
Dr. Azam Nurmohamed, internist-nefroloog, VUmc Amsterdam

Parallelsessie IX – Basaal 2 — Hendrik Marsmanzaal

Voorzitters: *Prof. dr. Frederike J. Bemelman, internist-nefroloog, AMC Amsterdam*
Prof. dr. Roel Goldschmeding, patholoog UMC Utrecht

Thema: **Biomarkers gerelateerd aan rejectie na orgaantransplantatie**

Voordrachten in het Engels, spreektijd 8 minuten, discussietijd 4 minuten.

09.00 CD16+ monocytes and skewed macrophage polarization towards M2 type hallmark heart transplant acute cellular rejection (p. 73)
T.P.P. van den Bosch[1], K. Caliskan[2], M.D. Kraaij[1], A.A. Constantinescu[2], O.C. Manintveld[2], P.J.M. Leenen[3], J.H. von der Thüsen[4], M. Clahsen-van Groningen[4], C.C. Baan[1] and A.T. Rowshani[1], [1]Dept of Internal Medicine and Transplantation, [2]Dept of Cardiology, [3]Dept of Immunology and [4]Dept of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands

Parallelsessie IX – Basaal 2 **Hendrik Marsmanzaal**

09.12 Liquid biopsies: non-invasive rejection detection after heart transplantation (p. 74)
L.S.M. Hofste[1], A. Vink[1], J. van Kuik[1], E. Siera-de Koning[1], F. Ahmadi[1], N. de Jonge[2], R.A. de Weger[1] and M.M.H. Huibers[1], Dept of [1]Pathology and [2]Cardiology, University Medical Center, Utrecht, The Netherlands

09.24 Hypothermic machine perfusion reduces reperfusion injury of the bile ducts after transplantation of donation after circulatory death livers (p. 75)
R. van Rijn[1,2], O.B. van Leeuwen[1,2], A.P.M. Matton[1,2], L.C. Burlage[1,2], R.H.J. de Kleine[1], M.T. de Boer[1], A.S.H. Gouw[3] and R.J. Porte[1], [1]Section of Hepatobiliary Surgery and Liver Transplantation, Dept of Surgery, [2]Surgical Research Laboratory, Dept of Surgery, [3]Dept of Pathology, University of Groningen, University Medical Center Groningen, The Netherlands

09.36 MicroRNAs differentiate between antibody and T-cell mediated renal allograft rejection (p. 76)
T.P.P. van den Bosch[1], M.C. Clahsen-van Groningen[2], F. Rezaee[3], D. Nieboer[4], E.W. Steyerberg[4], C.C. Baan Ph.D[1] and A.T. Rowshani[1], [1]Dept Internal Medicine, Section of Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, [2]Dept of Pathology, Erasmus University Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, and Dept of Cell Biology, University Medical Center Groningen, Groningen, [4]Dept Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands

09.48 Compartmental infiltration of kidney allograft with monocyte-macrophage subtypes defines the type of rejection (p. 77)
T.P.P. van den Bosch[1], M.C. Clahsen-van Groningen[2], F. Rezaee[3], D.A. Hesselink[1], D. Nieboer[3], E.W. Steyerberg[3], C.C. Baan[1] and A.T. Rowshani[1], [1]Dept of Internal Medicine, Section of Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, [2]Dept of Pathology, Erasmus University Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, and Dept of Cell Biology, University Medical Center Groningen, Groningen, Dept of Public Health, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands

Parallelsessie IX – Basaal 2 **Hendrik Marsmanzaal**

10.00 Identification of kidney transplant patients at risk for skin cancer by differentially methylated regions in t cells (p. 78)
F.S. Peters[1], A.M.A. Peeters[1], P.R. Mandaviya[2], J. van de Wetering[1], M.G.H. Betjes[1], C.C. Baan[1] and K. Boer[1], [1]Dept of Internal Medicine, Nephrology and Transplantation, [2]Dept of Clinical Chemistry, Erasmus Medical Center, University Medical Center Rotterdam, The Netherlands

10.12 Antibodies against apoptotic cells present in end-stage lung disease patients do not correlate with clinical outcome after lung transplantation (p. 79)
K. Budding[1], E.A. van de Graaf[2], T. Kardol-Hoefnagel[1], E-J.D. Oudijk[3], J.M. Kwakkel-van Erp[2], C.E. Hack[1,4] and H.G. Otten[1], [1]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, [2]Dept of Respiratory Medicine, University Medical Center Utrecht, Utrecht, [3]Center of Interstitial Lung Diseases, St. Antonius Hospital, Nieuwegein, [4]Depts of Rheumatology and Dermatology, University Medical Center Utrecht, Utrecht, The Netherlands

10.24 **Prijsuitreiking**

10.30 Koffiepauze

Parallelsessie X – Verpleegkundig — Willem Pijperzaal

Voorzitters: *Marion J.C. Wessels, MA, verpleegkundig specialist, UMC Utrecht*
Judith M. Wierdsma, Msc, verpleegkundig specialist, UMC Utrecht

Voordrachten in het Nederlands, spreektijd 8 minuten, discussietijd 4 minuten.

09.00 Risk factors and impact on outcomes of trajectories of anxiety and depression after liver transplantation: a prospective cohort study (p. 80)
C. Annema[1], G. Drent[2], P.F. Roodbol[3], R.E. Stewart[4], H.J. Metselaar[5], B. van Hoek[6], R.J. Porte[7] and A.V. Ranchor[3], [1]School of Nursing & Health, University Medical Center Groningen, [2]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, [3]Dept of Health Psychology, University Medical Center Groningen, [4]Dept of Public Health, University Medical Center Groningen, [5]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, [6]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, [7]Dept of Surgery and Liver Transplantation, University Medical Center Groningen, The Netherlands

09.12 EXPloring attitudes and factors influencing reproductive Choices in renal Transplant patients (EXPeCT-study) (p. 81)
M. van Buren[1], D. Beck[1], P. de Haan[2], J. van de Wetering[1] and E. Massey[1], [1]Dept of Internal Medicine, Erasmus University Medical Center Rotterdam, [2]Dept of General Surgery, Erasmus University Medical Center Rotterdam, The Netherlands

09.24 Posttraumatic stress disorder in liver transplant recipients before and after transplantation: prevalence, symptom occurrence, and intrusive memories (p. 82)
C. Annema[1], G. Drent[2], P.F. Roodbol[3], H.J. Metselaar[4], B. van Hoek[5], R.J. Porte[6], M.J. Schroevers[3] and A.V. Ranchor[3], [1]School of Nursing & Health, University Medical Center Groningen, [2]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, [3]Dept of Health Psychology, University Medical Center Groningen, [4]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, [5]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, [6]Dept of Surgery and Liver Transplantation, University Medical Center Groningen, The Netherlands

Parallelsessie X – Verpleegkundig **Willem Pijperzaal**

09.36 Dried Blood Spot Monitoring After Lung Transplantation: Patients Perspectives (p. 83)
M.J.C. Wessels-Bakker[1], E.M. van Maarseveen[2], M.E. Janssen[1], H.D. Luijk[1], E.A. van de Graaf[1], A.C. Egas[2] and J.M. Kwakkel-van Erp[1], [1]Dept of Heart and Lung, University Medical Center Utrecht, Utrecht, [2]Dept of Clinical Pharmacy, University Medical Center Utrecht, Utrecht, The Netherlands

09.48 Providing guidance to patients with Hepatic Encephalopathy who are on the waiting list for liver transplantation: a quality improvement project (p. 84)
M. Heida, J. van der Wal and G. Drent, Dept of Gastroenterology and Hepatology, University Medical Center Groningen, The Netherlands

10.00 Cystic fibrosis related diabetes mellitus and lungtransplantation (p. 85)
I.M. IJgosse and H.W. de Valk, Dept of Internal Medicine, University Medical Center Utrecht, Utrecht, The Netherlands

10.12 From proposal to practice: participation of compatible donor-recipient pairs in the Dutch kidney exchange program (p. 86)
M. de Klerk, W.C. Zuidema, E.K. Massey, W. Weimar, J. van de Wetering, Dept of Internal Medicine, Section of Nephrology and Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands

10.24 **Prijsuitreiking**

10.30 Koffiepauze

Parallelsessie XI – Klinisch 3 — Johan de Meesterzaal

Voorzitters: *Dr. Maarten H.L. Christiaans, internist-nefroloog, Maastricht UMC*
Dr. Raechel J. Toorop, vaat-/transplantatiechirurg, UMC Utrecht

Early Bird sessie 2

Voordrachten in het Nederlands, spreektijd 8 minuten, discussietijd 4 minuten.

08.00 Impact of C3d-fixing donor-specific HLA antibodies on long-term kidney graft survival (p. 87)

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.E. van Reekum[4], A.D. van Zuilen[4], M. 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], C.E. Voorter[8], L. Wieten[8], E.M. van Duijnhoven[9], M. Gelens[9], M.H.L. Christiaans[9], F.J. van Ittersum[10], S.A. Nurmohamed[10], N.M. Lardy[11], W. Swelsen[11], K.A. van der Pant[12], N.C. van der Weerd[13], I.J.M. ten Berge[13], F.J. Bemelman[13], A. Hoitsma[14], P.J.M. van der Boog[14], J.W. de Fijter[14], M.G.H. Betjes[15], S. Heidt[16], D.L. Roelen[16], F.H. Claas[16] and H.G. Otten[1], [1]Laboratory of Translational Immunology, UMC Utrecht, Utrecht, [2]Laboratory Medicine, Lab. Medical Immunology, Radboud University Medical Center, Nijmegen, [3]Dept of Nephrology, Radboud University Medical Center, Nijmegen, [4]Dept of Nephrology, UMC Utrecht, Utrecht, [5]Julius Center for Health Sciences and Primary Care, UMC Utrecht, Utrecht, [6]Dept of Nephrology, University of Groningen, UMC Groningen, Groningen, [7]Dept of Laboratory Medicine, University of Groningen, UMC Groningen, Groningen, [8]Dept of Transplantation Immunology, Tissue Typing Laboratory, Maastricht UMC, Maastricht, [9]Dept of Internal Medicine, Division of Nephrology, Maastricht UMC, 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]Dutch Organ Transplant Registry (NOTR), Dutch Transplant Foundation (NTS), Leiden, [14]Dept of Nephrology, Leiden University Medical Center, Leiden, [15]Dept of Internal Medicine, Nephrology, Erasmus Medical Center, Rotterdam, Dept of Nephrology, Rotterdam, [16]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands

Parallelsessie XI – Klinisch 3 **Johan de Meesterzaal**

08.12 A standard frailty indicator for predicting postoperative complications after kidney transplantation (p. 88)
L. Schopmeyer[1], M. El Moumni[1], G.J. Nieuwenhuijs-Moeke[2], S.P. Berger[3], S.J. Bakker[3], R.A. Pol[1], Dept of [1]Surgery, [2]Anaesthesiology and [3]Nephrology, University Medical Center Groningen, The Netherlands

08.24 Self-monitoring creatinine after transplantation: the (un)reliability of patient reported data (p. 89)
C.L. van Lint[1]; W. Wang[2]; S. van Dijk[1,4]; W-P. Brinkman[2]; T. Rövekamp[3]; M. Neerincx[2]; A.J. Rabelink[1] and P.J.M. van der Boog[1], Dept. of Nephrology[1], Leiden University Medical Centre, Leiden; Dept. of Computer Science[2], Delft University of Technology, Delft; Dept. of Technology in Healthcare, Prevention and Health[3], TNO, Leiden; Dept. of Health, Medical and Neuropsychology & Behavioural Sciences[4], Leiden University, The Netherlands

08.36 Combined Measurement of Immunosuppressive Agents, Creatinine and Hematocrit in a Single Dried Blood Spot Using LC-MSMS and Near-infra-Red Spectrometry (p. 90)
A.C. Egas ,[1]M.J. Wessels-Bakker, [2]M.J.M. Kwakkel-van Erp, [2]M.E. Janssen, [2]B. Luijk, [2]E.A. van de Graaf, [3]M. Oostendorp, [3]El Amrani and [1]E.M. van Maarseveen, [1]Clinical Pharmacy, University Medical Center Utrecht, Utrecht, [2]Respiratory Medicine, University Medical Center Utrecht, Utrecht, [3]Division of Heart and Lung, University Medical Center Utrecht, Utrecht, [3]Dept of Clinical Chemistry and Haematology, University Medical Center Utrecht, Utrecht [2]Current address: Máxima Medical Center Veldhoven, Clinical Laboratory, Veldhoven, The Netherlands*

08.48 Prognostic impact of rejection in biopsies taken during delayed graft function (p. 91)
N. Sajadjan[1], M.C. van den Heuvel[2], T.M. Huijink[3], R.A. Pol[2] and S.P. Berger[1], Dept of [1]Nephrology and [2]Pathology and [3]Surgery, University Medical Center Groningen, The Netherlands

Parallelsessie XII – Klinisch 4 — Johan de Meesterzaal

Voorzitters: *Dr. Dries E. Braat, chirurg, Leids UMC*
Dr. Neelke C. van der Weerd, internist-nefroloog, AMC

Thema: **Pretransplantatie en donatie**

Voordrachten in het Nederlands, spreektijd 8 minuten, discussietijd 4 minuten.

09.00 The effect of starting enteral tube feeding in patients with end-stage cystic fibrosis before lung transplantation (p. 92)
F.M. Hollander[1A3], B.C. Broersen[2], G. Belle-van Meerkerk[1], N.M. de Roos[2] and E.A. van de Graaf[3], [1]Internal Medicine and Dermatology, [A]Dept of Dietetics, University Medical Center Utrecht, [2]Division of Human Nutrition, Wageningen University, [3]Cystic Fibrosis and Lung Transplantation Center, University Medical Center Utrecht, The Netherlands

09.12 Iliac peripheral arterial disease before kidney transplantation: the influence of intervention (p. 93)
M.A. van der Zijden[1], M. Laging[1], J.A. Kal-van Gestel[1], M.J. Poldervaart[1], H.J.A.N. Kimenai[2], S. ten Raa[2] and J.I. Roodnat[1], Dept of [1]Internal Medicine and [2]Surgery, Erasmus Medical Center University Medical Center, Rotterdam, The Netherlands

09.24 The agonal phase of DCD donors: parameters of success? (p. 94)
H. Peters Sengers[1], R.W. Klaasen[1], J.A.M. Hagenaars[2], M.I. Idu[3], J.J. Homan van der Heide[1], J.I. Roodnat[2] and F.J. Bemelman[1], [1]Renal Transplant Unit, Academic Medical Center Amsterdam, [2]Renal Transplant Unit, Erasmus Medical Center Rotterdam, [3]Dept of Surgery, Academic Medical Center Amsterdam, The Netherlands

09.36 Abdominal organ procurement in The Netherlands – An analysis of quality and clinical impact (p. 95)
J.D. de Boer[1,2], W.H. Kopp[2], K. Ooms-de Vries[1], B.J.J.M. Haase-Kromwijk[1], C. Krikke[3], J. de Jonge[4], L.W.E. van Heurn[5], A.G. Baranski[2], J.A. van der Vliet[6] and A.E. Braat[2], [1]Dutch Transplant Foundation, Leiden University Medical Center, [2]Dept of Surgery, University Medical Center Groningen, [3]Dept of Surgery, Erasmus Medical Center Rotterdam, [4]Dept of Surgery, Maastricht University Medical Center, [5]Dept of Surgery, Radboud University Nijmegen Medical Center, [6]Dept of Surgery, The Netherlands

Parallelsessie XII – Klinisch 4 **Johan de Meesterzaal**

09.48 Influence of Ischemic Agonal Phase on Hepatic Ischemia / Reperfusion Injury and Postoperative Outcomes in DCD Liver Transplantation (p. 96)
M. Kalisvaart[1], J.E. de Haan[2], W.G. Polak[1], J.N.M. IJzermans[1], D.A.M.P.J. Gommers[2], H.J. Metselaar[3], and J. de Jonge[1], [1]Dept of Surgery, Division of Transplant Surgery, [2]Dept of Intensive Care, [3]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

10.00 DonorDialoog Rotterdam: Niet willen, Niet mogen of Niet weten? (p. 97)
Y. van Hemmen and J. Reiger, Nederlandse Transplantatie Stichting, The Netherlands

10.12 Validation and calibration of the prognostic Kidney Donor Risk Index (KDRI) scoring system of deceased donors for renal transplantation in The Netherlands (p. 98)
H. Peters-Sengers[1], M.B.A. Heemskerk[2], J.J. Homan van der Heide[1], S.P. Berger[3] and F.J. Bemelman[1], [1]Renal Transplant Unit, Academic Medical Center, Amsterdam, [2]Dutch Transplant Foundation, Leiden, [3]Renal Transplant Unit, University Medical Center Groningen, The Netherlands

10.24 Koffiepauze

Donderdag 9 maart 2017

Sessie XIII – Plenair **Hendrik Marsmanzaal**

Voorzitters: *Dr. Nicolaas de Jonge, cardioloog, UMC Utrecht*
Drs. Bernadette J.J.M. Haase-Kromwijk, directeur NTS

Thema: **Patiëntenparticipatie: keuzes in de orgaantransplantaties: kwantiteit of kwaliteit**

11.00 Kwaliteit
Dr. Hanneke M. Kwakkel-van Erp, longarts, UMC Utrecht

11.20 Kwantiteit
Prof. dr. Herold J. Metselaar, maag-darm-leverarts, Erasmus MC Rotterdam

11.40 Na deze stellingname door beide artsen zal er een patiëntenpanel in gesprek gaan met de voorgaande sprekers, waarbij uiteraard ook de toehoorders in de zaal vragen kunnen stellen of deelnemen aan de discussie.

Aan het patiëntenpanel nemen deel:

Hayo Patrick Angerman (Nederlandse Leverpatiënten Vereniging)
Henk Bakker (HartenTwee)
Nico v.d. Meij (Nederlandse Cystic Fibrosis Stichting)
Bart Pijpers (Nierpatiënten Vereniging Nederland)
Sandra Renting (Nederlandse Cystic Fibrosis Stichting)

12.10 Samenvatting van de voordrachten en de discussie.
Drs. Bernadette J.J.M. Haase-Kromwijk, directeur NTS

12.15 Lunchpauze

Vanaf 13.30 *is er in de Zocherzaal een interactieve sessie van de NVN (max. 50 deelnemers): 'Samen beslissen rond nierfunctievervangende behandeling*'

Postersessie – Klinisch I

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

12.30 – 12.45

Moderator: Dr. Dennis A. Hesselink, internist-nefroloog, Erasmus MC, Rotterdam

1. Panel reactive antibodies is a debatable indicator of post-transplant function and survival (p. 107)
M. Mc-Cahery[2], M.C. Clahsen-van Groningen[2], K.A.L. Mauff[2], J.A. Kal-van Gestel[1] and A.T. Rowshani[1], [1]Dept of Nephrology & Transplantation, Erasmus MC, Rotterdam, [2]Dept of Pathology, Erasmus MC, Rotterdam, The Netherlands

2. A search for a biomarker to predict belatacept-resistant rejection in kidney transplantation (p. 108)
G.N. de Graav[1], C.C. Baan[1], M.C. Clahsen-van Groningen[2], R. Kraaijeveld[1], M. Dieterich[1], W. Verschoor[1], D.L. Roelen[3], M. Cadogan[1], J. van de Wetering[1], J. van Rosmalen[4], W. Weimar[1], and D.A. Hesselink[1], [1]Dept of Internal Medicine, Div of Nephrology and Kidney Transplantation, Erasmus MC, Rotterdam, [2]Dept of Pathology, Erasmus MC, Rotterdam, [3]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, [4]Dept of Biostatistics, Erasmus MC, Rotterdam, The Netherlands

3. DSA presence does not affect renal histology and clinical outcome in chronic active antibody mediated rejection (p. 109)
K.A. Sablik[1], M.C. Clahsen–van Groningen[2], C.W.N. Looman[3], J. Damman[2], D.L. Roelen[4], M. van Agteren[1] and M.G.H. Betjes[1], [1]Dept of Nephrology and Transplantation, Erasmus MC, [2]Dept of Pathology, Erasmus MC, [3]Dept of Biostatistics, Erasmus MC, [4]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Center, The Netherlands

4. Urine neutrophil gelatinase-associated lipocalin (NGAL) after revascularization is indicative of renal graft recovery in children (p. 110)
K. Cransberg[1], K. Meys[2], A.J.M. Zwiers[3], E.A.M. Cornelissen[4], A.H. Bouts[5], M. Pheninckx[1], Y.B. de Rijke[6], H. de Jong[1] and C.E.J. Sloots[7], [1]Dept Ped. Nephrology, Erasmus MC, Rotterdam, [2]Dept Radiology, Maastricht UMC, Maastricht, [3]Dept of Anesthesiology, Erasmus MC, Rotterdam, [4]Dept Ped. Nephrology,

Postersessie – Klinisch I

Radboud UMC, Nijmegen, [5]Dept Ped. Nephrology, Academic Medical Center, Amsterdam, [6]Dept Clin. Chemistry, Erasmus Medical Center, Rotterdam, [7]Dept Ped Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

5. Pretransplant numbers of CD16+ monocytes as a novel biomarker to predict acute rejection after kidney transplantation; a pilot study (p. 111)
T.P.P. van den Bosch[1], L.B. Hilbrands[2], R. Kraaijeveld[1], N.H.R. Litjens[1], F. Rezaee[3], D. Nieboer[4], E.W. Steyerberg[4], J.A. van Gestel[1], C.C. Baan[1] and A.T. Rowshani[1], [1]Dept Internal Medicine, Section of Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, [2]Dept of Nephrology, Radboud University Medical Center, Nijmegen, [3]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, and Dept of Cell Biology, University Medical Center Groningen, Groningen, [4]Dept of Public Health, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands

Postersessie – Klinisch 2

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

12.45 – 13.00

Moderator: Dr. Azam Nurmohamed, internist-nefroloog, VU medisch centrum

6. Towards a conditional approach to anonymity in the Netherlands? – a multi-center prospective study among anonymous donors and recipients (p. 112)
M. Pronk[1], D. Slaats[1], I. Dooper[2], D. Pilzecker[2], J. Vervelde[3], K. van der Pant[3], R. Meijer[4], M. van Vliet[5], C. Schrauwers[5], F. van Reekum[6], J. Wierdsma[6], J. Dackus[7], P. Ulrichts[7], F. Dor[1,8], W. Weimar[1], J. van de Wetering[1], W. Zuidema[1] and E. Massey[1], [1]Dept of Internal Medicine, Nephrology and Transplantation, Erasmus Medical Center, Rotterdam, [2]Dept of Nephrology, Radboud UMC, Nijmegen, [3]Dept of Internal Medicine/Nephrology, Renal Transplant Unit, Academic Medical Center, University of Amsterdam, Amsterdam, [4]Dept of Nephrology, UMCG, Groningen, [5]Dept of Nephrology,

VUmc Amsterdam, [6]Dept of Nephrology, UMC Utrecht, [7]Dept of Nephrology, UMC Maastricht, The Netherlands, [8]West London Renal and Transplant Center, Dept of Renal and Transplant Services, Hammersmith Hospital, Imperial College, London, United Kingdom

7. Predictors for delayed graft function in living donor kidney transplantation (p. 113)

T.M. Huijink[1,3], G.J. Nieuwenhuijs-Moeke[2], N. Sajadjan[3], R.A. Pol[1] and S.P. Berger[3], Dept of [1]Surgery, [2]Anesthesiology and [3]Nephrology, University Medical Center Groningen, The Netherlands

8. Improving recognition of potential tissue donors; a quality improvement project by a hospitalist in training in The Netherlands (p. 114)

M.L. de Boom[1], J. Blok-Singerling[2], M. Huijzer-den Toom[2], D.C. Grootendorst[3], M. Franken-de Koster[4] and C. Brumsen[5], [1]Dept of Hospital Medicine, Haaglanden Medical Center, The Hague, [2]Dept of Organ- and Tissuedonation, Haaglanden Medical Center Haaglanden, The Hague, [3]Landsteiner Institute, Haaglanden Medical Center Haaglanden, The Hague, [4]Dept of Quality & Safety, Haaglanden Medical Center Haaglanden, The Hague, [5]Dept of Internal Medicine, Haaglanden Medical Center Haaglanden, The Hague, The Netherlands

9. Wat is er en wat moet er komen?
Het scholingsaanbod voor donatieprofessionals in Nederland (p. 115)

H.M. Dentz[1], A.H. Brunsveld-Reinders[2], M.E.C. Willems- van der Haak[3], C.W.F. Ultee[4] and M. Volbeda[5], [1]Nederlandse Transplantatie Stichting Leiden, [2]Leids Universitair Medisch Centrum, Leiden, [3]Maastricht Universitair Medisch Centrum, Maastricht, [4]Academisch Medisch Centrum, Amsterdam, [5]Universitair Medisch Centrum Groningen, The Netherlands

10. Does "the eye of the donor surgeon" predict kidney transplant outcome? (p. 116)

E.L. Tierie[1,2], J.I. Roodnat[2] and F.J.M.F. Dor[1,3], [1]Dept of Surgery, Division of HPB & Transplant Surgery, [2]Dept of Nephrology, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands, Imperial College Renal and Transplant Center[3], London, United Kingdom

Postersessie – Klinisch 3

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

13.00 – 13.15

Moderator: Dr. Niels P. van der Kaaij, thoraxchirurg UMC Utrecht

11. The golden hour: length of total warm ischemia time presages development of severe acute kidney injury after DCD liver transplantation (p.117)
M. Kalisvaart[1,2], I. Umbro[3], J. de Haan[4], I. Scalera[2], A. Schlegel[2], J. IJzermans[1], T. Perera[2], J. Isaac[2], A. Mitterhofer[3], P. Muiesan[2] and J. de Jonge[1], [1]Dept of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Dept of HPB Surgery and Liver Transplantation, University Hospitals Birmingham, Birmingham, United Kingdom, [3]Dept of Clinical Medicine, Nephrology and Dialysis B, Sapienza University, Rome, Italy, [4]Dept of Intensive Care, Erasmus Medical Center, Rotterdam, The Netherlands

12. Mental disorders among unspecified living kidney donors (p. 118)
S.Y. Ismail[1], W.C. Zuidema[2], J. van de Wetering[2], M.T. Hilhorst[3], L. Timmerman[2], E.K. Massey[2], J.N.M. IJzermans[4], J.J.V. Busschbach[1] and W. Weimar[2], Dept of [1]Psychiatry, [2]Internal Medicine, [3]Medical Ethics and Philosophy and [4]Surgery, Erasmus Medical Center, University Hospital Rotterdam, The Netherlands

13. Living kidney donation a major life event - What do the donors say? (p. 119)
M.C. Pronk[1], L. Timmerman[1], S. Janki[2], J. van de Wetering[1], W.C. Zuidema[1], J.N.M. IJzermans[2], J.J. van Busschbach[3], W. Weimar[1], E.K. Massey[1]. Dept of Internal Medicine[1], Dept of Surgery[2], Dept of Medical Psychology and Psychotherapy[3], Erasmus Medical Center, Rotterdam, The Netherlands

14. Predictive value of renal transplant scintigraphy for the duration of delayed graft function (p. 120)
S. Benjamens[1,2], R.A. Pol[1], A.W.J.M. Glaudemans[2], S.P. Berger[3], R.H.J.A. Slart[2,4], [1]Dept of Surgery - Transplantation, University Medical Center Groningen, [2]Dept of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, [3]Dept of Internal Medicine - Div of Nephrology, University Medical Center Groningen, [4]Dept of Biomedical Photonic Imaging, University of Twente, Enschede, The Netherlands

Postersessie – Klinisch 3

15. Kidney Retransplantation in the Ipsilateral Iliac Fossa: A Surgical Challenge (p. 121)
K. Muller[1], L.S.S. Ooms[1], J.I. Roodnat[2], F.J.M.F. Dor[1], T.C.K. Tran[1], H.J.A.N. Kimenai[1], J.N.M. IJzermans[1] and T. Terkivatan[1], [1]Dept of HPB and Transplantation Surgery, [2]Dept of Nephrology, Erasmus Medical Center, Rotterdam, The Netherlands

Postersessie – Klinisch 4

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

12.30 – 12.45

Moderator: Dr. Mariëlle A.C.J. Gelens, internist-nefroloog, MUMC

16. Comparison of estimated and measured Glomerular Filtration Rate in Longitudinal Follow-up after Living Kidney Donation (p. 122)
M. van Londen, J.S. Sanders, J.J. de Vries, M.F.C. de Jong, R.A. Pol, S.P. Berger, G.J. Navis and M.H. De Borst, University Medical Center Groningen, Groningen, The Netherlands

17. Results of the second decade of the Trans-Atlantic Airlift for renal transplantation recipients from the Dutch Antilles: an unique program comes of age (p. 123)
Z.A. Choudry[1], H. Peters Sengers[1], N. Ajubi[2], W. de Velter[2], R. Kock[3], J. Lardy[4], N.C. van der Weerd[1], J.J.H. van der Heijde[1], K.A. van der Pant[1], M.M. Idu[5] and F.J. Bemelman[1], [1]Renal Transplant Unit, Dept of Nephrology, [2]St. Elisabeth Hospital, Curaçao, [3]Dr. Horacio E. Oduber Hospital, Aruba, The Dutch Antilles, [4]Dept of Immunogenetics, Sanquin Diagnostic Services, Amsterdam, [5]Dept of Surgery, Academic Medical Center Amsterdam, The Netherlands

18. A single-center retrospective study of kidney graft survival after transplantation with a DCD-II donor kidney (p. 124)
N. Slebioda, L.B. Hilbrands and M.C. Baas, Dept of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands

Postersessie – Klinisch 4

19. Conversion from tacrolimus-based to everolimus-based immune-suppressive therapy 3 months after living-donor kidney trans-plantation: A randomized-controlled clinical trial (p. 125)
R. Bouamar[1], N. Shuker[1,2], J.A.J. Osinga[1,2], M.C. Clahsen-van Groningen[3], J. Damman[3], C.C. Baan[2], J. van de Wetering[2], A.T. Rowshani[2], J. Kal-van Gestel[2], W. Weimar[2], T. van Gelder[1,2] and D. A. Hesselink[2], [1]Dept of Hospital Pharmacy, [2]Dept of Internal Medicine, [3]Dept of Pathology, Erasmus Medical Center, Rotterdam, The Netherlands

20. The effectiveness of non-surgical interventions in biliary duct complications after liver transplantation (p. 126)
F.J.M. Roos[1,3], J.W. Poley[1], B.E. Hansen[1], A. Moelker[2], W.G. Polak[3] and H.J. Metselaar[1], [1]Dept of Gastroenterology and Hepatology, Erasmus Medical Center Rotterdam, Rotterdam, [2]Dept of Interventional Radiology, Erasmus Medical Center Rotterdam, Rotterdam, [3]Dept of Surgery, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

Postersessie – Klinisch 5

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

12.45 – 13.00

Moderator: Drs. Femke M. Molenaar, internist-nefroloog, UMC Utrecht

21. Overweight kidney transplant recipients are at risk of being overdosed following standard bodyweight-based tacrolimus dosing (p. 127)
L.M. Andrews[1], B.C.M. de Winter[1], J.T. Tang[2], N. Shuker[1], R. Bouamar[1], R.H.N. van Schaik[3], B.C.P. Koch[1], T. van Gelder[1,4] and D.A. Hesselink[4], [1]Dept of Hospital Pharmacy, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Dept of Laboratory Medicine, West China Hospital of Sichuan University, Chengdu, China, [3]Dept of Clinical Chemistry, [4]Dept of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

Postersessie – Klinisch 5

22. Opposite Acute Potassium and Sodium Shifts During Transplantation of Machine Perfused Human Liver Grafts (p. 128)
L.C. Burlage[1,2], L. Hessels[3], R. van Rijn[1,2], N. Karimian[1,2], A.C. Westerkamp[1,2], A.P.M. Matton[1,2], K. Reyntjens[4], I. Petzold[4], M.W. Nijsten[3] and R.J. Porte[1]. [1]Section of Hepatobiliary Surgery and Liver Transplantation, Dept of Surgery, [2]Surgical Research Laboratory, Dept of Surgery, [3]Dept of Critical Care, [4]Dept of Anesthesiology, University of Groningen, University Medical Center Groningen.

23. Coagulatory state in renal transplants recipients. Is there a differrence between dialysis patients and pre-emptively transplanted patients? (p. 129)
G.J. Nieuwenhuijs-Moeke[1], T.A.J. van den Berg[2], S.J.L. Bakker[3], T. Lisman[4] and R.A. Pol[2], [1]Dept of Anesthesiology, University Medical Center Groningen, Groningen, [2]Dept of Surgery, Div of Transplantation Surgery, University Medical Center Groningen, Groningen, [3]Dept of Nephrology, University Medical Center Groningen, Groningen, [4]Surgical Research Laboratory and Section of Hepatobiliary Surgery and Liver Transplantation, Dept of Surgery, University Medical Center Groningen, Groningen, The Netherlands

24. Hair matters: underrated side effect of immunosuppressive therapy in children (p. 130)
A.H.M. Bouts[1] and M.A. Middelkamp-Hup[2], [1]Dept of Pediatric Nephrology, [2]Dept of Dermatology, Academic Medical Center, Amsterdam, The Netherlands

25. "What if this is my chance to save my life?" The patient perspective on public solicitation of living kidney donors (p. 131)
M.C. Pronk[1], D. Slaats[1*], W.C. Zuidema[1], M.T. Hilhorst[2], F.J.M.F. Dor[1, 3], M. Betjes[1], W. Weimar[1], J. van de Wetering[1], E.K. Massey[1]. *Shared first authorship; [1]Dept of Internal Medicine, Nephrology and Transplantation, Erasmus MC, University Medical Center, Rotterdam, The Netherlands; [2]Dept of Medical Ethics and Philosophy, Erasmus MC, University Medical Center Rotterdam, The Netherlands; [3] West London Renal and Transplant Centre, Dept of Renal and Transplant Services, Hammersmith Hospital, Imperial College, London, United Kingdom*

Donderdag 9 maart 2017

Postersessie – Verpleegkundig

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

13.00 – 13.15

Moderator: John Dackus, verpleegkundig specialist, Maastricht UMC

26. Niet harder maar slimmer werken (p. 132)
D. Pilzecker, Y. Hooghof, I. Dooper, H. Kloke, Dept of Nephrology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

27. The influence of surgical site infections on quality of life in live kidney donors (p. 133)
K. Muller, R.C. Minnee, H.J.A.N. Kimenai, L.S. Ooms, S. Janki, E.N. Bossenbroek, T. Terkivatan, J.N.M. IJzermans, Dept of HPB and transplantation surgery, Erasmus Medical Center, Rotterdam, The Netherlands

28. Intimiteit, seksualiteit en veilig vrijen na transplantatie (p. 134)
J. van der Laan[1], I. Saro[2], G. Bolt[3], [1]Niertransplantaties, Universitair Medisch Centrum Groningen, [2]Levertransplantaties, Universitair Medisch Centrum Groningen, [3]Groningen Transplantatie Centrum, Groningen, The Netherlands

29. SIEB: suikers in eigen beheer (p. 135)
M.J.M. van Helden, M.C. Baas, Nierziekten, Radboud UMC, Nijmegen, The Netherlands

30. Vitamine D suppletie bij Cystic Fibrosis patiënten na longtransplantatie (p. 136)
M.E. Janssen, M.J.C. Wessels-Bakker, J.M. Kwakkel-van Erp, E.A. van de Graaf. Divisie Hart & Longen, Universitair Medisch Centrum Utrecht

Postersessie – Basaal 1

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

12.30 – 12.45

Moderator: Dr. Bauke G. Hepkema, medisch immunoloog, UMC Groningen

31. PRISM: A Fast, Compact, In-line, High Yield, Human Pancreatic Islet Isolation Method (p. 137)
J.B. Doppenberg, M.A. Engelse and E.J.P. de Koning, Leiden University Medical Center, Leiden, The Netherlands

32. Bacterial translocation after liver transplantation is associated with biliary complications (p. 138)
J.W. Selten[1], F.J.M. Roos[1], C.J. Verhoeven[1], H.J. Metselaar[2], J.N.M. IJzermans[1] and L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus Medical Center Rotterdam, Rotterdam, [2]Dept of Gastroenterology and Hepatology, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

33. Bile Duct Strictures after Liver Transplantation are Associated with a Donor Glypican-6 Polymorphism Linked to the Biliary Stem Cell Niche (p. 139)
J.W. Selten[1], F.J.M. Roos[1], C.J. Verhoeven[1], H.J. Metselaar[2], J.N.M. IJzermans[1] and L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus Medical Center Rotterdam, Rotterdam, [2]Dept of Gastroenterology and Hepatology, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

34. Effective delivery of Mesenchymal Stromal cells during isolated liver machine perfusion to promote graft repair on the pump (p. 140)
M.M.A. Verstegen[1], K. Wang[1], L. Mezzanotte[2], J.P. van Kooten[1], S. van den Hoek[1], I. Schurink[1], P.E. de Ruiter[1], R. Yanto Ridwan[2], M.J. Hoogduijn[3], J.M. Sierra Parraga[3], C.W.G.M. Löwik[2], J.E. de Haan[4], P.A.C. de Specht[4], L.J.W. van der Laan[1] and J. de Jonge[1], [1]Dept Surgery, [2]Dept Radiology, [3]Dept Internal Medicine and [4]Dept of Intensive Care, Erasmus Medical Center, Rotterdam, The Netherlands

35. Treating ischemically damaged porcine kidneys with mesenchymal stromal cells during normothermic machine perfusion (p. 141)
M.B.F. Pool[1], J.M. Sierra Parraga[2], M. Roemeling-van Rhijn[3], M.E.J. Reinders[4], M.J. Hoogduijn[2], R.J. Ploeg[1,5], H.G.D. Leuvenink[1] and C. Moers[1], [1]Dept of

Postersessie – Basaal 1

Surgery – Organ Donation and Transplantation, University Medical Center Groningen, University of Groningen, Groningen, [2]Dept of Internal Medicine, Erasmus Medical Center, University of Rotterdam, Rotterdam, [3]Dept of Internal Medicine, University Medical Center Groningen, University of Groningen, Groningen, [4]Dept of Nephrology, Leiden University Medical Center, University of Leiden, Leiden, The Netherlands, [5]Oxford Transplant Center, University of Oxford, Oxford, United Kingdom

Postersessie – Basaal 2

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

12.45 – 13.00

Moderator: Dr. Erik M. van Maarseveen, ziekenhuisapotheker, UMC Utrecht

36. Tacrolimus-based immunosuppression only marginally affects monocyte activation after kidney transplantation (p. 142)
*N.M. Kannegieter[1], D.A. Hesselink[1], M. Dieterich[1], G.N. de Graav[1], R. Kraaijeveld[1], A.T. Rowshani[1], P.J.M. Leenen[2] and C.C. Baan[1], Dept of [1]Internal Medicine, *Section Nephrology and Transplantation, and [2]Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands*

37. The effect of tacrolimus and mycophenolic acid on CD14+ monocyte activation and function (p. 143)
*N.M. Kannegieter[1], D.A. Hesselink[1], M. Dieterich[1], R. Kraaijeveld[1], A.T. Rowshani[1], P.J.M. Leenen[2] and C.C. Baan[1], Dept of [1]Internal Medicine, *section Nephrology and Transplantation, and [2]Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands*

38. Variations in DNA methylation of interferon gamma and programmed death 1 in allograft rejection after kidney transplantation (p. 144)
K. Boer[1], L.E.A. de Wit[1], F.S. Peters[1], D.A. Hesselink[1], L.J. Hofland[2], M.G.H. Betjes[1], C.W.N. Looman[3], C.C. Baan[1], Dept of Internal Medicine, section Nephrology and Transplantation[1], section Endocrinology[2], Dept of Public Health[3], Erasmus University Medical Center, Rotterdam, The Netherlands

Postersessie – Basaal 2

39. In Vivo Anti-microRNA Treatment In a Humanized Mouse Model for Allograft Vasculopathy (p. 145)
M.M.H. Huibers[1], L. Qin[2], G. Li[2], J. Renes[1], C.L. Venema[1], E. Siera-de Koning[1], J. van Kuik[1], A.L.M. Peeters[1], G. Tellides[2], R.A. de Weger[1], [1]Dept of Pathology, University Medical Center, Utrecht, the Netherlands, [2]Dept of Surgery, Yale University School of Medicine, New Haven, Connecticut, USA

40. Healthcare law analyses of the Donor Registry in the Netherlands: Is registered consent to organ donation legally binding after death? (p. 146)
D.C. Georgieva[1], N.E. Jansen[2], B.J.J.M. Haase-Kromwijk[3], [1]lawyer at the Dutch Transplant Foundation, [2]researcher and senior policy maker at the Dutch Transplant Foundation, [3]director of the Dutch Transplant Foundation

Postersessie XV – Basaal 3

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

13.00 – 13.15

Moderator: Dr. Junior M. Lardy, medisch manager, Sanquin, Amsterdam

41. CD4+CD28null T Cells Require Exogenous Cytokines to Become Allo-reactive (p. 147)
B. Dedeoglu, N.H.R. Litjens, R. Kraaijeveld, W. Verschoor, C.C. Baan, M.G.H. Betjes, Dept of Internal Medicine, section Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands

42. Taking the HLA-specific memory B cell elispot to the next level: assaying the full donor HLA repertoire (p. 148)
G.E. Karahan[1], Y. de Vaal[1], J. Krop[1], D. Roelen[1], F.H.J. Claas[1], S. Heidt[1], [1]Dept of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands

Postersessie XV – Basaal 3

43. Computational approaches to facilitate epitope-based HLA matching in solid organ transplantation (p. 149)
K. Geneugelijk[1], J. Wissing[1], D. Koppenaal[1], M. Niemann[2], and E. Spierings[1], [1]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands, [2]PIRCHE AG, Berlin, Germany

44. Ectopic lymphoid structures are present in type I T-cell mediated kidney transplant rejection (p. 150)
K. de Leur[1,2], M.C. Clahsen-van Groningen[3], G.N. de Graav[1], D.A. Hesselink[1], J.N. Samsom[4], C.C. Baan[1], K. Boer[1], [1]Dept of Internal Medicine, Section Transplantation & Nephrology, [2]Dept of Surgery, Division of HPB & Transplant Surgery, [3]Dept of Pathology, [4]Dept of Pediatrics, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands

45. Patients with renal failure have a pERK-dependent defective TCR-mediated activation of CD4+ T cells (p. 151)
L. Huang, N.H.R. Litjens, N.M. Kannegieter, M. Klepper, C.C. Baan, M.G.H. Betjes, Division of Nephrology and Transplantation, Dept of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands

Donderdag 9 maart 2017

Sessie XIV – Plenair — Hendrik Marsmanzaal

Voorzitters: *Dr. Erik Spierings, medisch immunoloog, UMC Utrecht*
Prof. dr. Marianne C. Verhaar, hoogleraar experimentele nefrologie, UMC Utrecht

Thema: **Big Data**

13.30 **PROCARE**
Dr. Henny G. Otten, immunoloog, UMC Utrecht

14.00 **iGene TRAiN**
Prof. dr. Folkert W. Asselbergs, cardioloog, UMC Utrecht

Parallelsessie XV – Basaal — Hendrik Marsmanzaal

Voorzitters: *Drs. Kirsten C.A. Geneugelijk, onderzoeker i.o., UMC Utrecht*
Prof. dr. Cees C. van Kooten, onderzoeker, Leids UMC

Thema: **Moleculaire analyses en het adaptieve immuunsysteem in orgaantransplantatie**

Abstract presentaties in het Engels, spreektijd 8 minuten, discussietijd 4 minuten.

14.30 Targeting inflammatory kidney disease locally using liposomal prednisolone (p. 99)
C.M.A. van Alem[1], T. Bezhaeva[1], M. Boonstra[2], R.A. Lalai[1], A. Koudijs[1], J.M. Metselaar[3,4], M.E. Reinders[1], C. van Kooten[1] and J.I. Rotmans[1], [1]Dept of Nephrology[1], Leiden University Medical Center, [2]Dept of Surgery, Leiden University Medical Center, [3]Enceladus Pharmaceuticals, Naarden, The Netherlands, [4]Experimental Molecular Imaging, University Clinic, RWTH-Aachen University, Aachen, Germany

14.42 The autoimmune-associated single nucleotide polymorphism within PTPN22 correlates with clinical outcome after lung transplantation (p. 100)

K. Budding[1], J. van Setten[2], E.A. van de Graaf[3], 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, University Medical Center Utrecht, Utrecht, [2]Dept of Cardiology, University Medical Center Utrecht, Utrecht, [3]Dept of Respiratory Medicine, University Medical Center Utrecht, Utrecht, [4]Center of Interstitial Lung Diseases, St. Antonius Hospital, Nieuwegein ,[5]Dept of Rheumatology and Dermatology, University Medical Center Utrecht, Utrecht, The Netherlands

14.54 CMV-specific CD4+ T cells in CMV-IgG-seronegative individuals protect from CMV viremia following transplantation with a CMV-seropositive donor kidney (p. 101)

L. Huang, N.H.R. Litjens, B. Dedeoglu, R.W.J. Meijers and M.G.H. Betjes, Dept of Internal Medicine, Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands

15.06 IL-21R antagonist inhibits differentiation of B cells towards plasmablasts upon alloantigen stimulation (p. 102)

K. de Leur[1,2], F.J.M.F. Dor[2], M. Dieterich[1], L.J.W. van der Laan[2], R.W. Hendriks[3] and C.C. Baan[1], [1]Dept of Internal Medicine, [2]Dept of Surgery, Division of HPB & Transplant Surgery, [3]Dept of Pulmonary Medicine, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands

15.18 Multiplex PCR Screening of MicroRNAs in Graft Preservation Fluid during Liver Transplantation for Biomarker Discovery (p. 103)

J.W. Selten[1], H.P. Roest[1], A.J.M. Gillis[2], L.C.J. Dorssers[2], J. de Jonge[1], L.H.J. Looijenga[2], J.N.M. IJzermans[1] and L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus Medical Center, Rotterdam, [2]Dept of Pathology, Erasmus Medical Center, Rotterdam, The Netherlands

15.30 MinION Single Molecule Sequencing: the new way of HLA allele resolution typing in low and high volume laboratories (p. 104)

M. Groeneweg, C.E.M. Voorter, T.W.M. Slangen, C.M. Meertens, F. Palusci and M.G.J. Tilanus, Transplantation Immunology, Tissue Typing Laboratory, Maastricht University Medical Center, The Netherlands

Parallelsessie XV – Basaal **Hendrik Marsmanzaal**

15.42 Differential effects of immunosuppressive drugs on DNA methylation in T cells (p. 105)
F.S. Peters[1], A.M.A. Peeters[1], L.J. Hofland[2], M.G.H. Betjes[1], K. Boer[1] and C.C. Baan[1], Dept of [1]Internal Medicine, Nephrology and Transplantation, [2]Endocrinology, Erasmus University Medical Center, Rotterdam, The Netherlands

15.54 Einde abstractsessie

16.00 Theepauze

Parallelsessie XVI – Young investigators **Copijnzaal**

Voorzitters: Dr. Manon M.H. Huibers, onderzoeker, UMC Utrecht
Drs. Laura A. Michielsen, arts-onderzoeker, UMC Utrecht

14.30 **Young investigators sessie**
Jonge wetenschappelijke onderzoekers vinden het vaak lastig om kort en aantrekkelijk over hun onderzoek te vertellen. Ze willen hun verhaal het liefst zo genuanceerd en correct mogelijk over het voetlicht brengen en dat botst met een kernachtige presentatie. Daarnaast zijn jonge onderzoekers vaak te bescheiden over opmerkelijke resultaten. Toch hopen velen dat hun onderzoeksresultaten uiteindelijk ten goede komen aan de maatschappelijke praktijk

Tijdens de young investigators sessie zal er een workshop gegeven worden waarbij de deelnemers de essentie van hun verhaal vaststellen en leren zich kernachtig uit te drukken en boeiende verhalen te vertellen. Uitgangspunt is dat de deelnemers zoveel mogelijk aan het werk zijn en kunnen oefenen.

16.00 Koffiepauze

Parallelsessie XVII - Transplantatie coördinatoren Johan de Meesterzaal

Voorzitters: *Drs. Maaike A. Sikma, intensivist UMC Utrecht*
Maaike J.J. Sperber, transplantatie-coördinator UMC Utrecht

14.30 **Zorg om donatie, zorg na donatie en zorg voor donatie**

Deze door WTCN georganiseerde sessie is toegankelijk voor alle geïnteresseerde congresdeelnemers

Tijdens een interactieve sessie wordt aandacht gegeven en uw mening gevraagd over verschillende onderwerpen die voor, tijdens en na een postmortale orgaandonatie procedure een rol spelen.

16.00 Koffiepauze

Sessie XVIII – Prijsuitreikingen Hendrik Marsmanzaal

Voorzitters: *Dr. Marlies E.J. Reinders, voorzitter NTV, internist-nefroloog LUMC*
Dr. Arjan D. van Zuilen, voorzitter LOC, internist-nefroloog UMCU

16.15 Astellas Trans(p)la(n)t(at)ionele Research Prijs
Uitreiking prijs 2017

Lezing door prijswinnaar 2016: Drs. Tim C. van Smaalen, MUMC

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

16.28 LWTV Innovatie-kwaliteitsprijs
Uitreiking prijs 2017 door Louise Maasdam, voorzitter LWTV

Lezing door prijswinnaar 2016: Drs. Coby H. Annema-de Jong, UMCG

Donderdag 9 maart 2017

Sessie XVIII – Prijsuitreikingen — Hendrik Marsmanzaal

16.38 Uitreiking Distinguished Research Award 2017
door Dr. Marlies E.J. Reinders, voorzitter NTV

16.43 Gauke Kootstraprijs 2017
Uitreiking door Prof. dr. Gauke Kootstra, naamgever van de prijs
Lezing door de prijswinnaar

17.00 Sluiting door Dr. Arjan D. van Zuilen, voorzitter LOC

Ledenvergadering NTV — Hendrik Marsmanzaal

17.00 Algemene Ledenvergadering NTV

18.00 Vertrek

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The role of recipient epithelial cells in regeneration after liver transplantation: Different kinetics of chimerism for hepatocytes and bile duct epithelial cells

F.J.M. Roos[1], J.W. Selten[1], W.G. Polak[1], M.M. Verstegen[1], H.F.B.M. Sleddens[2], M. Doukas[2], H.J. Metselaar[3], J.N.M. IJzermans[1] and L.J.W. van der Laan[1], [1]Dept of Surgery, Erasmus Medical Center Rotterdam, Rotterdam, [2]Dept of Pathology, Erasmus Medical Center Rotterdam, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

Impaired regeneration of the biliary tree after liver transplantation has been linked to post-operative biliary complications and, more specific, to non-anastomotic bile duct strictures (NAS). Ischemic damage of stem cell populations in the graft may impair regenerative processes of both hepatocytes and bile duct epithelial cells (cholangiocytes). It has been hypothesized that recipient-derived (stem) cells may contribute to the restoration of the damaged graft and thereby establishing epithelial chimerism. Therefore, the aim of this study is to determine the extent and kinetics of recipient-derived hepatocytes and cholangiocyte repopulation in transplanted livers after graft explantation due to NAS and other reasons.
We retrospectively identified recipients which required a re-transplantation for various indications between 2001 and 2015. Recipient-derived cells in the liver explant were determined using immunohistochemistry for HLA-A2 and X- and Y-chromosome fluorescent in situ hybridization (FISH). Bile ducts were located by cytokeratin 19 staining.
Overall, 13 explants for which a re-transplantation was performed were included in this study, of which five for NAS. All were HLA-A2 positive recipient who received a HLA-A2 negative liver graft. Additionally, four grafts were of female donors transplanted in male recipients. Median time until re-transplantation was 167 days. In all grafts, extensive repopulation of hepatocytes and cholangiocytes by recipient cells was observed. These results were confirmed by XY-FISH analysis. The repopulation of hepatocytes was time dependent. A significant difference was observed between early and late re-transplantations (<180 days mean 8.3% ±SD 6.4 vs. 31.8% ±23.5 >365; p=0.03). In contrast, the percentage of recipient derived cholangiocytes in the same grafts was not time-dependent (10.8% ±12.9 vs. 8.5% ±8.5; p=0.75). No clear differences in hepatocyte repopulation was observed between NAS and the non-NAS group (11.8% ±9.6 vs. 26.0% ±27.2; p=0.38) though there was a trend toward more cholangiocyte repopulation in the NAS livers (13.8% ±12.7 vs. 3.5% ±4.4 p=0.054).

Conclusion: extensive epithelial chimerism occurs after liver transplantation. The kinetics of hepatocyte and cholangiocyte chimerism is significantly different, suggesting distinct underlying regenerative mechanisms.

Regeneration of kidney vasculature with human kidney-derived endothelial cells in decellularized rat and human kidneys

D. Leuning[1], A. de Graaf [1], C.W. van den Berg[1], E. Lievers[1], L. Wiersma[1], H. de Boer[1], C. Avramut[2], B. van den Berg[1], C. van Kooten[1], M. Reinders[1], M. Takasato[3], M. Little[4,5], M. Engelse[1] and T. Rabelink[1], [1]Nephrology, LUMC, Leiden, [2]Cell Biology, LUMC, Leiden, The Netherlands, [3]RIKEN Center for Developmental Biology, Kobe, Japan, [4]Murdoch Childrens Research Institute, Melbourne,[5]Pediatrics, The University of Melbourne, Australia

As there is a shortage of donor organs, there is an urgent need for new alternatives. One future alternative could be a bioengineered kidney by recellularization of a kidney scaffold with patient-derived cells. In order to achieve a functional bioengineered kidney, the vasculature should be intact. Here we study regeneration of kidney vasculature with human kidney-derived endothelial cells in both rat- and human kidney scaffolds.
Kidney scaffolds were obtained by decellularizing rat- and human transplant grade kidneys (n=3) with 1% SDS and 0.1% TritonX-100. Preservation of structure, integrity and glycosaminoglycan (GAG) landscape of the scaffolds was analyzed with immunofluorescence for collagen type IV, fibronectin, vitronectin, laminin and heparan sulfate proteoglycans. Scaffolds were preloaded with resp. 0, 10 and 100 ng/ml vascular endothelial growth factor (VEGF). Rat whole organ and slices of human decellularized kidney were recellularized with human primary glomerular-derived microvascular endothelial cells (hgMVEC) or human induced pluripotent stem cell-derived endothelial cells (iPS-EC). Rat kidney scaffolds were recellularized via both the renal artery and renal vein and cultured for 7 days in a custom-made organ chamber. Cell survival, adherence and coverage were analyzed by CD31 immunofluorescence and confocal microscopy.

To conclude, human and rat kidneys showed a preservation of structure, integrity and GAG landscape after decellularization. Site specific binding of the growth factors VEGF and basic fibroblast growth factor (bFGF) was observed on these scaffolds. hgMVEC cell adherence of 20% coverage was observed in the absence of VEGF, while preloading the kidney scaffold slices with 100 ng/mL VEGF increased cell adherence to 55% coverage ($P<0.001$). iPS-EC showed a similar capacity to adhere to human kidney scaffold slices. Rat decellularized kidneys showed intact vascular integrity as shown by fluorescent bead perfusion via resp. the renal artery, renal vein and urether. We show that recellularization of rat kidney scaffolds with hgMVEC via both the artery and the vein gave the highest coverage of endothelial cells in both the glomeruli and the peritubular vessels without leakage towards the tubuli.
Here we show an extensive characterization of both rat- and human kidney scaffolds for the GAG landscape and established an increase in human kidney-derived endothelial cell adherence after loading of the scaffold with VEGF. Moreover, we show a novel recellularization method of rat kidney scaffolds in an organ chamber where long term organ-culture could be achieved. These results are a promising step towards a bioengineered kidney.

Expansion and characterization of peribiliary gland-resident stem cells using organoid cultures

M.M.A. Verstegen[1], M. de Wolf[1], K. Burka[1], M.J.C. Bijvelds[2], H. Gehart[3], J.N.M. IJzermans[1], H.R. de Jonge[2] and L.J.W. van der Laan[1], [1]Dept of Surgery, [2]Gastroenterology & Hepatology, Erasmus Medical Center-University Medical Center, Rotterdam, [3]Hubrecht Institute, Utrecht, The Netherlands

Integrity of the biliary tree is imperative for liver function. Though evidence suggests that peribiliary glands (PBG) harbor stem cells which contribute to bile duct homeostasis and repair during disease and injury, these biliary stem cells are still not well characterized. In addition, the PBG may also play a role in repairing ischemic damage during liver transplantation. Therefore, the aim of this study is to expand and characterize biliary stem cells using 3-dimensional (3D) organoid cultures from bile ducts. Human extra-hepatic bile ducts (n=32) were collected from donor liver grafts or explant patient livers at time of liver transplantation. Biliary organoid cultures were initiated using similar conditions as described for human liver biopsies and propagated by weekly passaging for over 6 months. RNA expression analysis (q-PCR) and immunohistochemistry was performed. Transporter channel function was measured using Ussing chamber technology and Forskolin Induced Swelling (FIS) assays. In addition, the hepatocyte differentiation potential of biliary stem cells was studied.

Organoids were efficiently grown from the common bile duct for many passages (>6 months) and compared to liver parenchyma-derived organoids. As expected, bile duct organoids stain positive for biliary cell markers CK19, Epcam and MUC1. RNA analysis showed expression of stem cell markers LGR5, PDX1 and Sox9 and showed less hepatic differentiation capacity of biliary organoids compared to liver organoids. Preliminary results suggest the presence of functional transport channels in the biliary organoids, as they were responsive to forskolin, vasoactive intestinal peptide (VIP) and bicarbonate. Extensive characterization of the 3D cultures using proteomics and gene-array analysis are ongoing.

This study demonstrates the presence of LGR5-positive stem/progenitor cells in human extra hepatic bile duct. These organoids can be propagated long-term, express hepato-biliary genes and proteins, and show functional transporter channel activity. Biliary organoids could potentially be used to model biliary disease and biliary strictures after liver transplantation.

Ageing of bone marrow and umbilical cord derived MSC during culture expansion

S.F.H. de Witte[1], E.E. Lambert[1], A.M. Merino[1], T. Strini[1], J.C.W. Douben[2], S.J. Elliman[3], P.N. Newsome[4], J.E.M.M. de Klein[2], C.C. Baan[1] and M.J. Hoogduijn[1], [1]Nephrology and Transplantation, Dept of Internal Medicine, [2]Dept of Clinical Genetics Medicine, Erasmus Medical Center, Rotterdam, The Netherlands, [3]Orbsen Therapeutics Ltd., Galway, Ireland, [4]Dept of NIHR Liver Biomedical Research Unit and Center for Liver Research, University of Birmingham, United Kingdom

Mesenchymal stromal cells (MSC) are used as experimental immunotherapy. Extensive culture expansion is necessary to obtain clinically relevant cell numbers, although the impact of this on MSC stability and function is unclear. Also, for clinical standardization it is relevant to identify up until when MSC maintain their properties to secure therapeutic efficacy. Here we study the effects of long-term *in vitro* culture expansion on the stability and function of MSC.

Human bone marrow derived MSC (bmMSC) and umbilical cord derived MSC (ucMSC) were *in vitro* expanded. During expansion their proliferative capacity was examined. At passages 4, 8 and 12 multiple analyses were carried out on MSC cultures to investigate the ploidy, metabolic stability, telomere length and immunophenotype. In addition, their potential to suppress lymphocyte proliferation and susceptibility to NK cell lysis was examined by FACS.

Both bmMSC and ucMSC showed decreasing proliferative capacity over time, whilst their telomere lengths and mitochondrial activity remained stable. The percentage of aneuploidy in cultures was unchanged after extensive expansion. In addition, expression of MSC markers CD13, CD73, CD90, CD105 and markers potentially associated with stress or ageing such as HLA type I and II and PDL-1 remained unchanged in both cultures. Reduced suppression of CD4 and CD8 T-cell proliferation was observed at passage 8 and 12 ucMSC compared to passage 4. Finally, susceptibility of bmMSC and ucMSC to NK cell lysis was similar among all passages.

We showed that after long-term expansion, the phenotype of bmMSC and ucMSC remains stable and cells exhibit similar immunogenic properties compared to lower passage cells. However, the immunosuppressive properties of MSC are reduced after long term culture. These findings reveal the consequences of application of higher passage MSC in the clinic, which will indeed help increase the total yield of therapeutic MSC, but may interfere with their efficacy.

Changes in Myocardial Microvascularisation After Heart Transplantation and During Cardiac Allograft Vasculopathy

M.M.H. Huibers[1], F. van Pijpen[1], H.J.H. Kirkels[2], N. de Jonge[2], A. Vink[1] and R.A. de Weger[1], [1]Dept of Pathology and [2]Cardiology, University Medical Center Utrecht, The Netherlands

Cardiac allograft vasculopathy (CAV) is a major threat to long-term survival of heart transplantation (HTx) recipients. Impaired microvascular structure and function have been shown to be present in heart failure and contribute to disease progression. However, limited research has been conducted into myocardial microvasculature after HTx and development of CAV. The aim of this study is to investigate microvascular density in the myocardium of HTx recipients and relate this to angiogenic gene expression. We hypothesize microvascular density to be decreased and angiogenic pathways to be downregulated in CAV patients.
Transversal mid ventricular heart slices were obtained from HTx recipients at autopsy. The cohort consists of 16 CAV negative patients who died within 0.5 years following HTx and 18 CAV positive patients who were diagnosed with CAV via histological evaluation of the coronary arteries post-mortem. Immunohistochemical staining (CD31) was used to study microvascular density in three layers of the myocardium (inner,- mid-, and outer myocardium). qPCR targeting 10 established angiogenesis and/or CAV related genes was performed to study gene expression (angiogenesis inhibitors: PF4, ET-1, TSP-1 and angiogenesis stimulating: VEGF-A, VEGF-C, Hif-1α, CD105, Notch1, FGF1, NOS3).
Microvascular density was increased in the outer layer of the heart of CAV positive HTx recipients compared to CAV negative recipients. Interestingly, the CAV positive group show much more interindividual variance in microvascular density compared to the CAV negative group. For overall gene expression, a trend towards upregulation was seen both the CAV positive and the CAV negative group compared to the cardiac tissue without transplantation. A mixed profile of pro- and anti-angiogenic genes was found to be upregulated in CAV positive patients.
Microvascular density is increased in the outer layer of the heart of HTx recipients with CAV compared to HTx recipients without CAV. An increased expression of angiogenesis stimulating and inhibiting genes was found in CAV patients. Combined, these findings suggest the activation of compensatory mechanisms. Due to the differences in microvascular density in the different layers of the heart, endomyocardial biopsies might not give a representative estimation of microvascular density for other layers in the heart.

Inflammatory conditions dictate the effect of MSC on B cell function

F. Luk[1], L. Carreras-Planella[2], S.S. Korevaar[1], S.F.H. de Witte[1], F.E. Borràs[2], M.G.H. Betjes[1], C.C. Baan[1], M.J. Hoogduijn[1] and M. Franquesa[1, 2], [1]Nephrology and Transplantation, Dept of Internal Medicine, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands, [2]Nephrology and Transplantation, Institut d'Investigació Germans Trias i Pujol, Badalona, Spain

The immunomodulatory capacity of mesenchymal stem or stromal cells (MSC) makes them a promising therapeutic tool for immune disease and organ transplantation. The effects of MSC on B cells are characterized by an abrogation of memory and plasmablast formation and induction of regulatory B cells. It is however unknown how MSC interact with B cells under inflammatory conditions.
In the present study MSC were isolated from adipose tissue and pre-treated with 50 ng/ml IFN-γ for 72h (MSC-IFN-γ) to simulate inflammatory conditions. Mature B cells were obtained from spleens by $CD43^-$ selection. B cells were co-cultured with MSC at a 10:1 ratio and stimulated with anti-IgM, anti-CD40 and IL-2. B cell proliferation and phenotype were analyzed by flow cytometry, and IgG and IL-10 production quantified by ELISA.
MSC were not capable of inhibiting the proliferation of B cells, while MSC-IFN-y significantly reduced B cell proliferation and were more potent in inhibiting IgG production by B cells. In contrast, MSC increased the percentage of IL-10 producing regulatory B cells ($CD19^+CD24^{hi}CD38^{hi}$), whereas MSC-IFNy lacked this capacity. Culturing B cells with MSC-IFN-y in a transwell system in order to investigate the mechanisms of action abolished the effect on B cell proliferation. Indoleamine 2,3 dioxygenase (IDO) expression was highly induced in MSC-IFN-y. By abolishing the effect of IDO by the addition of tryptophan (TRP), B cell proliferation and induction of regulatory B cells was restored.
Therefore, immunological conditions dictate the effect of MSC on B cell function: under immunological quiescent conditions MSC stimulate regulatory B cell induction, whereas under inflammatory conditions MSC inhibit B cell proliferation and IgG production through depletion of TRP. This knowledge is useful for designing of MSC therapy for specific purposes by appropriate pre-treatment of MSC.

In vivo tracking of live and dead mesenchymal stromal cells

S.F.H. de Witte[1], M. Gargesha[4], A.M. Merino[1], S.J. Elliman[4], P.N. Newsome[3], D. Roy[4], C.C. Baan[1] and M.J. Hoogduijn[1], [1]Nephrology and Transplantation, Dept of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Orbsen Therapeutics Ltd., Galway, Ireland, [3]Dept of NIHR Liver Biomedical Research Unit and Center for Liver Research , University of Birmingham, United Kingdom, [4]BioInVision Inc., Mayfield Village, OH, United States of America

Introduction: Mesenchymal stromal cells (MSC) are under investigation as an experimental immunomodulatory therapy. Their administration is commonly by intravenous (IV) infusion, although previous studies have reported that MSC infused by this method are trapped in the lungs and mostly disappear within a day. It is unclear what happens to MSC after their disappearance from the lungs. In the present study we examined the bio distribution and survival of MSC after IV infusion with CryoViz 3D imaging technology.

Material and Methods: Human umbilical cord derived MSC were double-labelled with Qtracker605 beads, which are contained in live cells, and Hoechst3242, which is a DNA stain visible in live and dead cells. Labelled MSC were infused via the tail vein (120 000) into C57Bl/6 mice. To analyse the bio distribution of live and dead cells, whole body imaging of mice was performed at 5 minutes and 24 hours after MSC infusion via 3D imaging using CryoViz.

Results: Directly after administration, the majority of MSC were alive and located in the lungs (86±11% from the total amount of cells present), with a small percentage located in the liver (2±0.5%). A small percentage of live MSC were identified in other organs at 5 min (16±9%) and 24 hours (2±1%). After 24 hours a significant decrease in the numbers of live MSC in the lungs was observed, whereas, an accumulation of dead cells was observed in the liver after 24 hours.

Discussion: From these data we can conclude that after getting trapped in the lungs, MSC are relocated to the liver after 24 hours, although at this stage most of the MSC are dead. The biological effect of the accumulation of dead MSC in the liver is yet unknown. These findings help us further understand the fate of MSC after IV infusion, which is useful for understanding the mechanisms of MSC therapy.

Association of repeated HLA mismatches with graft survival in kidney transplantation: data from the Dutch transplant registry

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Background: Kidney re-transplantation is a risk factor for decreased allograft survival. Among other factors, repeated mismatched HLA antigens potentially trigger an alloimmune memory response against the graft resulting in antibody mediated rejection or chronic allograft nephropathy. After the introduction of calcineurin inhibitors as standard immunosuppressive therapy, the question rises whether transplantation with a repeated HLA mismatch (RMM) is still a risk for decreased kidney allograft survival. Literature on this subject is inconclusive. Furthermore, the policy in transplant centers in the Netherlands for accepting a RMM differ substantially.
Objective: To evaluate the risk of a RMM (on the A, B or DR locus) on kidney allograft survival in the Dutch transplant registry (NOTR).
Methods: Between 1994 and 2014 records of 1698 re-transplants were found in the Dutch transplant registry (deceased donors and living donors). Of 160 transplantations no clinical data were available and of 517 transplantations it could not be determined whether there was a RMM, due to missing HLA data of a (previous) transplantation leaving 1,021 transplantations available for the current analyses. Patients were followed up for graft failure and mortality. The primary end point was graft failure with a potential immunological cause. Cox regression analysis was performed to calculate hazard ratios (HR) in RMM transplantations. Adjustments were performed for donor and recipient characteristics, year of transplant and PRA. Multiple imputation with 5 repetitions was performed to account for missing covariates.
Results: 919 transplantations (90%) were performed with a kidney without a RMM and 102 transplantations (10%) had a RMM on the A,B or DR locus (or both). Baseline characteristics were comparable between the groups, except for a higher percentage of living donation in the RMM group (57% versus 31%) and a subsequent shorter cold-ischemic time. 299 death-censored graft failures were registered of which 192 (64%) were classified as graft failures with a potential immunological cause. Of these graft failures, 19 occurred in the RMM group. After a median follow-up of 5.9 years, a significant decreased death-censored graft survival was observed for a DR RMM. Further analysis revealed an adjusted hazard ratio for immunological graft failure of 2.12 (1.09-4.09) for a HLA-DR RMM and 1.01 (0.49-2.06) for a HLA-A or HLA-B RMM. There was correlation of a RMM with patient survival.

Conclusion: A HLA-DR, but not HLA-A or -B RMM confers a substantial increased risk for graft failure. The risk of a HLA-DR RMM has to be weighed against the risk of staying on dialysis.

Course of donor specific anti-HLA antibodies after induction therapy with rituximab in renal transplantation

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The presence of pre-existing or de novo donor-specific antibodies against HLA (DSA), is associated with a worse graft outcome after renal transplantation. B-cell depletion protocols have shown to reduce DSA and chronic antibody mediated rejection. We aimed to study the effects of rituximab as a single-agent induction therapy on the titers of pre-existent or *de novo* DSA after renal transplantation and relate this to rejection free and overall graft survival.
We collected sera in participants of a prospective double-blind randomized study on the efficacy and safety of the prophylactic use of rituximab, added to standard immunosuppressive treatment (prednisolone, tacrolimus and mycophenolate mofetil) in comparison with standard immunosuppressive treatment alone in renal transplantation (www.clinicaltrials.gov, NCT00565331). 280 patients were included in this trial (142 received placebo, 138 rituximab). Serum before transplantation and at 12 months after transplantation was available in 127 placebo and 119 rituximab treated patients (total 246 patients).
At the moment of transplantation, 12.6% of placebo- and 8.4% of rituximab treated patients had anti-HLA class 1 antibodies. Pre-existent class 1 DSA were present in 7/127 (5.5%) placebo- and 5/119 (4.2%) rituximab treated patients (NS). In both groups all class 1 DSA disappeared at month 12 after transplantation.
Anti-HLA class 2 antibodies were present in 9.4% of placebo- and 8.4% of rituximab treated patients at the time of transplantation. Pre-existent class 2 DSA were present in 6/127 (4.7%) placebo- and 1/119 (0.8%) rituximab treated patients (NS). In the placebo group, class 2 DSA disappeared in 3 patients and persisted in the other 3. Class 2 DSA persisted in the patient treated with rituximab
2/127 (1.6%) placebo- and 2/119 (1.7%) rituximab treated patients developed *de novo* class 1 DSA (NS).
De novo class 2 DSA developed in 7/127 (5.5%) placebo-treated patients at 12 months and in only 1 patient treated with rituximab (0.8%, $p = 0.04$).
In conclusion, pre-existent class 1 DSA disappeared at 12 months after transplantation independent of rituximab induction therapy. Pre-existent class 2 DSA are less likely to disappear. Although only very few patients developed de novo DSA, rituximab induction therapy might inhibit the formation of *de novo* class 2 DSA.

Alemtuzumab is superior to ritxumab as induction therapy in ABO incompatible kidney transplantation

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Introduction: The standard protocol for ABO-incompatible (ABOi) kidney transplantation uses rituximab (RTX) as induction therapy. However, the results the ABOi program in our center showed a relative high rate of rejection compared to the ABO-compatible program and international reports from ABOi patient series. Alemtuzumab (ATZ) induction has been shown to reduce biopsy-proven acute rejection (BPAR) in both ABOc and ABOi kidney transplantation. Therefore, RTX induction was replaced for ATZ from April 2015 onwards.

Methods: All consecutive ABOi patients from 2006 till March 2015 received rituximab (RTX) 375 mg/m^2 4 weeks prior to transplantation. From April 2015 ATZ induction 30 mg was administered subcutaneously 3 weeks prior to transplantation, except for CMV negative patients with a CMV positive donor who received RTX. The protocol was the same in both groups and consisted of tacrolimus, mycofenolate mofetil and prednisone two weeks, immunoadsorption depending on baseline anti-A/B IgG titer 1 week and IVIG 1 gr/kg one day before transplantation. BPAR within three months and serum BK and CMV replication within one year were documented.

Results: 84 ABOi patients received RTX and 13 patients ATZ induction. Baseline characteristics were similar, especially for blood group (67 vs 58% type O in RTX vs ATZ), initial anti-A/B titer (median 32), peakPRA (median 4%in both groups) and total HLA MM (median 4 vs. 3.5 in ATZ). ATZ administration was well tolerated, but the majority of patients developed fever within 48 hours (7/13 patients documented fever >38.5 C with CRP max 92 mg/L). No case of BPAR developed in ATZ treated patients (0/12 versus 35/84 in RTX, $p < 0.005$). Major infectious complications consisted of Candida esophagitis and TBC after ATZ induction in the same patient from an endemic area for TB with negative interferon-gamma release assay and her transplantation was canceled. BK and CMV replication is not more common in ATZ treated patients (BK 13% vs 8% and CMV 15% vs 0% in RTX vs ATZ, both $p > 0.1$).

Conclusion: Alemtuzumab instead of rituximab induction in the ABOi desensitization protocol, significantly reduces the incidence of BPAR without an increase in opportunistic viral infections.

The value of repeat biopsies in kidney allograft recipients with delayed graft function

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Background: Delayed graft function (DGF) is a frequent complication after deceased donor kidney transplantation. It is general practice to perform kidneys biopsies during the period of DGF to exclude early allograft rejection. These biopsies are usually performed at roughly 10 days after transplantation. It is less clear whether biopsies should be repeated if DGF persists after 2 weeks. Hence, we evaluated the timing and diagnostic value of repeat biopsies in patients with DGF.

Methods: We included 619 deceased donor kidney transplantations performed between 2000 and 2007 at our centre. DGF was defined as the need for dialysis in the first week after transplantation. All biopsy reports were re-evaluated in accordance to the BANFF '09 classification. The results of the repeat biopsies were compared with the initial biopsy.

Results: A total of 199 cases (32.2%) were identified as DGF, of which 73 cases (36.7%) underwent at least 2 biopsies during the DGF period. The initial biopsies (B1) were performed at 13±12 (mean±SD) days after transplantation and the repeat biopsies (B2) at 23±10 (mean±SD) days. B1 revealed 19 cases (26.0%) with rejection and 54 cases (74.0%) without rejection. At B2 there were 34 cases (46.6%) with rejection and 39 cases (53.4%) without rejection. From B1 to B2 we observed 31 new cases (57.4%) of rejection in patients who had no rejection in the initial biopsy ($P<0.001$). When looking at the repeat biopsies in patients who had rejection at B1, 8 of 19 cases (42.1%) had resolution of rejection at B2 despite persisting DGF ($P=0.001$). Of the other 11 cases with persistent rejection at B2, 4 had the same BANFF score, 4 a higher BANFF score and 3 a lower BANFF score in the repeat biopsy.

Conclusions: There is a significant rate of new rejection cases in patients with persistent DGF if a kidney biopsy is repeated roughly 2 weeks after the first biopsy. Repeat biopsies during persisting DGF in patients with rejection at the first biopsy may prevent unnecessary escalation of rejection treatment. Our findings underscore the importance of repeat biopsies in patients with persistent DGF.

The role of donor-specific anti-HLA antibodies in kidney transplant survival revisited!

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The presence of donor-specific anti-HLA antibodies (DSA) is associated with increased risk of graft failure after renal transplantation. However, clinical relevance of DSA for graft survival is mainly studied in deceased-donor and not living-donor transplantations. In this Dutch multicenter study we investigated the impact of non-donor-specific HLA antibodies (NDSA) and DSA, assessed by using Luminex single antigen bead assay, on long-term graft survival in 3237 deceased- and 1487 living-donor renal transplantations. We found that after deceased-donor transplantation, patients with NDSA or DSA had a 10-years graft survival of 71% and 63%, which was significantly lower ($P<0.0001$) compared to the 77% graft survival rate of patients without HLA-antibodies. In contrast, (N)DSA had minimal effect on living-donor transplantations. In deceased-donor recipients, especially the combination of DSA but also NDSA against HLA class-I and -II had detrimental effects, showing a long-term graft survival of 54% and 67% respectively. Furthermore, both DSA and NDSA were associated with graft failure after 1 year, while only DSA showed an association with graft failure thereafter. In conclusion, DSA are associated with increased risk for graft failure but only in deceased- and not living-donor transplantations. In addition, on the long-term (N)DSA especially against HLA class-I and II are associated with increased graft failure in deceased-donor transplantations. Based on these results we suggest that patients with (N)DSA should be treated as a patients for higher risk for graft rejection unless transplanted with living-donor transplants.

Predicted Indirectly ReCognizable HLA epitopes presented by HLA-DRB1 (PIRCHE-II), a novel tool to identify permissible HLA mismatches in kidney transplantation

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Individual HLA mismatches may have differential effects on graft survival after kidney transplantation. Therefore, there is a need for a reliable tool to define permissible HLA mismatches in kidney transplantation. We previously demonstrated that Predicted Indirectly ReCognizable HLA epitopes of donor origin presented by recipient HLA class-II (PIRCHE-II) play a role in *de novo* DSA formation after kidney transplantation. In the present Dutch multi-center study we evaluated the possible association between PIRCHE-II and kidney graft failure in 3,061 donor-recipient couples that were transplanted between 1995 and 2005. For these donors-recipients couples, PIRCHE-II was determined and was related to graft survival in both univariate and multivariable analyses. Adjusted for confounders, the natural logarithm of PIRCHE-II was associated with a higher risk for graft failure (HR:1.11, 95% CI:1.04-1.17, p=0.001). Univariately analyzed, patients with low PIRCHE-II numbers had a better 10-years graft survival than patients with higher PIRCHE-II numbers (p=0.001; PIRCHE-II strata: <9, ≥9-<35, ≥35-<90, and ≥90 with 82%, 76%, 73%, and 70% 10-year graft survival). Our data suggest that the PIRCHE-II algorithm is a valuable tool to discriminate between permissible HLA mismatches and high-risk HLA mismatches in kidney transplantation. Inclusion of PIRCHE-II in donor-selection criteria may eventually lead to an improved kidney graft survival.

Two promoter polymorphisms in the genes encoding for complement regulating proteins CD46 and CD59 in kidney donors are associated with biopsy proven acute rejection

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Complement regulating proteins, including CD46, CD55 and CD59, protect cells against self-damage. Because of their expression on the donor endothelium, they are hypothesized to be involved in accommodation. Polymorphisms in their promoter regions may affect transcription. In lung transplantation, an insertion in the CD59 promoter in donors was associated with bronchiolitis obliterans syndrome. The aim of this study was to investigate if donor polymorphisms in complement regulating proteins influence kidney transplant outcomes.
We have included 317 kidney transplantations between 2005 and 2010. Five frequent polymorphisms in the promoters of CD46 (rs2796267 and rs2796268), CD55 (rs150046210 and rs283715831) and CD59 (rs147788946) were genotyped. Log-rank analyses were used to compare survival curves.
The absence of an insertion in the CD59 promoter (rs147788946) of donors was associated with a lower freedom from biopsy proven acute rejection or acute borderline rejection (BPAR) within the first year (p=0.04). Although the 5-year graft survival curve suggests an impaired graft survival, mainly early posttransplantation, this was not significant (p=0.13). Furthermore, for a single nucleotide polymorphism (SNP) in the CD46 promoter (rs2796267, A/G) we found that the presence of at least one G allele resulted in a lower freedom from BPAR within the first year (p=0.03). There was no correlation with 5-year graft survival (p=0.73). Next, we compared the presence of both protective genotypes in donors (n=24) to the presence of both risk genotypes (n=145). The results indicated an even more distinct difference in freedom from BPAR within the first year between both groups (p=0.007). Moreover, the presence of both protective genotypes was also correlated with an improved 5-year graft survival (p=0.04). Finally, a second SNP in the CD46 promoter (rs2796268, A/G) showed a trend towards a lower freedom from BPAR in the presence of at least one G allele (p=0.08). CD55 promoter SNPs did not significantly correlate with transplant outcomes.

These results suggest that two promoter polymorphisms in CD46 (rs2796267) and CD59 (rs147788946) in kidney donors correlate with a lower freedom from BPAR within the first year. Although numbers are relatively low, the combined presence of both protective genotypes appeared to have an additional preservative effect on freedom from BPAR and 5-year graft survival.

Colorectal carcinoma after renal transplantation: Screening looks like a valuable option

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Introduction: The risk of developing colorectal carcinoma (CRC) is increased after transplantation. Screening for CRC is performed from the age of 55 years in the Netherlands. We investigated the incidence and characteristics of CRC in Dutch renal transplant recipients (RTRs) and evaluated whether and when screening is required after transplantation.
Methods: After linking the Dutch Organ Transplant Registry (NOTR) with the Dutch Cancer Registration (IKNL), we registered all RTRs who developed CRC. We calculated the incidence rate of CRC in the RTRs in total, per age category, per year after transplantation and per years of immunosuppression, using the incidence in the general population as reference. Further statistical analysis calculated survival, age at diagnosis and mean time till diagnosis of CRC.
Results: Between 1968 and October 2014, 21016 renal transplantations were performed in 17771 RTRs in the Netherlands. 198 Patients developed 208 CRCs after transplantation. Overall incidence of CRC in our renal RTRs was increased by a ratio of 2.34 (2.04-2.86). When divided per age group at diagnosis we found significantly increased ratios; 35-39 yrs.: 5.26(1.97-14.03), 45-49 yrs.: 2.48(1.41-4.36) and 50-54 yrs.: 2.38(1.61-3.53), when compared with the general population. The incidence ratio gradually increased along the years of immunosuppression. An exposure of 5 yrs. resulted in a relative risk of 1.4(1.08-1.82), till 4.8(2.59-8.13) after 31-35 years of immunosuppression. RTRs developed CRC at a mean age of 60-64, compared to 70-74 years in the general population. The absolute risk of CRC in RTRs was comparable to that of a 10-year older person in the general population. Median survival time after diagnosis of CRC is 2 years (range 0-19). Using a binary logistic regression, we found that more years of immunosuppression (starting at 1-5 yrs, using 5 year categories) respectively gave a RR of 1.3, 2.3, 2.8, 4.4 and 5.2 of developing CRC. Higher age at transplantation is also associated with increased risks (using categories 26-40, 41-55, 56-70 and 71-100; 1.4, 2.2, 4.0, 5.0 respectively). There was no interaction.
Discussion: Age at transplantation and years of immunosuppressive treatment significantly increased the incidence for CRC in Dutch RTRs compared with the general population. The absolute risk of CRC in RTRs at the age of 45 years is similar to that of the general population at 55 years, which makes it necessary to start screening 10 years earlier.

Actieve ziekte pre-transplantatie is een onafhankelijke risicofactor voor terugkeer van primaire scleroserende cholangitis (PSC) post-levertransplantatie

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Primaire scleroserende cholangitis (PSC) is een chronische leverziekte, welke kan leiden tot levercirrose of recidiverende cholangitis. Levertransplantatie (LTx) is de enige curatieve optie. PSC kan echter terugkeren (recurrence of rPSC) met een negatief effect op transplantaat- en patiëntoverleving. De factoren die leiden tot deze terugkeer zijn niet opgehelderd. Deze studie is gericht op het identificeren van risicofactoren voor rPSC.
Inclusie criteria: Alle levertransplantaties voor PSC verricht in ons centrum tussen 1990-2015. Exclusie criteria: minder dan 6 maanden follow-up na LTx en a. hepatica trombose/stenose. De diagnose rPSC is gebaseerd op de Mayo Clinic criteria. Uitgebreide pre, peri-, en posttransplantatie gegevens zijn verzameld. Resultaten zijn weergegeven als gemiddelde (±SD) en mediaan (25th–75th%) en analyses middels Kaplan-Meier overlevingscurves, uni- en multivariabele (tijdsafhankelijke) Cox regressie.
In totaal zijn 191 transplantaties uitgevoerd voor PSC, waarvan 47 geëxcludeerd (n=33 wegens follow-up < 6 maanden en n=14 voor arteriële complicaties) en uiteindelijk 144 transplantaties geanalyseerd. LTx indicaties waren levercirrose (n=88), recidiverende cholangitis (n=40) en combinatie (n=16). Karakteristieken van de 1e LTx (n=121) zijn: leeftijd ontvanger 46.7 (±11.9) jaar; 85 (70.2%) mannen; gemiddelde follow-up 6.68 (±5.03) jaar; donor type DBD 103 (85.1%), DCD 15 (12.4%) en 3 levende donaties. Bij 29 (20.1%) transplantaties is rPSC vastgesteld, waarvan 19 na 1e LTx en 7 na retransplantatie. De gemiddelde tijd tot rPSC was 5.3 (±3.7) jaar. Patiëntoverleving op 1, 3, 5 en 10 jaar zonder rPSC was 95.5%, 92.4%, 89.8% en 78.4% en met rPSC 96.4%, 92.6%, 87.9% en 72.6% (HR 1.93; 95%CI 0.67-5.5; p=0.22). Op basis van de multivariabele analyse gaf alleen de indicatie voor transplantatie "recidiverende cholangitis" significant meer risico op rPSC (HR 2.91; 95%CI 1.34-6.36; p=0.01) in vergelijking met de indicatie "cirrose". Eerder beschreven risicofactoren voor rPSC als inflammatoire darmziekten, colectomie, perioden van rejectie en donorleeftijd konden in dit cohort niet worden bevestigd.
Onze studie suggereert dat patiënten die getransplanteerd zijn voor recidiverende cholangitis (actieve ziekte) vaker rPSC ontwikkelen na levertransplantatie in vergelijking tot patiënten getransplanteerd voor PSC cirrose (eind-stadium). Dit is een belangrijke nieuwe bevinding die verder bevestigd moet worden in grotere (multicenter) studies.

Mycophenolate Mofetil trough levels and Chronic Lung Allograft Dysfunction in lung transplant recipients

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Mycophenolate Mofetil (MMF) is standard immunosuppression in lung transplant (LTx) recipients. Research into MMF pharmacokinetics has revealed great variability of inter- and intrapatient MPA bio-availability. Advised target range in lung transplantation is 2,5-4.5 mg/L. However, daily dose is often reduced based on side effects irrespective of trough levels. We studied whether low MMF trough levels is related to the development of chronic lung allograft dysfunction (CLAD). A better understanding of MMF dose, trough level and its relation to CLAD may improve treatment strategies for LTx.

MMF mean trough level and development of CLAD was retrospectively studied in 142 LTx patients transplanted between 2009 and august 2014. Immunosuppression consisted of tacrolimus, MMF and prednisolone. Standard daily dose of MMF is 2x1000mg. MMF trough levels were routinely measured but MMF doses were not adjusted to these levels. Other variables were mean trough Tacrolimus level, BMI, sex, indication, age, and CMV status. Mortality, malignancies and infectious complications were also studied.

MMF dose was reduced in 117 of 142 pts. Mean trough level of MMF was 1,78 mg/L (SD 0,97) and 1,63 (SD 0,80) in the patients without and with CLAD respectively (p=NS). 119 out of 142 pts had a mean trough level below the advised range of 2.5-4.0 mg/L. Mean MMF trough level was lower in Cystic Fibrosis (CF) patients (1,35 vs 1,84 mg/L, P<0,025) but this did not result in a higher incidence of CLAD. A high Body Mass Index (BMI) at the moment of transplantation (p=0.001) and Female gender (p=0,047) were independently associated with CLAD.

We conclude that there is no relation between mean MMF trough level and CLAD and that our current strategy of reducing MMF dosage based on side effects seems to be safe in respect to CLAD. The currently advised range of MMF might be too high in the context of our triple immunosuppression.

Prognostic impact of rejection in biopsies taken during delayed graft function

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Background: Delayed graft function (DGF) is a frequent complication after deceased donor kidney transplantation. It is generally believed that DGF is associated with an increased risk of rejection. During DGF protocolled biopsies are usually performed roughly once every 10 days until stable kidney function is achieved. However, as inflammatory changes may also result from ischemia-reperfusion damage we questioned the predictive importance of BANFF lesions in DGF biopsies.

Methods: We included 619 deceased donor kidney transplantations performed between 2000 and 2007 at our centre. DGF was defined as the need for dialysis in the first week after transplantation. All biopsy reports were re-evaluated in accordance to the BANFF '09 classification. Allograft survival was retrieved from our centres transplant database.

Results: A total of 199 cases (32.2%) were identified as DGF, of which 147 cases (73.9%) underwent a biopsy. Of these 147 cases, 92 cases had *no rejection* (NR), 15 *borderline rejection* (BR), 19 *interstitial rejection* (IR) and 21 cases *vascular rejection* (VR). Compared to NR the diagnosis of IR had no impact (P=0.983) on graft survival in patients with DGF while VR was associated with poorer graft survival (P=0.027). Interestingly, lesions compatible with the diagnosis of BR were associated with improved graft survival (P=0.020).

Conclusions: As both BR and IR had no negative impact on graft survival our findings suggest that the corresponding lesions may not actually represent alloimmune reactions but rather inflammatory responses to ischemia-reperfusion damage. As expected, VR seems to represent harmful lesions. The finding that BR was associated with better graft survival is surprising and may suggest an immune-regulatory mechanism. Further analysis of the biopsies and the interaction with rejection treatment is necessary before firm conclusions can be drawn.

Oxalate deposition in the renal allograft biopsy within 3 months after transplantation

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Background and aims: Deposition of calcium oxalate (CaOx) may impair both native and transplant renal function. We analyzed the role of CaOx in postoperative transplant dysfunction.

Methods: We retrospectively analyzed all preimplantation renal biopsies (t0) for CaOx obtained in 2000-2001. Thereafter, we retrospectively investigated all for-cause renal allograft biopsies obtained within 3 months post-transplantation of patients transplanted in 2014-2015 for CaOx. Clinical data were collected. H&E stained slides were analyzed using polarized light.

Results: A total of 106 t0 biopsies (56 living, 50 deceased donor) were available for analysis, 1 showed CaOx (0.94%) (living donor). 388 patients were transplanted in 2014 and 2015; 77 had DGF, 148 (38.4%) had at least one biopsy within the first 3 months after transplantation. Twenty-four (16%) patients showed CaOx in their biopsy. No diagnosis (ATN, rejection or other) prevailed in the CaOx. DGF was more frequent with CaOx ($p=0.02$). Significantly more patients with CaOx had been on dialysis before transplantation ($p=0.023$). Other clinical parameters investigated were not significantly different between the groups. In the CaOx population 3 grafts failed (12.5%) and 2 patients died (8.3%) versus 8 (6.5%) and 6 (4.8%) in controls (ns).

Conclusion: One in 6 patients have CaOx in their renal allograft biopsy within 3 months after transplantation which can contribute to renal dysfunction. Prevalence was not significantly different between recipients of living or deceased donor kidney, but it prevailed significantly in patients that were on dialysis before transplantation. Patients with DGF significantly more often had CaOx.

A lower mean exposure to tacrolimus, not intra-patient variability is associated with chronic active antibody mediated rejection

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Chronic active antibody mediated rejection (caABMR) is one of the major causes of long-term kidney graft loss. It is hypothesized that frequent underexposure and suboptimal trough levels of immunosuppressive drugs, in particular CNI, are risk factors for the development of caABMR. Previously, it was found that high intra-patient variability in tacrolimus exposure is associated with poor long-term outcome in kidney transplantation and may serve as a substitute parameter for frequent underexposure and/or non-adherence. In this study we investigated the association between tacrolimus exposure and the development of caABMR.

To investigate the possible association between tacrolimus exposure and the development of caABMR, we retrospectively included 58 *biopsy proven* caABMR patients and compared them to 192 matched controls. Control cases were matched for age, year of transplantation and type of kidney donor. All patients were on a standard regimen of tacrolimus and MMF. The intra-patient variability (IPV) was calculated from pre-dose tacrolimus concentrations measured in the 3 years prior to caABMR diagnosis. The tacrolimus IPV for the matched controls was measured over a similar period of time dependent on the case's time to caABMR diagnosis. Besides IPV also mean trough tacrolimus levels and duration of tacrolimus underexposure were compared between both groups.

The median time after transplantation to caABMR diagnosis was 6 years [*range 2-14 years*]. The tacrolimus IPV was relatively high in both groups with 24.0% [*range 9.1%-48.3%*] for the caABMR patients versus 23.6% [*range 3.3%-45.8%*] for the controls (p=0.68). However, the mean tacrolimus trough levels showed a small but statistically significant difference with a tacrolimus concentration of 5.8 ng/mL for the caABMR patients and 6.3 ng/mL for the controls (P=0.03).

Conclusion: A lower mean exposure to tacrolimus but not a high intra-patient variability is associated with the development of caABMR.

The importance of Acute Kidney Injury in patients with Left Ventricular Assist Devices: A Multi-centre study addressing Incidence, Risk Factors and Impact on 1-year Mortality and Renal Function

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Continuous-flow Left ventricle assist devices (CF-LVAD) have become an important tool in the treatment of end-stage heart failure and are increasingly used as bridge-to heart transplantation (BTT). However, CF-LVADs has been recognised as destination therapy when heart transplantation is not possible. The success of this treatment depends on optimal patient selection and patient support after LVAD implantation. Data on the consequences of acute kidney injury (AKI) after CF-LVAD are scarce and inconsistent. In the current study, the incidence and predictors of AKI and its impact on mortality and renal function in the first year after LVAD implantation were evaluated.

A retrospective multicentre cohort study was conducted, including all patients (age ≥18) in who a LVAD was implanted (91% HeartMate II, 9% HVAD) between 2004 and 2015 in the two participating centers. The definition proposed by the Kidney Disease Improving Global Outcome criteria (KDIGO) was used to define AKI. Multivariable analysis was conducted for the association of clinical variables and the onset of AKI and the relation between AKI and renal function at one year.

Overall, 241 patients (mean age 52.4 ± 12.9 years, 76% male, 64% BTT) were included. AKI criteria were met in 169 (70%) LVAD patients, of whom 109 (45%) had AKI stage I, 22 (9%) stage II and 38 (16%) stage III. The need for inotropic support and pre-existent severe kidney failure (eGFR <30 ml/min/1.73 m2) were independently associated with the development of AKI and with the severity of AKI. Overall, 30-day mortality rates were 8.3%, 10.1%, 13.6% and 26.3% (p=0.038) for patients without AKI, stages I, II, and III. One-year mortality rates were 18.7%, 26.4%, 23%, and 51% in patients without AKI, AKI stages I, II and III, respectively (log-rank p=0.001). The mean eGFR at 1 year was 78, 72, 67 and 55 mL/min per 1.73 m^2, in patients without AKI, stages I, II, and III, respectively (p = 0.038). In multivariable analysis, AKI stages ≥ II were independently associated with a worse renal function at one year (p<0.01).

In conclusion, AKI is highly frequent after CF-LVAD implantation. More severe AKI stages are associated with impaired renal function one year after implantation and with a higher mortality rate in the first year after LVAD implantation. Prevention or mitigation of AKI after CF-LVAD implantation is therefore an important goal of perioperative care.

CD16+ monocytes and skewed macrophage polarization towards M2 type hallmark heart transplant acute cellular rejection

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During acute heart transplant rejection, infiltration of lymphocytes and monocytes is followed by endothelial injury and eventually myocardial fibrosis. To date, no information is available on monocyte-macrophage related cellular shifts and their polarization status during rejection. Here, we aimed to define and correlate monocyte-macrophage endomyocardial tissue profiles obtained at rejection and time-points prior to rejection, with corresponding serial blood samples in 25 heart transplant recipients experiencing acute cellular rejection. Additionally, 33 healthy individuals served as control.
Using histology, immunohistochemistry, confocal laser scan microscopy and digital imaging expression of CD14, CD16, CD56, CD68, CD80 and CD163 was explored to define monocyte and macrophage tissue profiles during rejection. Fibrosis was investigated using Sirius Red stainings of rejection, non-rejection and one-year biopsies. Expression of co-stimulatory and migration-related molecules on circulating monocytes, and production potential for pro- and anti-inflammatory cytokines were studied using flowcytometry.
At tissue level, striking CD16+ monocyte infiltration was observed during rejection ($p<0.001$). Significantly more CD68+CD163+ M2 macrophages were documented during rejection compared to barely present CD68+CD80+ M1 macrophages. Rejection was associated with severe fibrosis in 1-year biopsies ($p<0.001$). Irrespective of rejection status, decreased frequencies of circulating CD16+ monocytes were found in patients compared to healthy individuals. Rejection was reflected by significantly increased CD54 and HLA-DR expression on CD16+ monocytes with retained cytokine production potential.

CD16+ monocytes and M2- macrophages hallmark the correlates of heart transplant acute cellular rejection on tissue level, and seem to be associated with fibrosis on the long-term.

Liquid biopsies: non-invasive rejection detection after heart transplantation

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After heart transplantation (HTx) acute cellular rejection (ACR) can damage the allograft which leads to the release of donor cell free DNA (cfDNA) into the circulation of the recipient. The amount of donor cfDNA in the recipients blood (liquid biopsies) can be measured using digital PCR. The aim of our study is to implement this non-invasive liquid biopsy technique for donor cfDNA detection post-HTx.
50 HTx patients were selected with at least one year follow-up. Within this cohort 37 patients experienced ACR. The 13 non-ACR patients are used as controls. Eight common SNPs were used for the recipient-donor genotyping with qPCR. cfDNA was isolated from EDTA plasma from the recipients pre-HTx and at multiple timepoints post-HTx. With digital PCR the amount of donor cfDNA was measured in the recipients plasma by targeting the specific SNP of the donor.

Pilot data of 15 patients were gathered and post-HTx we detect donor cfDNA in the recipient plasma samples. A limit of detection (LOD) for every SNP was determined during validation of the assays. In the first month post-HTx the amount of cfDNA of both the donor and the recipient is fluctuating. The amount of donor cfDNA decreases to a baseline (BL) level after one month. In all plasma samples of the patients post-HTx elevated levels of donor cfDNA were detected after the biopsy proven ACR and in some patients the elevated levels of donor cfDNA also matched the biopsy proven ACR. Other clinical events explained peaks in cfDNA levels.

The eight SNPs were sufficient for typing the HTx recipients and donors. We can detect donor cfDNA in the recipients plasma post-HTx. Because cfDNA fluctuates within the first month, endomyocardial biopsies (EMBs) are still crucial in this period. After the first month liquid biopsies show promising results to limit the amount of EMBs, however this remains challenging as other medical issues might be interfering.

Hypothermic machine perfusion reduces reperfusion injury of the bile ducts after transplantation of donation after circulatory death livers

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Although donation after circulatory death (DCD) livers are increasingly used for transplantation, these organs are associated with an increased risk of biliary complications due to ischemia reperfusion injury (IRI). hypothermic machine perfusion (HMP) has been advocated as a method to reduce IRI after liver transplantation. The aim of this study was to determine whether oxygenated HMP reduces IRI of the bile ducts after transplantation of DCD livers. In a recently performed phase I trial ten DCD livers were preserved with end-ischemic oxygenated HMP prior to transplantation. Biopsies were obtained from the common bile duct at the end of static cold storage (before HMP; baseline) and after graft reperfusion in the recipient. The histological severity of biliary injury was graded according to an established semi-quantative grading system in a blinded fashion. Twenty DCD liver transplantations in our center that were not preserved with HMP served as controls. Baseline characteristics were comparable between the two groups. As expected, the degree of bile duct injury at baseline was similar between the study groups. After reperfusion, in the control group, the degree of biliary stroma necrosis (p=0.004) and injury of the periluminal peribiliary glands (p=0.017) increased compared to baseline. In contrast, in HMP preserved livers the degree of biliary injury after reperfusion did not increase compared to baseline. In accordance, there was less injury of the periluminal (p=0.043) and deep peribiliary glands (p=0.043) after graft reperfusion in the HMP group, compared to the control group. In conclusion, this study suggests that oxygenated HMP reduces IRI of the bile ducts after transplantation of DCD livers. Whether HMP leads to a decrease in the incidence of biliary complications after DCD liver transplantation, is currently investigated in a multicenter randomized controlled trial (Clinicaltrial.gov NTC02584283).

MicroRNAs differentiate between antibody and T-cell mediated renal allograft rejection

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MicroRNAs are important immune regulators of gene and protein expression. Both circulating and intragraft expression of microRNAs have been related to renal allograft rejection. To determine the mechansims that control cellular and antibody mediated rejection, we hypothesized that miRNA expression as (post)transcriptional regulator of gene expression could be different between rejecion subtypes. In this study, we investigated microRNA tissue expression of different histopathological types of kidney allograft rejection according to Banff 2013, i.e. to analyse the differences between acute cellulair rejection, and acute and chronic antibody mediated rejection. Results of such a study would help detect new biomarkers.

Microarray experiments and semiquantitative real-time reverse transcription polymerase chain reaction (QPCR) were performed using total RNA isolated from 46 fresh-frozen renal allograft biopsies showing rejection. Initial microarray analysis (miRCURY LNA™ microRNA Array platform, Exiqon) and subsequent QPCR revealed 5 microRNAs with significantly differential expression between the rejection biopsies.

Expression levels of miR-155 and miR-21 were significantly downregulated in acute antibody mediated rejection group (n=9) compared to acute cellular rejection biopsies (n=24) ($p=<0.05$) whereas miR-195 was upregulated ($p=<0.05$). miR-21 was significantly downregulated in chronic antibody mediated rejection group (n=13) compared to acute antibody mediated rejection biopsies ($p=<0.001$). The specific cell sources in rejecting kidney biopsies are now being investigated, as miR-155 and miR-21 has been repeatedly associated with the monocyte-macrophage lineage cells.

We found significant differences in expression of miR-155, miR-21 and miRNA195 between antibody mediated and cellular rejection. Future validation studies are needed to confirm these data.

Compartmental infiltration of kidney allograft with monocyte-macrophage subtypes defines the type of rejection.

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Rejection, regardless of the type and time, significantly worsens the graft function and survival. Emerging evidence has revealed a crucial role for the cells of monocyte-macrophage lineage in the pathogenesis of rejection. Here, we studied monocyte-macrophage compartmental infiltration of 62 kidney transplant biopsies with the diagnosis of 1) acute antibody mediated rejection (aABMR, n=9), 2) chronic antibody mediated rejection (cABMR, n=13), 3) acute cellular rejection type I (ACR I, n=11), 4) acute cellular rejection type II (ACRII, n=13), and 5) and 15 protocol biopsies from kidney transplants with stable function as controls. Next we studied the relationship between these findings and allograft function and survival in the long term.

Immunohistochemical and immunofluorescent stainings were applied to study monocyte-macrophage infiltration. The intensity of infiltration was quantified by ImageJ analysis and laser scan confocal microscopy. Infiltrating monocytes were characterized by double staining with CD14 and CD16. Infiltrating macrophages were identified by expression of CD68, CD80, CD163 as follows: CD68+CD80 (M1 type) and CD68+CD163 (M2 type). Histopathological data was analyzed and correlated to eGFR, creatinine and proteinuria levels at the time of biopsy, 3, 6 and 12 months post-rejection.

Overall, the presence of CD68+macrophages in kidney biopsies was significantly associated with rejection compared to stable patients regardless of histopathological subtype (p=<0,01). Overall, the presence of CD68+CD163+ macrophages was signigicantly associated with a lower eGFR at the time of biopsy, and at 3, 6 and 12 months after rejection (p<0,001). Glomerular infiltration by classical and intermediate monocytes and and the presence of non-classical monocytes in the interstitium were significantly associated with rejection regardless of rejection subtype (p=<0,01). cABMR was characterized by glomerular and tubulointerstitial CD68+ macrophage infitration, and glomerular and tubulointerstitial classical and intermediate monocyte distribution as compared to aABMR (p=<0,05). ACRI and ACRII were charactherized by vascular and tubulointerstitial distribuation of CD68+ cells as compared to aABMR rejection type (p=<0,05).

In sharp contrast to T cells, the presence of CD68+macrophages in a kidney transplant biopsy is significantly associated with rejection regardless of histopathological subtype.There are significant compartmental differences in the distribution of different macrophage and monocyte subtypes between aABMR and cABMR, as well as between ACR I/II and aABMR. These findings could be of interest for the histopathological classifcation of rejection type. Future clarification of the pathogenetical role and the cell specific markers could help detect new rejection biomarkers.

Identification of kidney transplant patients at risk for skin cancer by differentially methylated regions in t cells

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Skin cancer, specifically cutaneous squamous cell carcinoma (cSCC), is the most often occurring malignancy in patients after organ transplantation with an incidence of 100-200 times more compared to the general population. Biomarkers to predict post-transplant cSCC are unavailable. We hypothesized that epigenetic alterations in T cells, which are crucial in tumour immune surveillance, identify individuals at increased risk for cSCC after transplantation. Therefore, we studied genome-wide DNA methylation in T cells at time of transplantation and prior to the clinical onset of cSCC in kidney transplant (KTx) patients.

Pure T cells were isolated by FACS sorting from PMBCs of KTx patients with (n=46) and without cSCC after transplantation (n=46). Patients with post-transplant cSCC were matched to patients without cSCC. Genome-wide DNA methylation was measured using Illumina's Infinium 450K array. To find differentially methylated regions (DMRs) linear mixed modelling was applied to adjust for confounders followed by comb-p to find the regions.

The results showed 16 DMRs at time of transplantation between patients with post-transplant cSCC and those without post-transplant cSCC. The majority (11/16) of these DMRs were hypomethylated in patients with post-transplant cSCC and 13 of these 16 DMRs were located within the promoter region of a gene. After transplantation but prior to the clinical onset of cSCC, 7 DMRs were found of which the top results included an intragenic region of SERPINB9, an actively transcribed gene in T cells, and a known tumour suppressor microRNA. No overlap was found so far between the two groups.

These results support the hypothesis that differentially methylated regions have potential to serve as a predictive tool for the development of post-transplant cSCC both at time of transplantation and prior to the clinical onset of cSCC.

Antibodies against apoptotic cells present in end-stage lung disease patients do not correlate with clinical outcome after lung transplantation

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Antibodies against HLA and non-HLA are associated with transplantation outcome. Recently, pre-transplant serum IgG antibody levels against apoptotic cells were found to correlate with kidney allograft loss. We investigated the presence of these antibodies in lung transplantation (LTx) patients and evaluated the correlation of pre-LTx serum levels of IgG antibodies against apoptotic cells with LTx outcome. These cells included donor lung endothelial cells (EC) obtained from lung perfusion fluid collected during LTx procedure. Cells were isolated, expanded *in vitro*, and analyzed as targets for anti-apoptotic cell reactivity. Cultured cells exhibited EC morphology and were CD31+, CD13+ and vWF+ . End-stage lung disease patients showed elevated serum IgG levels against apoptotic lung EC (p=0.0018) compared to healthy controls. Interestingly, levels between cell systems did not correlate, hinting at target cell-specificity. We observed no correlation between chronic or acute rejection and pre-LTx serum levels of anti-apoptotic antibodies. Also, these levels did not differ between matched patients developing chronic rejection or not during follow-up or at the time of diagnosis, as they remained as high as prior to transplantation. Thus, circulating levels of anti-apoptotic cell antibodies are elevated in end-stage lung disease patients but our data do not correlate with outcome after LTx.

Risk factors and impact on outcomes of trajectories of anxiety and depression after liver transplantation: a prospective cohort study

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Background: Although the burden of psychological problems among liver transplant recipients is recognized, little is known about the course of symptoms of anxiety and depression over time. The aim of this study was to examine whether distinct trajectories of anxious and depressive symptoms are present among adult liver transplant recipients from before transplantation up until to two years after transplantation; to identify demographic, clinical, and individual characteristics associated with the distinct trajectories; and to examine the influence of distinct trajectories on outcomes.
Methods: Data were retrieved by questionnaire before and at 3, 6, 12, and 24 months after transplantation. Clinical data were retrieved by medical record review. Latent Class Growth Analysis was used to identify distinct trajectories and General Linear Mixed Models analysis was used to identify associated variables.
Results**:** Three distinct trajectories for symptoms of anxiety and depression were identified: "no symptoms," "resolved symptoms," and "persistent symptoms." The trajectory of persistent symptoms of anxiety comprised 23% of the transplant recipients. The trajectory of persistent depressive symptoms 29% of the transplant recipients. Several clinical and individual variables were found to be associated with the trajectories of persistent symptoms of anxiety and depression: experiencing more side-effects from the immunosuppressive medication, a lower level of personal control, more use of emotional coping, less use of task-oriented coping, less disclosure about the transplant, and experiencing more stressful life events. Transplant recipients within the trajectories of persistent symptoms, reported significantly worse medication adherence ($P < 0.02$) and lower scores for all domains of health-related quality of life ($P < 0.001$).
Conclusion: A significant subset of liver transplant recipients showed persistent symptoms of anxiety and depression. Our results emphasize the importance of psychological care in the transplant population. Assessment of risk factors early in the transplant process and continuous follow-up of psychological functioning are warranted. Based on these assessments appropriate interventions should be undertaken to enhance psychological functioning in liver transplant patients.

EXPloring attitudes and factors influencing reproductive Choices in renal Transplant patients (EXPeCT-study)

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The number of renal transplantations (RTX) among young women is increasing. Therefore the number of women who have the desire to have children after transplantation is also rising, despite the possible complications for both mother and child. While most literature focuses on the medical outcomes of pregnancy after transplantation, this qualitative study aims to explore the motives for pregnancy after transplantation and the psychosocial and medical factors considered. Furthermore, we explored the experience of being pregnant and raising children after RTX.
Women who were transplanted between 2008-2013 and became pregnant after transplantation were eligible for inclusion. These women were matched with women who had not been pregnant but were the same age (± 5 yrs) and transplanted at the same time (± 2 yrs). Semi-structured interviews were conducted and transcribed ad verbatim. Directed content analysis was carried out to identify general themes .
Between 01-01-2008 and 31-12-2013, 137 women £ 45 yrs were transplanted in our center. We invited 37 women, of which 20 women were willing to participate in the interviews. Preliminary analysis identified the following themes: physical loss; concerns about being able to take care of a child because of tiredness after RTX, but also loss of a child. Guilt was mentioned for different reasons, towards nephrologists for wanting to risk their renal transplant for a pregnancy, but also towards their children who will grow up with a sick mother. Calculating risks and trying to lower them was important because they want to stay in control. Information about pregnancy and RTX was minimal if women did not initiate a discussion with their nephrologist. Trust in their body to become pregnant was mentioned, and the difficulty discussing their desire to have children. One was dissuaded not to get pregnant by their nephrologist and did not dare to talk about it ever again. Two factors were identified as being crucial in the decision whether or not to become pregnant: the guidance/advice they received from the professional and the support from their social network.

Conclusion: Preliminary results show that discussing with the doctor the wish to conceive is of great importance and should be handled with care. Young women after transplantation with or without a desire to have children find it difficult to talk about this with their nephrologist. Because this threshold can be high for these women we suggest that the nephrologist or nurse practitioner pro-actively discusses this issue with every women in the child-bearing age to afford effective education and guidance.

Posttraumatic stress disorder in liver transplant recipients before and after transplantation: prevalence, symptom occurrence, and intrusive memories

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Background**:** Studies on posttraumatic stress disorder (PTSD) in organ transplant recipients mainly focused on assessing prevalence rates and identifying risk factors. Less is known about which aspects of the transplant process are traumatic in nature. This study aimed at increasing the understanding of PTSD in liver transplant patients by describing the course of PTSD from the waiting-list period up until one year after transplantation, symptom occurrence, psychological co-morbidity, and the nature of re-experiencing symptoms.

Methods**:** A prospective cohort study was performed among 95 liver transplant recipients. Data were retrieved by questionnaire before transplantation, and at 3, 6, and 12 months post-transplantation. Both quantitative and qualitative methods were used to analyze the data.

Results**:** Before transplantation, 32% of the respondents showed clinically relevant symptoms of PTSD, of which 10.5% fulfilled the criteria of full PTSD and 6.3% fullfilled the criteria of partial PTSD. In all cases, co-morbid conditions of anxiety and/or depression were present. After transplantation, ~15% of the respondents showed clinically relevant symptoms of PTSD, but no new onset of full PTSD was found, while new onset of partial PTSD was found in six respondents. Arousal symptoms, such as sleeping disorders and concentration problems, were the most frequently reported symptoms, but were found not to be distinctive for PTSD in transplant patients because of the overlap with disease- and treatment-related symptoms. Re-experiencing symptoms before transplantation were mostly related to waiting for a donor organ and the upcoming surgery. After transplantation re-experiencing symptoms were mainly related to aspects of the hospital stay, such as the stay on the Intensive Care Unit and experiencing a delirium.

Conclusions**:** In liver transplant patients, clinically relevant PTSD symptomatology is more present than caseness for full and partial PTSD, and both PTSD symptomatology and caseness is more prevalent in liver transplant candidates than in liver transplant recipients during the first year after transplantation. However, because of the overlap with disease and treatment-related factors, and with other psychological disorders, it is difficult to disentangle the differences. Therefore, when PTSD is suspected, referral to a clinician is warranted in order to confirm the diagnosis and subsequently initiate appropriate interventions.

Dried Blood Spot Monitoring After Lung Transplantation: Patients Perspectives

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After lung transplantation lifetime drug monitoring of the immunosuppressive drug tacrolimus is necessary because of a narrow therapeutic window and large inter- and intra-individual variability of the tacrolimus blood concentration. Since 2012 the dried bloodspot (DBS) testing of tacrolimus was introduced in our daily clinical practice in stable outpatient lung transplant recipients. The aim of this study was to evaluate patient satisfaction of DBS sampling. Methods: 39 stable lung transplant recipients at our center were recruited for the evaluation of the DBS testing. Patients with scleroderma were excluded. Patient satisfaction was evaluated using a written questionnaire 6 to 12 months after starting DBS. Eighty-two percent (32/39) of the patients responded. Two of the 32 patients admitted they never used the DBS and were therefore excluded. Native lung disease of the 7 non-responders was Cystic Fibrosis (86%) or Pulmonary Hemosiderosis (14%). Forty-three percent was male (median age 30 years; range 23-52). Native lung disease of the 30 responders was Cystic Fibrosis (77%), COPD (10%) and approximately 3% was A1ATD, sarcoidosis, IPF or Pulmonary Hypertension. Fifty percent of the responders was male (median age 32 years; range 21-64). On a scale from 0 to 10, patient satisfaction was 8.3 (range 2,5-10). Hundred percent of the patients were content with the patient information and the instruction. None of the responders experienced any inconvenience with the finger prick and all of them continued the DBS. Twenty-seven responders reported difficulties with applying the blood drop on the sampling paper because of tremors caused by tacrolimus. However, almost all bloodspot samples sent to our laboratory were valid. Finally, 40% percent of the responders reported that they would like to have an e-reminder to send the DBS sample in time.

Conclusion: Patient satisfaction with DBS method was high in our outpatient population. DBS testing of tacrolimus is considered patient friendly. DBS sampling of tacrolimus can be performed at home and can reduce the outpatient clinic visits. All patients continued to use the DBS. Home sampling is a promising tool to improve quality of life for lung transplantation patients.

Providing guidance to patients with Hepatic Encephalopathy who are on the waiting list for liver transplantation: a quality improvement project

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Hepatic encephalopathy (HE) is a severe complication in patients on the waiting list for liver transplantation. HE often affects patients with decompensated liver cirrhosis. It is a neuropsychiatric syndrome caused by a high level of ammonia in the blood, which crosses the blood-brain barrier. Mental and neuromuscular symptoms are present in patients with HE. Teaching patients and their caregivers how they can recognize the first symptoms of HE can prevent both worsening of the condition and hospitalization. At present, patients and their caregivers are concerned about HE because they are unaware of the symptoms of the condition.
The main goal of this study is to provide guidance to patients and their caregivers on how to manage HE. Furthermore, nurses require clinical training that helps them to inform and instruct patients and their caregivers about HE.

Patients and their caregivers were interviewed about recognizing symptoms of HE and about their knowledge of appropriate actions. The nurses from the ward were invited to fill out a survey on knowledge of HE and skills they require to teach patients and their partners.
A total of ten patients and their caregivers were interviewed. Patients with a first episode of HE were concerned about the symptoms and had little knowledge of HE. Patients who had been through multiple episodes of HE had some knowledge of the symptoms. Most caregivers saw a difference in the behavior of patients with HE, but were not able to connect this altered behavior to HE. They all stated that while an information leaflet on HE would be informative, they also wanted to learn how to manage its symptoms and how to prevent deterioration. Fifteen nurses (65%) from the ward filled out the survey. Respondents indicated they were in need of clinical training on managing HE as well as information on causes, symptoms, and treatment options. Based on these results, a clinical training was prepared and an information leaflet was designed, including a diary (weight, frequency of defecation) and a number connection test to assess the degree of HE.

The conclusion of this study is that providing information about HE helps patients and their caregivers to gain a sense of control and to prevent worsening of the condition. A follow-up study will be performed to verify whether this information leaflet increases knowledge, improves quality of life, and decreases the number of HE episodes.

Cystic fibrosis related diabetes mellitus and lungtransplantation

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Cystic fibrosis is een erfelijke ziekte waarbij er gestoorde electrolytransport over de slijmvliezen is, vooral in de long. Dit proces leidt tot terugkerende infecties en verlies van longfunctie, vaak eindigend in longfalen (FEV1<30%). De helft van volwassen patiënten ontwikkelen diabetes: Cystic Fibrosis Related Diabetes (CFRD). Afgezien van schade door de diabetes, wordt hyperglycaemie als oorzaak gezien van verslechtering tijdens pulmonale infecties. Longtransplantatie (LTx) is de ultieme therapie voor longfalen. Insuline toediening en conventionele zelfmetingen van bloedglucoses door vingerprikken (SMBG) is niet altijd voldoende.

Methode: We beschrijven een 34 jarige vrouw met CFRD. Patiënte werd behandeld met insulinepomptherapie, gekoppeld aan een continu glucose meting (CGM). In 2012 onderging patiënte haar LTx. Wegens verlaagd FEV1 en dreigende afstoting in december 2014, kreeg patiënte hoge doseringen steroïden en twee keer een afweeronderdrukkende behandeling. Tijdens deze periodes was patiënte niet in staat om te eten. Om deze reden werd sondevoeding gestart. Wegens angst voor hypoglycaemieen durfde patiënte weinig insuline te bolussen. Hiermee ontstonden grote glcuosefluctuaties. In januari 2016 onderging patiënte een her-transplantatie. In deze post-transplantatie periode was de glucose variabiliteit hoog.
Met patiënte werd in multidisciplinair verband besloten om te starten met een insulinepomp welke de insulinetoediening stopt en herstart op basis van de sensorwaarde. De verpleegkundig specialist (VS) diabetes nam in dit proces de regie. Door educatie en communicatie kon patiënte deze advanced technology adequaat toepassen.

Resultaat: Insulinebehoefte van patiënte daalde van 45 naar 20,5 eenheden per dag. Hypoglycaemieen kwamen niet voor. Hyperglycaemieen waren acceptabel. Patiënte ervoer een groot zelfvertrouwen in haar diabetes.

Aanbevelingen voor de praktijk: In samenspraak met de patiënt overwegen om bij kwetsbare patiënten pre- en posttransplantatie te starten met complexe insuline-pomptherapie samen met CGM.

From proposal to practice: participation of compatible donor-recipient pairs in the Dutch kidney exchange program

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Background: Since 2004 incompatible donor-recipients pairs have participated in the Dutch living kidney exchange program. Between 2009 and 2012 5 compatible pairs decided to donate in the exchange program, which resulted in 14 instead of 5 transplants. Enrolment of compatible pairs could help increase the success rate in the kidney exchange program. However, how should we educate compatible donors and recipients about this participation. Here we discuss the implementation of a protocol for these pairs to participate in the exchange program and describe a study designed to evaluate the decision-making process.
Methods: Our transplant team discussed the protocol to minimize undue influence, as well as the moment of education. A questionnaire was developed to evaluate the protocol and the decision-making process regarding participation.
Results: In June 2016 we introduced the compatible pairs program. We developed a leaflet with neutral, objective information about the program. This information was also available on our website. Education about living donation programs was standardized. All new patients and donors who visit the outpatient clinic for the first time will be informed in the same way about these programs. The first consultation with the coordinator about the living donation/transplant programs take place at the time that donor-recipient pair do not know if they are compatible or not. The information leaflet about voluntary participation in the exchange program is handed out at this point. The second consultation with the coordinator takes place when the compatible pair visit the outpatient clinic for the immunological results. If the cross-match is negative and they are blood type and HLA compatible, we discuss the willingness to participate in the exchange program. When the pair has made a decision, we ask them to participate in a survey study on their decision-making process. The questionnaire can be filled in at home. Specific versions of the questionnaire were developed for participants and for non-participants, and for patients and donors respectively.
In conclusion: Education takes place to raise awareness that a living donor can always give the kidney in a indirect way. This can be the case if it's medical necessary or voluntary on an altruistic basis to help other pairs. With the questionnaire we aim to gain insights into patients and donors motivation to their decision. Acceptable and unacceptable conditions of the program will be evaluated.

Impact of C3d-fixing donor-specific HLA antibodies on long-term kidney graft survival

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The presence of complement fixing antibodies against donor human leukocyte antigens (HLA) prior to transplantation is considered a contraindication for transplantation. Detection of these antibodies by crossmatching is widely used in donor exclusion. HLA antibody detection by single antigen bead array (SAB) is much more sensitive than complement-dependent crossmatches and allows finer definition of antibody specificity. However, the exact clinical significance of SAB detected donor-specific antibodies (DSA) that do not cause a positive crossmatch is not clear. Although most studies showed a relation between SAB-defined DSA and impaired graft outcome, the presence of HLA antibodies in pre-or posttransplant sera not always resulted in graft loss. This raises the question how to define clinically relevant DSA using SAB, which is important as inclusion of irrelevant specificities in patients' antibody profiles would result in dismissal of appropriate kidney donors. A recent modification of the pan-IgG SAB assay allows detection of HLA antibodies binding C1q and C3d. As early humoral graft rejection is considered to be complement mediated, these novel SAB-based techniques may provide a valuable tool in the identification of patients at risk for graft loss. C1q-fixing ability of DSA has already been shown to be strongly associated with kidney graft loss. Studies defining the potential of C3d as marker of complement fixation (e.g. assay developed by Immucor) are scarce and include low number sera from patients included up till now. In the Dutch PROCARE consortium study more than 6000 kidney transplantations performed between 1995-2006 were analyzed. The presence of non-donor-specific HLA antibodies (NDSA) and DSA against HLA-A/B/DR/DQ antigens was defined in 4724 pre-transplant sera using the pan-IgG SAB assay. Next, the 806 (17%) sera with DSA were further tested with the C3d-SAB assay. We found that 190/806 (24%) of the pretransplant sera contained at least one C3d-fixing DSA and 616/806 (76%) of the sera had no C3d-fixing DSA. At 10 years after transplantation, patients with C3d-fixing antibodies had a graft survival of 62%, while patients without C3d-fixing antibodies had a graft survival of 69%. Patients without any HLA antibodies had a 10-year graft survival of 79%. We conclude that the presence of pretransplant C3d-fixing DSA is associated with increased risk for graft rejection.

A standard frailty indicator for predicting postoperative complications after kidney transplantation

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Currently there is a lack of tools that help predict the 30-day post-surgery outcome after kidney transplantation. Frailty is a clinically recognizable condition, also called syndrome or phenotype, that estimates physiologic reserves resulting from aging-associated processes. These changes are responsible for an increased vulnerability and decreased ability to cope with physical stressors, resulting in a serious deterioration in health. Frailty has recently emerged as a possible predictive factor for post-surgical outcomes.
This study aims to assess whether frailty is a reliable tool for predicting short term (30 days) postoperative complications after kidney transplantation with the aim to optimize treatment decisions and preventive arrangements.
From January 2015 to October 2016 all kidney transplant recipients (N=150) were prospectively included. At admission, frailty was assessed using a standardized frailty indicator consisting of 15 items, classified in 8 separate groups, consistent with the domains of functioning. Frailty was defined as a score ≥ 4 on the frailty scale ranging from 0 to 15. Postoperative complications were recorded and analysed using the Comprehensive Complication Index (CCI). Using a linear regression model, the correlation between 30-day postoperative complications and frailty was adjusted for important confunders and risk factors like sex, age, ASA Score, Charlson Comorbidty Index, hypertension, BMI, smoking, dialysis, duration of dialysis, type of transplantation and retransplantation.
The mean frailty score for the tested population was 2.07 and 23 patients had a frailty score of 4 or higher. The mean CCI score for 30-day post-surgery was 17.9; the mean CCI score for "frail" patients (≥ 4) was 30.1 compared to 15.5 for "non frail" patients (<4). Frailty (13.4 point increase in CCI, 95% CI: 5.5-21.3; p=0.001) and type of transplantation (10.5 point increase in CCI for postmortal transplantations, 95% CI: 0.5-20.5; p=0.04) were statistically significant factors associated with a higher risk of postoperative complications after kidney transplantation, independent of potential confounders.

In conclusion, frailty and type of transplantation are both factors significantly associated with 30-day postoperative complications measured by the CCI. The simplicity of determining frailty using a standardized frailty indicator makes it well applicable in daily clinical practice and can improve short and possibly long-term outcome.

Self-monitoring creatinine after transplantation: the (un)reliability of patient reported data.

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Background: Self-monitoring creatinine is a promising new health care strategy to reduce number of outpatient visits after kidney transplantation. The current study used data from a self-management intervention to investigate whether it is safe to rely on patients' reported self-measurements.
Methods: During the first year post-transplantation 54 patients registered their self-measured creatinine values in an online Self-Management Support System (SMSS) which provided automatic feedback on the registered values (e.g. contact hospital). Values registered in the SMSS were compared to those logged in the creatinine device to study reliability of registered data. Adherence to measurement frequency was determined by comparing number of requested with number of performed measurements. To study adherence to provided feedback, SMSS logged feedback and information from the electronic hospital files were analysed.
Results: Eighty-seven percent of all registered creatinine values was entered correctly, although values were often registered several days later. In case of a difference between (number of) measured and registered values, registered creatinine values were significantly lower than the measured ones, suggesting active selection of lower creatinine values. Level of adherence to measurement protocol was highest during month 2-4 post-transplantation with over 90% of patients performing at least 75% of the requested measurements. Adherence to SMSS feedback ranged from 53-85% depending on the specific feedback.
Discussion: Patients' tendency to select lower creatinine values for registration and to postpone registration and the suboptimal adherence to the SMSS provided feedback might challenge the safety of self-monitoring. These issues can mostly be overcome by transferring measured data automatically.

Combined Measurement of Immunosuppressive Agents, Creatinine and Hematocrit in a Single Dried Blood Spot Using LC-MSMS and Near-infra-Red Spectrometry

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Purpose: Biomarker and drug monitoring and are essential to diagnose and prevent toxicity and rejection in lung transplant recipients. To date, whole blood sampling is 'the golden standard' for quantification of drugs and biomarker in either whole blood of serum. Nevertheless, whole blood sampling in stable transplant recipients usually takes place at the outpatient clinic and is rarely carried out by patients themselves at home. Therefore, we have developed a practical method for rapid and easy quantification of hematocrit (Ht), creatinine (Creat) and immunosuppressive agents (IMx) in dried blood spot (DBS) samples.
Methods: For Ht measurement near-infrared (NIR) spectrometry combined with an in-house developed NIR-model and Büchi NIRcal 5.5 software were used to nondestructively quantitate Ht in DBS. Thereafter, DBS samples were extracted under ultrasonication for 15 minutes. IMx and Creat were detected with a Thermo Scientific triple quadrupole Quantum Access with positive ionization. Following analytical validation methods were clinically validated by comparing DBS results with whole blood and serum reference methods. Venous whole blood samples of 30 patients on cyclosporin A, tacrolimus, sirolimus and everolimus were used to prepare DBS. Ht, IMx and Creat concentrations determined by DBS and whole blood or serum methods were compared by Passing & Bablok regression analysis.
Results: A good correlation was demonstrated yielding linear regression coefficients of R2 >0.95. for all compounds and Ht. Low, medium and high controls are all <15% in all cases. The average concentrations of Ht, IMx and Creat in the population were within the 95% limits of agreement.
Conclusion: A rapid and combined dried blood spot analysis suitable for patient home monitoring of immunosuppressants, creatinine and hematocrit in lung transplant recipients using a single sample was successfully developed.

A sudden increase in delayed graft function in living donor kidney transplantation and a changed peroperative fluid regimen

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The first half of 2016 an increase in delayed graft function (DGF) in our living donor kidney transplantation (LDKT) population was noticed. The incidence of DGF (defined as need for dialysis 1st week after transplantation) and functional DGF (fDGF, defined as failure of a fall in serum creatinine of 10% on 3 consecutive days in the 1st week after transplantation) had increased from respectively 1.4%-4.4% (DGF) and 8.4%-8.9% (fDGF) in 2014-2015 up to 11.3% and 26.4% in the first half of 2016. During 2015 we changed our peroperative fluid regimen from a standard amount of 4-5 liter balanced cristalloids to a goal directed fluid therapy approach. This approach aims to optimize the volume state based on the Frank Starling curve and individualized goals. For kidney transplantation the goal was set to a stroke volume variation (SVV) <10% at time of reperfusion. We questioned whether this adjustment in fluid regimen was related to the increase in fDGF. From January 2014 to June 2016 214 LDKT were performed in our center. Donor and recipient characteristics were obtained from hospital records. Intraoperative data were retrieved from our digital patient data monitoring system. Analysis comprised an univariable analysis, analysis over time and multivariable logistic regression. As half of the population was transplanted preemptively two groups were made: fDGF (n=26, also including patients meeting DGF criteria) and noDGF (n=188). Demographics of donors were comparable with the exception of age and length. Recipients on dialysis were more likely to develop fDGF after transplantation compared to preemptively transplanted patients (P<0.001). Univariable analyses detected various risk factors for fDGF. Recipients developing fDGF received less peroperative fluid, 34.3 (25.3-41.5) ml/kg vs 43,7 (34,2-53,6) ml/kg (P=0.006) and were treated more frequently with noradrenaline, 79% vs 52% (P 0.010). Sacrifice of an artery occurred more frequently in fDGF (P 0.043). In the unadjusted analysis, the effect of the amount of fluid on developing fDGF was 0.962 (B-0,039, 95% CI 0.932-0.993 P=0.016). When adjusted for dialysis, sacrifice of an artery and the use of noradrenaline, the amount of fluid remained independently associated with DGF (OR=0.96, 95%CI 0.931-0.997, P=0.032) Goal-directed fluid management towards an SVV of 10% has led to reduced peroperative fluid administration. This seems to be an independent risk factor for development of fDGF in living donor kidney transplantation. A more liberal fluid management using other goals might be more appropriate.

The effect of starting enteral tube feeding in patients with end-stage cystic fibrosis before lung transplantation

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Background & aims: Lung transplantation (LTx) is an established treatment option for end-stage lung disease in patients with cystic fibrosis (CF). A body mass index (BMI) below 18.5 kg/m^2 is often used as a preclusion for LTx. Pre-transplant nutrition management is aimed to maintain or improve nutritional status, in order to meet the criteria for LTx. Enteral tube feeding (ETF) is widely used to improve nutritional status in CF patients. Previous studies suggest a gender difference; CF women have a higher risk for malnutrition and detoriation of pulmonary function than men. The aim of this retrospective study was to investigate whether ETF improves body weight, BMI and pulmonary function and induces cystic fibrosis related diabetes (CFRD) equally in men and women with CF before lung transplantation.
Methods: End-stage CF patients using ETF for at least 6 months between 2000 to 2014 were included. Outcomes were collected at the usual outpatient clinic visits and data on body weight and BMI are necessary according to Lung Allocation Score (LAS) implemented in April 2014. Data were extracted from patient files from six months before to 6 months after starting ETF and were analyzed for men and women separately.
Results: Twenty-six adult patients with end-stage CF (19 women; 73%) were included. Six months before the start of ETF, 9 of the 19 women had a BMI less than 18.5 kg/m^2. In women, mean BMI significantly decreased before the start of ETF ($p<0.05$) and increased significantly 1.4 kg/m^2 after the start of ETF ($p<0.05$). Mean body weight increased by 3.3 kg (95%CI, 1.7 to 4.9 kg). In men, the increase in mean BMI of 0.3 kg/m^2 over time was not significant. Body weight increased by 4 kg after the start of ETF but this was also not significant (95% CI, -1.2 to 9.1 kg). In women, pulmonary function (FEV_1%pred) decreased significantly from 34% 6 months before starting ETF to 29.5% 6 months after ($p<0.05$). In men, FEV_1%pred declined from 22.5% in the 6 months before to 21.5% 6 months after the start of ETF. At the start of ETF, 10 women and 3 men suffered from CFRD. Of the 13 patients with CFRD, only 1 woman developed CFRD after the start of ETF.
Conclusion: ETF can help to improve body weight and BMI and may contribute to a stabilization of pulmonary function in patients with end-stage CF. This is an important outcome for patients waiting for lung transplantation. We found no indication that the effect was different for men and women.

Iliac peripheral arterial disease before kidney transplantation: the influence of intervention

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Background: Peripheral arterial disease may exclude kidney transplantation when vascular connectivity is hampered. Stenotic or calcified iliac vessels without symptoms are not an indication for vascular treatment. How important is peripheral artery disease for survival and what is the influence of intervention before transplantation?
Methods: Our retrospective study included 1728 patients transplanted between 2000-2012. Peripheral vascular disease was scored as: stenosing or dilating disease, dissection, and vascular intervention in the iliac region. Separately microvascular disease (amputations in diabetes mellitus) and ≥3 transplantations were scored. Other variables included are: recipient age, PRAmax, transplant-year, number of HLAmismatches, donor type, donor age, CNI-use, and the RoCKeT score after extraction of peripheral arterial disease, which was used to correct for comorbidities. Multivariable Cox proportional hazards analyses were performed to test the independent influence of peripheral vascular disease variables, corrected for variables with a known significant influence.
Results: There were 325 graft failures and 215 deaths in the period studied. There were missing values in 5 cases. In multivariable Cox analysis graft failure censored for death was significantly influenced by peripheral vascular disease (n=141, p=0.021, RR=1.59) and by the known variables but not by the adjusted RoCKeT score. In a separate multivariable analysis occlusive vascular disease did significantly influence outcome (n=91, p=0.007, RR=1.93), while dilating disease (n=55) did not influence outcome. Furthermore, untreated arterial disease significantly influenced outcome (n=77, p=0.013, RR=1.91), while treated disease (n=72) did not influence outcome. Patient death was significantly influenced by peripheral arterial disease (p=0.003, RR1.75) and the adjusted RoCKeT score (p<0.001).
Conclusion: Graft survival is negatively influenced by the presence of peripheral arterial occlusive disease, but not by the presence of dilating vascular disease. Patients untreated for arterial disease before transplantation have increased graft of graft failure while treated patients do not have an increased risk.

The agonal phase of DCD donors: parameters of success?

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Background: Donation after circulatory death (DCD) is an important source for kidney transplantation in the Netherlands. Data from experimental animal studies showed that prolonged warm ischemia time and hypoxemia can have deleterious consequences for the quality of the DCD donor kidney. Hemodynamic profiles during the agonal phase—i.e. the period between withdrawal of life-sustaining treatment to cardiac arrest—vary widely among DCD donors, raising the possibility that agonal phase characteristics are associated with recipient transplant outcome.
Methods: We investigated the association between the parameters of saturation (SpO2, measured with finger pulse) and systolic blood pressure (SBP) during agonal phase and primary non-function (PNF), delayed graft function (DGF), and 3-year graft survival rate. Graft survival was defined as graft loss or patient death or a permanent eGFR < 15 ml/min/m^2. Parameters during agonal phase were dichotomized into minutes of SpO2 > 60% or SpO2 < 60%, and minutes of SBP > 80 mmHg or SBP < 80 mmHg. We included 409 recipients (≥18y) from two Dutch transplant centers, transplanted from January 2006 to January 2014 with a circulatory-death donor (≥18y) kidney, and followed them till May 2015.
Results: Median duration of agonal phase was 16 min (IQR 11-23). After the switch-off, median SBP > 80 mmHg lasted longer than SpO2 > 60% (4 min, IQR 2-9 *vs.* 7 min IQR 7-13). Median SpO2 < 60% was 10 min (6-16) and median SBP < 80 was 7 min (IQR 4-13) till the heart stops beating. Median 1st warm ischemic time (WIT) from cardiac arrest to cold perfusion was 16 min (IQR 13 – 20). Median cold ischemic time (CIT) was 17.4 hours (IQR 13.9 – 21.0). Primary non-function rate was 6%, delayed graft function rate was 64%, and graft survival at 3 years was 77%. Longer periods of agonal phase were (borderline) significantly associated with primary non-function (p=.065), delayed graft function (p=.012), and graft survival (p=.098). Multiple regression analysis—adjusted for donor age, donor cause of death, donor creatinine, 1st WIT, and cold ischemic time—showed that 1 min increase of SBP < 80 mmHg was independently associated with DGF (OR 1.06, p=.004), and graft failure (HR 1.02, p=.002), whereas 1 min increase of SBP > 80 was independently associated with PNF (OR 1.02, p=.025). Associations were not found for SpO2.
Conclusions: We conclude that duration of agonal phase is associated with early transplant outcome. SBP during agonal phase shows better discrimination for transplant outcome of DCD donor kidneys than SpO2. Relevant cut-offs for SPB and other methods to measure SpO2 needs further investigation.

Abdominal organ procurement in The Netherlands – An analysis of quality and clinical impact

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In 2012 the quality form system was initiated to evaluate the quality of organ procurement in The Netherlands. In this study we analysed all completed quality forms from March 2012 till August 2013. Of all 754 accepted and shipped organs, 591 (78%) forms were filled out. These included 133 livers (23%), 38 pancreata (6%) and 420 kidneys (71%). Response rate for each organ was 87% (133/153) livers, 90% (38/42) pancreata and 75% (420/559) kidneys.
In 133 cases (23%) there was a discrepancy between the data from the procuring and transplanting surgeons. Injuries were seen in 148 (25%) organs of which 12 (2%) led to discard of the organ; 1/133 (0.8%) livers, 5/38 (13%) pancreata and 6/420 (1.4%), kidneys ($p<0.001$). Higher donor BMI is a risk factor for procurement related injury in all organs (OR 1.06, 95% CI 1.01 – 1.11, $p=0.011$) and DCD donation in liver procurement (OR 2.31, $p= 0.034$). DCD donation is also associated with more pancreata being discarded due to injury (OR 10.333, $p=0.046$). Furthermore, an association between a higher center procurement volume and less injuries is shown in the pancreata (OR= -0.95, $p=0.013$) and kidneys (OR=-0.91, $p=0.012$). Despite the relative high incidence of non-critical injuries there is no statistical significant difference in 1-year graft survival between (repaired) injured and intact organs for any organ.

In conclusion, the quality form system efficiently monitors the quality of organ procurement. Although there is a relatively high rate of organ injuries, the discard rate is low and it does not significantly affect 1-year graft survival for any organ. We identified higher BMI as a risk factor for injury in abdominal organs and DCD as a risk factor in livers. A higher procurement volume per center is associated with less injuries.

Influence of Ischemic Agonal Phase on Hepatic Ischemia / Reperfusion Injury and Postoperative Outcomes in DCD Liver Transplantation

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Donation after circulatory death (DCD) grafts are increasingly used in liver transplantation, but the use of these marginal grafts is associated with biliary complications and impaired graft survival rates. The DCD-specific extra donor warm ischemia time (DWIT) exposes the graft to a longer period of warm ischemia, which potentially aggravates hepatic ischemia/reperfusion injury. Our aim was to analyse the impact of DWIT on the severity of hepatic ischemia/reperfusion injury and subsequent recipient outcomes in DCD liver transplantation. We performed a retrospective single centre cohort study of all DCD liver transplantation from 2008 until 2016. DWIT was divided into two periods: ischemic agonal phase (time after treatment withdrawal that saturation drops below 80% or MAP below 50 mmHg to circulatory arrest) and asystolic phase (time from circulatory arrest to start of cold perfusion). Postoperative peak serum AST levels (72h) were used to quantify the severity of hepatic ischemia/reperfusion injury. A total of 93 recipients were included in this study. The mean length of ischemic agonal phase and asystolic phase was 13 and 16 minutes, respectively. Only the length of ischemic agonal phase was correlated with hepatic ischemia/reperfusion injury (Spearmans' rho 0.399; $p<0.001$) and multilinear modelling identified length of ischemic agonal phase ($p<0.001$), but not asystolic phase, as a factor associated with postoperative peak serum AST levels. Further analysis of the impact of ischemic agonal phase on recipient outcomes showed higher in-hospital severe complication ($p=0.001$) and mortality rates ($p=0.030$) in recipients with a ischemic agonal phase longer than 13 minutes. The 1-year graft survival was also inferior for recipients with a longer agonal phase (<=13 minutes, 92%; >13 minutes, 74%; $p=0.016$).

In conclusion, this study provides new insight on the relation between ischemic agonal phase and hepatic ischemia/reperfusion injury. Furthermore, the impact on recipient outcomes are significant and further studies are required to identify poor DCD liver grafts.

DonorDialoog Rotterdam: Niet willen, Niet mogen of Niet weten?

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Met DonorDialoog Rotterdam onderzocht de Nederlandse Transplantatie Stichting (NTS) hoe ze specifieke groepen - lager opgeleiden en niet-westerse allochtonen - beter kan bereiken, informeren en overtuigen van het belang van registratie in het Donorregister.
Van de hoger opgeleiden in Nederland staat 60% in het Donorregister geregistreerd. Van de lager opgeleiden is dit 20%. Ruim 41% van de hoger opgeleiden in Nederland zegt Ja, ik wil donor zijn, tegenover 11% van de lager opgeleiden. Van de autochtone bevolking staat 44% in het Donorregister, van de Surinaamse Nederlanders is dit 19%, van de Marokkaanse Nederlanders 13% en van de Turkse Nederlanders is dit 10%. De toestemmingspercentages in deze laatste drie groepen zijn lager dan 6%. Tegelijkertijd hebben ook veel mensen uit deze groepen een orgaan nodig: 44% van de wachtlijst voor een donornier in 2010 was van niet-westerse afkomst.
Deze cijfers, afkomstig van het CBS, waren voor de NTS aanleiding te zoeken naar manieren waarop zij lager opgeleiden en niet-westerse inwoners beter kan bereiken, informeren en overtuigen van het belang van registratie voor orgaandonatie. Hierbij speelde de vraag of men zich bewust niet wilde registreren, of dat men te weinig informatie heeft om een keuze te kunnen maken.
In samenwerking met vier maatschappelijke Rotterdamse organisaties en het Erasmus MC werden 20 voorlichters met een Marokkaanse, Turkse, Surinaamse, Antilliaanse, Kaap Verdische, Nigeriaanse, Kameroense en Eritrese achtergrond getraind in het verzorgen van voorlichtingen en het voeren van gesprekken over donatie en transplantatie. De voorlichters gaven binnen hun eigen gemeenschappen in totaal ca. 50 voorlichtingen en voerden ca. 100 'peer-to-peer'- gesprekken. Daarmee bereikten zij ca. 1.000 Rotterdammers. Bij de voorlichtingen zijn effectmetingen afgenomen die nieuwe inzichten hebben opgeleverd.
De resultaten van het project (naast - veel nieuwe inzichten op basis van de ervaringen en effectmetingen, - een toolbox met filmpjes, - standaardpresentaties en- informatiebrochures in diverse talen) delen we graag met u op het BOOT congres. Duidelijk is geworden dat een belangrijke reden voor het niet registeren een gebrek aan kennis is. Veel mensen uit de doelgroepen weten te weinig over het onderwerp om een weloverwogen keuze te kunnen maken. Ze staan er echter wel voor open. De voorlichtingen en de materialen voorzien dan ook in een behoefte.

Validation and calibration of the prognostic Kidney Donor Risk Index (KDRI) scoring system of deceased donors for renal transplantation in the Netherlands

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Background: The prognostic Kidney Donor Risk Index (KDRI)—developed and internally validated (c-statistic 0.62) in the US—is a widely used tool to predict transplant outcome of a deceased donor kidney.
Methods: We aimed to externally validate and calibrate the KDRI as proposed by Rao et al. (2009), containing 10 donor ($KDRI_{donor\text{-}only}$) and 4 transplant factors ($KDRI_{original}$), with stratification on recipient age. We used the Dutch Organ Transplantation Registry to include 3147 recipients (≥18y) from all Dutch centers, transplanted from 2002 to 2012 with a first brain-death or circulatory-death donor (≥18y) kidney, and followed them till September 2015.
Results: The median Dutch KDRI was increased to 1.21 compared with reported by Rao et al. in 2009, and comparable with the year 2012 in US (median of 1.24). Kidneys in the highest $KDRI_{original}$ quintile (1.45+) had an adjusted 5-year graft survival of 68.9%, whereas the lowest quintile (<0.79) showed survival rate of 84.7%. Discriminative ability (Harrell's C) of the $KDRI_{original}$ was 0.63 (95%CI 0.62-0.64), and slightly lower for the $KDRI_{donor\text{-}only}$ 0.62 (95%CI 0.61-0.63). Worse KDRI donors (>1.45) show less discrimination in elderly (65+) recipients than younger recipients, suggesting that in the elderly population other risk factors than the KDRI contribute to graft loss. The calibration-slope of the $KDRI_{original}$ was 0.98 (SE 0.13) and $KDRI_{donor\text{-}only}$ was 0.97 (SE 0.14), both not significant from 1 (p=.850; p=.844, respectively), indicating that discrimination of the KDRI was almost identical in the Dutch cohort. A joint test of all KDRI factors in cox regression—including the KDRI as offset term—indicated overall evidence of lack of fit ($\chi^2[13]=46.5$, p<.001). We found misspecification of the following donor factors: hypertension (p=.064), length (p=.003), weight (p<.001), and cold ischemic time (p<.001). The following donor factors delivered no added value in terms of model fit to the KDRI: atherosclerosis, smoking, HLA-A mismatches, and inotropes prior to donation.
Conclusion: The KDRI scoring system for deceased donors shows equivalent discrimination and accuracy as compared with the US. The C statistic is too low to consider the KDRI as a useful decision-making tool for the individual recipient. However, the KDRI could be used to assist allocation for longevity matching between cohorts of donors and recipients.

Targeting inflammatory kidney disease locally using liposomal prednisolone

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Background: Treatment with systemic high-dose corticosteroids (GCs) often leads to severe side effects. Liposomal encapsulation could facilitate local delivery of GCs in inflamed organs as circulating liposomes can hold their payload until they extravasate at sites of inflammation where they encounter phagocytic cells, resulting in local GC bioactivity instead of systemic exposure. This study focusses on the effect of liposomal prednisolone (LP) on macrophages, and the targeted delivery of liposomes to the kidney in a renal ischemia reperfusion injury (IRI) model in the rat.

Methods: Male Lewis rats (9 per group) were subjected to 45 minutes clamping of the left renal blood vessels and were injected intravenously with a) fluorescent liposomes or b) 10 mg/kg LP, 10mg/kg prednisolone (P), an equal volume of empty liposomes (EL), or saline (S). At 96 hours, the kidneys were imaged using a near infrared fluorescence camera and removed for histological analysis and RT-PCR. In vitro, LPS-activated human macrophages were incubated with 10 µg/mL LP, 10 µg/mL P, E, or S, and IL-6 production was measured using an ELISA.

Results: In vivo imaging revealed that fluorescent liposomes accumulated in the injured kidneys when compared to the contralateral kidneys (MFI 10.6±3.1 vs 7.3±2.5, $P<0.05$). While treatment with LP and P did not affect influx of CD68(+) macrophages upon IRI, treatment with LP led to more anti-inflammatory CD163(+) macrophages compared to P-, EL- and S-treatment (2.8±1.5 vs 0.9±1.9%, 0.3±0.1%, 0.6±0.6%, $p<0.05$). In addition, MCP-1 mRNA was reduced from 8.7±2.4% to 3.5±2.0, and 4.8±2.9 ($p<0.05$) after S vs LP and P treatment. In vitro, both P or LP incubation of macrophages revealed a 73% decreased IL-6 production compared to cells incubated with S (0,18±0,06 and 0,27±0,11 vs 1,0±0,0, $p>0,05$).

Conclusions: LP treatment of the inflamed kidney leads to increased local uptake and a shift of the infiltrate towards M2 macrophages, which is accompanied by a reduced production of pro-inflammatory cytokines. Liposomal encapsulation is therefore a promising strategy for targeted delivery of GCs to the inflamed kidney.

The autoimmune-associated single nucleotide polymorphism within PTPN22 correlates with clinical outcome after lung transplantation

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Obstructive chronic lung allograft dysfunction (BOS) is the major limiting factor for lung transplantation (LTx) outcome. Both T cell an B cell mediated autoimmunity contribute to the development of autoantibodies associated with the development of chronic rejection. *PTPN22* is described as the hallmark autoimmunity gene, and one specific single nucleotide polymorphism (SNP), rs2476601, is associated with multiple autoimmune diseases, impaired T cell regulation and autoantibody formation. Taking into consideration the contribution of autoimmunity to LTx outcome, we hypothesized that polymorphisms in the *PTPN22* gene could be correlated to BOS incidence. Therefore, we identified six selected SNPs within *PTPN22* and analyzed both patient and donor genotypes on BOS development post-LTx. A total of 145 patients and matched donors were included, and individual SNPs and haplotype configurations were analyzed. We found a significant association between patients carrying the heterozygous configuration of rs2476601 and a higher risk for BOS development (p=0.005, OR: 4.400, 95%CI: 1.563–12.390). This was confirmed via Kaplan-Meier analysis which showed that heterozygous patients exhibit a lower BOS-free survival compared to patients homozygous for rs2476601 (p=0.0047). Furthermore, one haplotype, which solely contained the heterozygous risk variant, was associated with BOS development (p=0.015, OR: 7.029, 95%CI: 1.352–36.543).
Our results show that LTx patients that are heterozygous for SNP rs2476601 are more susceptible for BOS development and indicate a deleterious effect of the autoimmune-related risk factor of *PTPN22* in patients on LTx outcome.

CMV-specific CD4+ T cells in CMV-IgG-seronegative individuals protect from CMV viremia following transplantation with a CMV-seropositive donor kidney

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A primary infection with cytomegalovirus (CMV) is one of the major threats following transplantation of a CMV-IgG-seropositive donor organ into a CMV-IgG-seronegative individual. Therefore, prophylactic treatment with valganciclovir is given in these individuals. However, CMV-specific T-cell immunity may exist without measurable anti-CMV IgG. The frequency and clinical relevance of solitary CMV-specific T-cell immunity is not known. The aim of this study is to assess the frequency of solitary CMV-specific T cells in a cohort of CMV-IgG-seronegative individuals and the clinical relevance with respect to CMV-infection following transplantation.
In a cohort of 28 CMV-IgG-seronegative and 14 CMV-IgG-seropositive individuals, CMV-specific cytokine-producing and proliferating T cells were assessed prior to transplantation using the CD137 multi-parameter assay and CFSE-dilution, respectively. CMV-specific humoral immunity was evaluated using the B-cell ELISPOT assay.
In 46% of CMV IgG-seronegative individuals CMV-specific $CD137^+$IFN-g-producing $CD4^+$ T cells were detected above background (median values amounted to 0.01% versus 0.58% in CMV-IgG-seropositive individuals). CMV-specific proliferating $CD4^+$ T cells were detected above background in 55% of the CMV-IgG-seronegative individuals (median values amounted to 0.4% versus 6.34% in CMV-IgG- seropositive individuals). CMV-specific IgG-producing antibody secreting cells (ASC) were barely detected in CMV-IgG-seronegative individuals (median values amounted to $3/10^5$ cells versus $48/10^5$ cells in CMV-IgG-seropositive individuals). However, a positive association was observed for CMV-specific $CD137^+$IFN-g-producing $CD4^+$ T cells and CMV-specific IgG ASC ($Rs=0.52$, $P<0.05$). In 46% of CMV IgG-seronegative individuals a CMV-viremia developed following transplantation. CMV-specific $CD137^+$IFN-g-producing $CD4^+$ T cells were associated with protection from a CMV-viremia following transplantation, i.e. positive responses were detected in 10/15 non-viremic versus 3/13 viremic recipients of a kidney transplant from a CMV-IgG-seropositive donor ($P=0.02$).
A solitary CMV-specific T-cell response without detectable anti-CMV antibodies is frequent and clinically relevant as it yields significant protection to infection following transplantation with a kidney from a CMV-IgG-seropositive donor.

IL-21R antagonist inhibits differentiation of B cells towards plasmablasts upon alloantigen stimulation

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Antigen-specific antibody responses rely on IL-21+ T follicular helper (Tfh) cells that regulate B cell differentiation. In transplantation, a large proportion of renal allograft recipients develop a donor-specific antibody response which is associated with an increased risk for acute and chronic rejection. Current immunosuppressive agents are mainly aimed at T-cell-mediated alloimmunity, whereas agents that effectively target humoral effectors are still insufficient. Therefore, to prevent rejections, there is a need to develop such agents. Here, we tested in an allogeneic setting whether Tfh cell help signals control B cell differentiation with its dependency on IL-21.

Patient PBMCs obtained pre kidney transplantation (n=17) were FACS sorted into CD4+CXCR5+ Tfh cells and CD19+CD27+ memory B cells and *in vitro* stimulated with alloantigen of the corresponding donor in the presence or absence of an IL-21 receptor antagonist (αIL-21R). Phospho-flow cytometry was used to determine the STAT3 phosphorylation levels of IL-21 stimulated T and B cells.

Stimulation of Tfh and memory B cells with alloantigen initiated expression of the activation markers ICOS and PD-1 on Tfh cells, and a shift towards a mixed Tfh2 and Tfh17 phenotype. The co-culture also initiated memory B cell class switch recombination and differentiation towards IgM and IgG producing plasmablasts. In the presence of αIL-21R, a dose dependent inhibition of STAT3 phosphorylation, a downstream activation molecule of the IL21R, was measured in both T and B cells. Blockade of the IL-21R did not have an effect on PD-1 and ICOS expression on Tfh cells but significantly inhibited B cell differentiation. The proportion of plasmablasts decreased by 78% in the presence of αIL-21R (p=0.004). Moreover, secreted IgM and IgG2 levels were significantly lower in the presence of αIL-21R (p=0.004, p=0.004, respectively).

Our results demonstrate that IL-21 produced by alloantigen activated Tfh cells controls B cell differentiation towards antibody producing plasmablasts. The IL-21R might therefore be a useful target in organ transplantation to prevent alloantibody mediated immune responses leading to graft failure.

Multiplex PCR Screening of MicroRNAs in Graft Preservation Fluid during Liver Transplantation for Biomarker Discovery

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Introduction: MicroRNAs (miRNAs) have been extensively investigated in recent years as biomarkers in liver transplantation. A variety of miRNAs in serum, tissue and bile have been demonstrated to correlate to rejection, early allograft dysfunction (EAD) and biliary complications after transplantation. However, the global miRNAs profiles in graft perfusion fluids during liver preservation have not been reported. In this study we aimed to identify perfusate miRNA profiles and investigate their potential to predict graft outcomes after transplantation.

Material & methods: Cell-free preservation fluids of 32 liver grafts at the end of cold storage were analyzed for miRNA content using Taqman microRNA array card A. 50% of grafts were from donation after brain death (DBD) and 50% from donation after circulatory death (DCD). For both donor types 8 grafts resulting in EAD and 8 resulting in non-EAD were included. Bioinformatics analysis was performed using the R-package HTqPCR on Ath miR-159a normalized datasets.

Results: 220 miRNAs were reliably detectable in perfusates. A difference in miRNA levels was seen between DCD and DBD livers for miR-523-3p, miR-525-5p, miR-382, miR-7a and miR-200a ($p<0.01$). Furthermore, 11 miRNAs were identified as significantly different between EAD and non-EAD grafts (miR-491-5p, miR-200c, miR-382, miR-220, miR-221, miR-510, miR-542, miR-518b, miR-379 miR-204 and miR-122, $p<0.01$), known to be liver abundant. Perfusates of liver grafts which developed biliary lesions after liver transplantation showed six new miRNAs (miR-455-5p, miR-191, miR-324-5p, miR-142, miR-302, miR-410, $p<0.01$).

Conclusion: In this discovery study we have identified several new miRNAs in graft preservation solutions of liver grafts related to donor type and post transplantation graft function. Further research is ongoing to validate the use of these miRNAs to assess graft quality during preservation in a larger cohort.

MinION Single Molecule Sequencing: the new way of HLA allele resolution typing in low and high volume laboratories

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The Human Leucocyte Antigen (HLA) complex plays a major role in the defense against foreign pathogens. In stem cell transplantation the highest possible resolution matching of patient and donor increases the chance of a successful outcome. In organ transplantation the detection of HLA antibodies against HLA epitopes urges HLA typing at the allelic level for patient and donor, especially in highly immunized patients. Allelic resolution HLA typing has evolved from PCR and probe based techniques to Sanger sequencing and Next Generation Sequencing nowadays applied in many HLA laboratories across the world. These techniques are rather expensive (Sanger sequencing) and/or time consuming (NGS). We have now developed the MinION single molecule sequencing for HLA class I and class II. This method is a cheap sequencing method, with sample preparation and sequencing taking only a few hours and it can be used by both low and high throughput laboratories. With this application ultra-long reads are created, up to 100,000 bases, which enables the production of reliable fully phased stretches of full length HLA sequences in contrast to NGS methods with short reads. Results from class I amplicon based MinION sequencing confirmed the reliability, validity and efficiency of the method with sufficient read depth, covering the full length gene from the start of the 5' UTR to the end of the 3' UTR. Initial results from class II full length sequencing already shows the applicability of this method for DQA1, DQB1, DPA1 and DPB1 with one amplicon, whereas for full length DRB1/3/4/5 two separate amplicons are needed due to the length of the gene. At the moment we are investigating the recently described probe captured method for the complete HLA region in combination with MinION sequencing, which would make the allelic resolution typing of deceased donors feasible within the limited time frame.

Differential effects of immunosuppressive drugs on DNA methylation in T cells

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DNA methylation controls cell functions by regulating gene expression. Changes in DNA methylation of immune-related genes can influence the immune response after transplantation. Here, we investigated the effect of tacrolimus and mycophenolic acid (MPA), two commonly prescribed immunosuppressive drugs, on changes in promoter DNA methylation of the pro-inflammatory cytokine interferon-gamma (IFN-γ) during immune activation in T cells.

Pure total T cells, naive ($CCR7^+CD45RO^-$) T cells and memory ($CD45RO^+$ and $CCR7^-CD45RO^-$) T cells were stimulated separately for 3 days with α-CD3/CD28, and in combination with tacrolimus (10 ng/mL) or MPA (0.2 μg/mL). 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 T cell differentiation and IFN-γ protein production.

DNA methylation of *IFN-γ* in total T cells significantly increased after stimulation from 46.6% to 54.1% at day 3 ($p=0.001$). Addition of tacrolimus or MPA did not affect this increase in methylation. To determine whether this observation is the result of T cell differentiation, we studied *IFN-γ* DNA methylation in isolated naive and memory T cells. After activation, naive T cells differentiated towards a memory-like phenotype (CD45RO+) and in parallel a decrease in *IFN-γ* DNA methylation from 79.3% to 69.8% ($p=0.002$) was found. Immunosuppressive drugs significantly inhibited the differentiation of naive T cells towards CD45RO+ cells ($p=0.02$) and differentially affected the DNA methylation changes. MPA neutralized the effect of stimulation (80.7% at day 0 to 78.2% at day 3) whilst tacrolimus showed a similar decrease after stimulation. DNA methylation and differentiation of the isolated memory population were unaffected by immunosuppressive drugs. IFN-γ protein production by these cells was significantly blocked by tacrolimus but not by MPA.

DNA methylation of *IFN-γ* was influenced by MPA but not by tacrolimus while the differentiation of T cells was inhibited by both immunosuppressive drugs. Changes in DNA methylation as a result of immunosuppressive medication can occur independently of changes in cell phenotype and these do not necessarily follow the same dynamics after immune activation.

POSTERS

Panel reactive antibodies is a debatable indicator of post-transplant function and survival

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Panel reactive antibodies (PRA) estimation is widely used in determining sensitization status and severity. Currently there is no strong evidence supporting that PRA% is predictive as a prognostic measurement for renal allograft outcome. Here, we investigated the value of PRA% as a prognostic indicator of post-transplant function and long-term renal allograft survival.

All patients who received a renal allograft at our Center from 2010 through 2014 were included. We retrospectively analyzed the association of current-pretransplant PRA% (cPRA%) and highest measured PRA% (hPRA%) (cut-off value 6%) with the incidence of rejection and it's association with kidney function. Patients were divided into three groups. Group 1, control group, is negative for cPRA% and hPRA%. Group 2 is hPRA% positive and cPRA% negative. Group 3 is cPRA% positive and hPRA% positive. Clinical data were collected.

A total of 942 patients was included and 866 for cause renal biopsies were obtained from 471 patients. Strikingly, there is no significant relation between hPRA% and increased biopsy proven rejection rate (P=0.08) No significant difference in eGFR at 3 and 12 months post-transplant was found between groups. The hPRA% positive groups had a trend in developing more proteinuria at 3 and 12 months post-transplant compared to the control group (P=0.05). Also no significant difference was found between the hPRA% positive group and the cPRA% and hPRA% positive group (P=1.00).

We conclude that cPRA% and hPRA% values do not predict the occurrence of rejection and are not associated with graft function and proteinuria up to one year after transplantation. We therefor question the use of PRA% in this setting in prioriting patients for eligibility for solid organ transplantation.

A search for a biomarker to predict belatacept-resistant rejection in kidney transplantation

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Belatacept, an inhibitor of the CD28-CD80/86 co-stimulatory pathway, allows for calcineurin-inhibitor free immunosuppressive therapy in kidney transplantation but has been associated with a higher acute rejection risk than ciclosporin. Thus far, no biomarker for belatacept-resistant rejection has been identified.
In this randomized controlled trial, 40 kidney transplant recipients were 1:1 randomized to belatacept or tacrolimus combined with basiliximab, mycophenolate mofetil and prednisolone. The 1-year incidence of biopsy-proven acute rejection (BPAR) was monitored. Potential biomarkers, namely $CD8^+CD28^-$, $CD4^+CD57^+PD1^-$ and $CD8^+CD28^{++}$ EMRA T-cells were measured pre-transplantation and correlated to BPAR after transplantation. Pharmacodynamic monitoring of belatacept was performed by measuring free CD86 on circulating monocytes.
The incidence of BPAR was higher among belatacept-treated than tacrolimus-treated patients: 50% *vs.* 10%; p = 0.01. The majority of rejections occurred within 3 months after transplantation. Three graft losses, due to BPAR, occurred in the belatacept group *vs.* none in the tacrolimus group. There were no differences in pre-transplant values of the biomarkers between rejectors and non-rejectors in the belatacept group. In univariable Cox regression analyses, the studied cell subsets were not significantly associated with the risk of developing BPAR. CD86 molecules on circulating monocytes in belatacept-treated patients were saturated at all time points.
Belatacept-based immunosuppressive therapy resulted in significantly higher and more severe acute rejection compared to standard, tacrolimus-based therapy. Neither cellular biomarkers nor insufficient blockade of the CD28-CD80/86 co-stimulatory pathway predicted BPAR.

DSA presence does not affect renal histology and clinical outcome in chronic active antibody mediated rejection

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Chronic active antibody mediated rejection (caABMR) is a major cause of long term renal allograft dysfunction. It is defined by the presence of microvascular inflammation (MVI), histopathological changes compatible with transplant glomerulopathy (TG) and the presence of donor specific antibodies (DSA). Ongoing activation of endothelial cells by circulating DSA is associated with MVI and the subsequent development of TG. Although considered mandatory for the diagnosis of caABMR, it is not uncommon for TG with MVI to present itself without detectable DSA. In this study we evaluated whether the presence or absence of DSA is associated with renal histology, allograft survival and response to therapy.

Forty-one biopsy-proven caABMR patients were included retrospectively between 2007 and 2014. All patients had progressive loss of allograft function and were treated similarly after diagnosis. DSA status was determined by single bead Luminex assay. Clinical characteristics, histomorphology, renal allograft function, response to therapy and allograft survival were compared between the DSA+ (N=17) and DSA- (N=24) caABMR patients. Possible variation in DSA detectability over time was assessed for the DSA- patients.

In all cases, DSA were de novo and the majority was directed against HLA-II being mostly anti-HLA-DQ antibodies. There were no statistically significant differences found in the clinical characteristics, renal allograft survival and histomorphologic lesions between patient groups. Both groups showed substantial and severe chronic histopathological damage and inflammation, consistent with caABMR. Decline in allograft function was similar without a statistically significant difference in treatment effect between the two groups (p=0.93).

However, C4d+DSA+ patients showed significantly poorer allograft function and better response to therapy prior to caABMR diagnosis when compared to C4d-DSA+ patients (p=0.01).

Conclusion. The presence or absence of detectable DSA has no significant association with renal histology and clinical outcome in caABMR patients. We did however find that, irrespective of DSA+, patients with caABMR and C4d+ in their biopsy responded better to therapy.

Urine neutrophil gelatinase-associated lipocalin (NGAL) after revascularization is indicative of renal graft recovery in children

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Introduction: Ischemia-reperfusion injury of transplanted donor kidneys results in tubular injury and subsequently the release of NGAL in the urine. We hypothesized that NGAL in the postoperative urine samples of transplanted kidneys reflects graft injury.

Methods: All children receiving a kidney transplantation at the 3 pediatric kidney transplantation centers in the Netherlands were eligible for this prospective observational study. Excluded were patients who did not have separate sampling of urine from donor kidney and native kidneys, except for patients without residual diuresis.

Urine was sampled pre-transplant, and at 3, 6, 12, 24, 36, and aiming at 48 and 72 hours post-revascularisation (RV), in separate portions from the splint (only graft urine), and from the bladder (mixed urine from native kidneys and the graft).

NGAL was assessed by immunoassay. In this study NGAL was analyzed as absolute concentration. Area under Curve (AUC) and maximal concentration (Cmax) was calculated by the Microsoft based program (PK Solver).

Half-life of the serum creatinine value acquired at RV was calculated by a linear trapezoidal method from the values measured at 6, 12, 24, 36 and 60 hours after RV. eGFR at 3 months was calculated. Data were analyzed using non-parametric tests.

Results: Sixty-six patients (37 boys; median age 10.2 yr, range 1.6-17.9) were included, of whom 15 (23%) received a deceased donor (DD) kidney and 39 (59%) had had previous dialysis treatment. Median half-life of serum creatinine was 33.6 hrs (IQR 13.5 – 109.5) for DD, and 7.8 hrs (range 5.1-12.0) for living-donor (LD) transplants No patient needed dialysis post-transplant.

Splint urinary NGAL was maximal at 3 (first sample) or 6 hours post-RV, with a median concentration of 150 ng/ml (IQR 42 – 629). Cmax was associated with creatinine half-life ($p< 0.001$), donor source (lower in LD, $p<0.001$), but not with recipients' age. Cmax was not predictive of eGFR at 3 months post-transplant.

The median AUC of NGAL in splint urine was 2394 uur.mcg/l (IQR 912-8086). The AUC was significantly associated with creatinine half-life ($p<0.001$) and donor source ($p<0.001$), but not with age, or eGFR at 3 months post-transplant.

Conclusion: Especially in recipients of DD kidneys both the Cmax and the AUC of NGAL in the urine of the graft is associated with the velocity of graft recovery. Urine Cmax of NGAL is a promising early predictor of graft recovery.

Pretransplant numbers of CD16+ monocytes as a novel biomarker to predict acute rejection after kidney transplantation; a pilot study

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Acute rejection is one of the major immunological determinants of kidney graft function and survival. Early biomarkers to predict rejection are lacking. Emerging evidence reveals a crucial role for the monocyte-macrophage lineage cells in the pathogenesis of rejection. We hypothesized that higher pre-transplant numbers of proinflammatory CD16+ monocytes can predict rejection.

The study cohort consisted of 104 kidney transplant recipients (58 non-rejectors and 46 biopsy-proven rejectors), and 33 healthy individuals. Posttransplant median±IQR follow up time was 14.7 (0.3-34) months. Pretransplantation blood samples were analyzed by flow cytometry for monocyte immunophenotypes. Groups were compared by Cox regression models for the occurrence of acute rejection.

We documented a significantly increased absolute number of pretransplant CD16+ monocytes in patients who developed biopsy proven rejection after transplantation compared to non-rejectors and healthy individuals (Hazard Ratio [HR], 1.60; 95% Confidential Interval [CI], 1.28 to 2.00; p<0,001 and HR, 1.47; CI, 1.18 to 1.82, p<0,001). In parallel, significantly less absolute numbers of CD16- monocytes were observed at pretransplant time point in rejectors vs non-rejectors (HR, 0.74; CI, 0.58 to 0.94; p<0,014).

A higher pre-transplant number of CD16+ monocytes is significantly associated with a higher risk of acute rejection after kidney transplantation.

Towards a conditional approach to anonymity in the Netherlands? – a multi-center prospective study among anonymous donors and recipients

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Anonymity of donors and recipients is a recurrent topic of discussion among transplant professionals . Studies on the donor and patient perspective on anonymity are scarce and mainly cross-sectional in nature, and/or were conducted over a decade ago, prior to the considerable growth in anonymous living programmes. Such studies are needed to include the opinion of donors and patients in policies on anonymity. This prospective study aimed to fill this gap by investigating donors' and patients' experiences with and attitude towards anonymity.

Individuals who anonymously donated or received a living donor kidney between July 2015 and May 2016 in the Netherlands were asked to complete a questionnaire before surgery (T0) and 3 months after surgery (T1). Questions concerned experiences with and satisfaction about anonymity; their attitude towards anonymity and demographic and medical characteristics. Due to the skewed distribution of the data, non-parametric tests were used to assess group differences and associations between attitude towards anonymity and demographic and medical characteristics, such as type of transplant program (unspecified/specified indirect).

Seventy-two donors and 50 recipients participated in the study (response rates 81% and 63% respectively). Participants were content with anonymity at T0 and T1. Fourteen percent of participants wanted to meet at T0 and 23% wanted to meet at T1. If the other party expressed the wish to meet, 50% (T0) and 55% (T1) would be open for a meeting. Two donors accidentally met their recipient. Most participants agreed with the principle of anonymity both before and after surgery, but also agreed that a meeting should be allowed if both parties agree to that. Attitude towards anonymity was not associated with type of transplant program and did not differ between donors or recipients and between T0 or T1.

Even though the majority of donors and recipients are satisfied with absolute anonymity (for their own procedure), they believed that (other) pairs should be allowed to meet if both parties agree to that. A conditional approach to anonymity would address this desire for autonomy. If such an approach were to be adopted, this would require effort from transplant professionals to accurately register individuals' wish to meet and to educate them on potential advantages and disadvantages of non-anonymity. Based on our findings we will provide recommendations for standardized education on anonymity.

Predictors for delayed graft function in living donor kidney transplantation

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Living donor kidney transplantation has experienced a marked increase in the Netherlands and despite the excellent results a risk of complications remains. Delayed graft function (DGF) is an uncommon complication after living donor kidney transplantation with a reported incidence of 5%. However, as DGF after living donor transplantation is unexpected, it has a major impact on post-operative care, resulting in numerous diagnostic procedures including early biopsies. The aim of this study was to evaluate possible predictive perioperative factors for developing DGF after living donor kidney transplantation.

All living donor kidney transplantations performed between 1993 and 2013 were extracted from our transplant database and analyzed. For each identified subject with DGF, three matched controls with similar recipient characteristics (gender, age and year of transplantation) were then included to form the control group. DGF was defined as the need for dialysis within the first week after transplantation. Recipient and donor characteristics (i.a. body mass index, preoperative dialysis, gender and HLA mismatches and ABO incompatibility) were evaluated in addition to various surgical and anesthesia parameters (i.a. right or left kidney, number of arteries and veins, ischemia times, duration of hypotension and anaesthetic and analgesic agents).

From a total of 690 living donor transplant patients, 4,1% developed DGF. Predominantly males were transplanted (62.2%), with a mean age of 49.0±12.9 years (mean ± SD). Only pre-transplantation dialysis (OR 3,069; 1,270-7,417; p=0.013) and transplantation of the right kidney (OR 3,786; 1,627-8,811; p=0.002) were predictors for the development of DGF after living donor kidney transplantation. Anesthetic management seemed to be of no influence during this period. Ischemia times and duration of hypotension did not correlate with the occurrence of DGF.

The finding that pre-transplantation dialysis is a risk factor for DGF after living donor kidney transplantation may be related to recipient volume status. Careful assessment of volume status and correction of hypovolemia prior to transplantation may be helpful in the prevention of DGF after living donor kidney transplantation. Our finding of the importance of the use of the right kidney requires further evaluation, but if confirmed, may be taken into consideration in kidney side selection.

Improving recognition of potential tissue donors; a quality improvement project by a hospitalist in training in The Netherlands

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The number of effectuated tissue donations has shown a decreasing trend in The Netherlands over the last years. The aim of this study was to assess the number of missed tissue donors and to develop an improvement plan. We retrospectively analyzed patient files of all deceased patients in 2014 for their potential as a tissue donor. Our primary aim was to determine the number of missed tissue donors. Our secondary aim was the percentage of correct identification of a possible tissue donor amongst all physicians and hospitalists in training. Additionally, three focus group discussions and a clinical audit determined the level of knowledge about, and adherence to the local and national protocols. This enabled us to suggest national and local improvements to lower the percentage of missed tissue donors. Patient files of 548 deceased patients were analyzed. The number of missed tissue donors was 94 (17.2%). The percentage of correct identification was 65.7% amongst all physicians (Cohen's Kappa Coefficient 0.557, p=<0.001). The percentage of correct identification was 57.1% amongst hospitalists in training (Cohen's Kappa Coefficient 0.492, p=<0.001). There was no statistical difference in correct identification. In 31 patients (32,4%), the reported contra-indication by physicians was not a contra-indication for tissue donation in The Netherlands. Better informing physicians about contra-indications and aiding them in the recognition of a tissue donor are the most potential improvements to increase the number of tissue donations.

Wat is er en wat moet er komen?
Het scholingsaanbod voor donatieprofessionals in Nederland

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Introductie: goede donatiezorg kan verleend worden als de zorgprofessionals die betrokken zijn bij postmortale orgaan- en weefseldonatie beschikken over voldoende kennis en vaardigheden. De Nederlandse Transplantatie Stichting (NTS) verzorgt scholing voor deze zorgprofessionals. Echter, er bestaat niet een gestandaardiseerd opleidingsprogramma binnen de ziekenhuizen. Onduidelijk is waar de behoefte van deze zorgprofessionals ligt. Wij hebben gekeken welke functies belangrijk zijn in het donatieproces en onderzocht welke scholing momenteel beschikbaar is, hoe deze scholing beoordeeld wordt, en een inventarisatie gemaakt welke scholing ontbreekt.
Methode: de diverse functies zijn geïdentificeerd door het donatieproces van begin tot het eind in kaart te brengen: van donorherkenning tot en met uitname van weefsels en organen. Vragenlijsten zijn ontwikkeld en digitaal verstuurd in een twee-stap methode namelijk 1. respondenten die rechtstreeks zijn benaderd en 2. respondenten die benaderd zijn via een tussenpersoon bij 1. genoemd. Functieprofielen van de professionals zijn bestudeerd en vergeleken met de antwoorden die de professionals gaven op de vragenlijsten.
Resultaten: in de ziekenhuizen zijn 19 functies geïdentificeerd die nauw betrokken zijn bij postmortale orgaan- en weefseldonatie. In totaal hebben 372 respondenten de vragenlijst ingevuld van wie 38 gedeeltelijk. Van de professionals geeft 44% aan te zijn ingewerkt en 71% van alle professionals heeft scholing gevolgd. Slechts 19% van de verpleegkundigen geeft aan te zijn ingewerkt; mortuariummedewerkers en ZUT-medewerkers scoren laag op zowel inwerktraject als scholing. De Communicatie rond Donatie training is het meest (48%) gevolgd en wordt als goed beoordeeld. Het aanbod van scholing is toereikend vindt 54% van de respondenten. Met het verplicht stellen van scholing is 66% van de respondenten het eens en accreditatie wordt belangrijk gevonden door 58%.
Conclusie: scholing wordt door de zorgprofessionals belangrijk gevonden en verdieping van het huidige aanbod is gewenst. De bestaande scholing bereikt niet alle zorgprofessionals. In een donatiecurriculum is de bestaande en gewenste scholing beschreven waarbij een onderverdeling is gemaakt in opleidingen waarbij de professional zich de benodigde kennis en vaardigheden eigen maakt (Basaal) en de 'Éducation permanente' waarbij de professional blijft (bij)leren.

Does "the eye of the donor surgeon" predict kidney transplant outcome?

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Previously, we demonstrated that the retrieval surgeon's subjective assessment of overall donor organ quality and perfusion best predicted the outcome of deceased donor kidney transplantation. In this study, we prospectively quantified the subjective impression of the donor surgeon to transplant outcomes.

Between 2014-2016, we performed a prospective regional pilot study for which a detailed organ assessment form was developed to be filled in by retrieval surgeons. Data scored were: temperature, kidney size, kidney perfusion, anatomical characteristics and abnormalities, atherosclerosis, degree of renal artery stenosis and overall quality of kidneys. Variables were scored categorically or on a 1-10 scale. Data on donor and recipient characteristics and graft function after transplantation were gathered. Correlations were made between organ assessment and graft function (immediate graft function (IGF) versus delayed graft function (DGF) or primary non-function (PNF)), and serum creatinine at 3 months post-transplantation.

In this study, 90 donors donated 178 kidneys of which 166 were transplanted (46.4% DBD, 53.6% DCD). The 12 discarded kidneys significantly more often were from DCD donors that were older, smoked, had lower BMI, lower quality parenchyma and acceptable perfusion from whom liver or pancreas were not retrieved. IGF was achieved in 55%, DGF in 35%, PNF in 4%, and unknown in 6% of the recipients. DGF/PNF occurred significantly more frequently in DCD kidneys (66% versus 49%, p=0.049), in donors with higher BMI (26.4±5.3 vs. 24.7±4.5, p=0.033), with less hypotensive episodes (10% vs. 29%, p=0.005), with lower perfusion quality (8.3±1.3 vs. 8.8±1.1, p=0.017), and larger kidneys (length: 11.8±1.6 vs. 11.1±1.3 cm, p=0.006, and width 6.1±0.9 vs. 5.8±0.9 cm, p=0.037), and in the presence of cysts (p=0.032) compared to IGF. The other variables were not significantly different between the groups. The data on serum creatinine at 3 months and 1 year after transplantation are incomplete and will be analysed in a later phase.

DGF/PNF after deceased donor kidney transplantation occurs more often in large kidneys that were poorly perfused as assessed by the donor surgeon. These kidneys would probably benefit most from reconditioning strategies, such as machine perfusion. A more precise scoring system might aid in decision-making towards acceptance, allocation, and potential reconditioning strategies.

The golden hour: length of total warm ischemia time presages development of severe acute kidney injury after DCD liver transplantation

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Acute kidney injury (AKI) is more frequently observed in DCD liver transplantation (LT). The DCD-specific donor warm ischemia time (DWIT) aggravates hepatic ischemia/reperfusion injury and thereby enhances renal impairment. Our aim was to analyse the impact of all warm ischemia periods on development of AKI after DCD LT. We performed a retrospective two Center study of all DCD LT (2008-2016). AKI was defined following KDIGO criteria. DWIT was divided into two periods: agonal phase (donor treatment withdrawal–circulatory arrest) and asystolic phase (circulatory arrest–cold perfusion). Total warm ischemia time was defined as the sum of DWIT and recipient warm ischemia time (RWIT). Multiple logistic regression was used to identify factors associated with development of severe postoperative AKI (KDIGO stage 2&3). A total of 368 recipients were included. 239 recipients (65%) developed AKI, including 151 recipients (41%) with severe AKI. The relation between all warm ischemia periods and AKI differed between Centers. In Center 1 only RWIT was longer in recipients with severe AKI (40 minutes) compared to recipients with no or mild AKI (36 minutes) ($p=0.003$). On the contrary, in Center 2 only agonal phase was longer in the severe AKI group (19 vs 15 minutes; $p=0.028$). Analysis of the entire cohort showed that the total warm ischemia time increased with severity of AKI: 61 minutes in recipients without AKI up to 69 minutes in recipients with AKI stage 3 ($p<0.001$). Multiple logistic regression identified length of TOTAL warm ischemia time as a factor associated with severe AKI (OR 1.032; 95%CI 1.014-1.051; $p<0.001$). In conclusion , the extra DWIT in DCD LT exposes grafts to more hepatic ischemia/reperfusion injury upon the warm ischemia prior to reperfusion. Although the composition of warm ischemia may differ between Centers, the length of total warm ischemia time is associated with development of severe AKI and should ideally not exceed 60 minutes.

Mental disorders among unspecified living kidney donors

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Background: In unspecified living kidney donation psychosocial screening is performed to determine whether donors are mentally stable enough to donate safely. The aim of this study is to investigate what proportion of these donors has been diagnosed with a post-donation mental disorder.
Methods: We retrospectively searched the medical records for individuals who were included as unspecified donors between May 2000 and November 2016 and registered which donors reported symptoms and/or a diagnosis of a mental disorder during the routine post donation medical check-up. We also recorded whether donors (partly) attribute their acquired mental disorder to the donation.
Results: In total, 142 unspecified donors donated. Within this group 8% reported psychopathology within three years post-donation namely, posttraumatic stress disorder (n=2), depression (n=1), bipolar disorder with suicidal gestures (n=2), unspecified psychiatric breakdown (n=1), personality disorder not otherwise specified (n=1) and depressive symptoms not meeting the full DSM-IV criteria (n=4). Four donors (partly) attributed their decrease in mental health to the donation.
Discussion: A small proportion of unspecified living kidney donors acquire mental disorders within three years post-donation. This percentage is comparable with the prevalence in the Dutch general population (9%). This finding could suggest that no additional care other than normal psychological care is warranted. Nevertheless, it is understandable that the donor and his/her surrounding attribute a decrease in mental health at least in some degree to the 'life event' of the donation. Such attribution is not necessarily wrong, and justifies a duty of care. These findings emphasize the need for a detailed psychological follow-up of these donors in order to identify those at risk and to provide early psychological intervention where necessary. Using such follow-up data, studies can identify the association between the characteristics of the donor and donation process on the one hand and the change in mental status on the other.

Living kidney donation a major life event - What do the donors say?

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Introduction: professionals suggest that living kidney donation is a major life event, given that living kidney donors (LKDs) have to adjust their daily activities for a couple of weeks. To date it is unknown whether LKDs themselves experience the donation as a major life event and what the relative impact is compared to other life events. Insights into these questions are important for the education of potential LKDs.
Methods: data from 2 studies were combined. LKDs were interviewed 3 (n=111) and 12 months (n=127), or ≥36 months (n=614) postdonation. The last group was asked whether they experienced the donation as a major life event (yes/no). All LKDs were asked to recall all other events that impacted their lives in the past year (e.g. birth of a child and death of a parent). They completed two 10-point scales for each event and the donation: whether they have experienced the event as negative/positive and the impact of the event on their lives. Higher scores indicated a more positive experience and a higher impact. All life events were ranked based on their experience and impact score. The experience score of the donation was categorized as a negative (0-5) or positive (5.1-10) event. Multiple logistic regression analyses were conducted to examine whether donors' and recipients' medical complications were associated with the impact and experience score.
Results: 45% of the donors experienced the donation as a major life event. The majority (95%) experienced the donation as positive. The median score for experience of the donation was 9 (range 0-10), which was comparable with ratings of marriage/cohabitation and moving house. Median scores for impact of the donation were 5, range: 0-10 (3 and 12 months postdonation) and 6, range: 1-10 (≥ 36 months postdonation). These were comparable with marriage/cohabitation and retirement. Donors who experienced more (recipient) medical complications evaluated the donation more often as a negative and impactful event.
Conclusions: living kidney donation is generally experienced as a positive event with a relatively moderate impact on donors' lives. Less than half of LKDs labeled the donation as a major life event. These findings can be used to inform potential LKDs and their families about the impact of living kidney donation. Nevertheless, professionals should be aware of the elevated impact of donation in case of (recipient) medical complications and provide these donors extra support if needed.

Predictive value of renal transplant scintigraphy for the duration of delayed graft function

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Background: renal scintigraphy (RS) is a widely used test for the assessment of the transplanted kidney (KTX). As RS cannot reliably distinguish between rejection and acute tubular necrosis we questioned whether RS could predict the expected duration of delayed graft function (DGF) and thus help guide the timing of a renal biopsy. This study focused on RS results, quantitatively analyzed and qualitatively graded, related to the duration of DGF. Improving the predictive value and clinical applicability of qualitative and quantitative RS indices may result in a more reliable prediction of the duration of early graft dysfunction, resulting in a reduction of the number of diagnostic biopsies and faster treatment.
Methods: from 2000 to 2014, all post-KTX RS procedures performed in patients with early transplant dysfunction were included. The duration of DGF was defined as the number of days of dialysis-based and/or functional DGF. All RS procedures were performed using Technetium-99m mercaptoacetyltriglycine (MAG3) with an intravenous administration dose of 80 MBq and were reanalyzed for the purpose of this study. RS results were qualitatively graded and various quantitative indices (*Retention to Uptake ratio* (*R20/3*), *Tubular Function Slope* (*TFS*), *corrected Tubular Extraction Rate* (*cTER*), *Uptake corrected for injected dose* (*MUC10*)) were combined with a new index (*Average upslope)*.
Results: a total of 177 patients were included, the mean age (± SD) was 49 ± 14 years, 57% were male, 17% received transplant after living-(un)related KTX, 41% after donation after brain death, and 42% after donation after circulatory death. A total of 136 (77%) patients experienced DGF ≥7 days of which 96 (54%) ≥14 days. Qualitative grading for the prediction of DGF >7 days had sensitivity and specificity of respectively 88% and 70%. The quantitative indices with the most optimal results for the prediction of DGF≥7 days were *cTER* (73% sensitivity, 85% specificity), and *Average upslope* (68% sensitivity, 84% specificity).
Conclusions: in conclusion, the qualitative RS-grading and the RS quantitative indices cTER and Average upslope seem accurate predictors of DGF duration, in particular for DGF > or < than 7 days post-transplantation. Analyses of RS allows the identification of patients in whom the duration of DGF is longer than predicted and thus may help in identifying the need and timing of renal biopsy after KTX.

Kidney Retransplantation in the Ipsilateral Iliac Fossa: A Surgical Challenge

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The aim of this study is to review the surgical outcome of kidney retransplantation in the ipsilateral iliac fossa in comparison to first kidney transplants.
The database was screened for retransplantations between 1995 and 2013. Each study patient was matched with 3 patients with a first kidney transplantation. Just for graft and patient survival analyses, we added an extra control group including all patients receiving a second transplantation in the contralateral iliac fossa. We identified 99 patients who received a retransplantation in the ipsilateral iliac fossa.
There was significantly more blood loss and longer operative time in the retransplantation group. The rate of vascular complications and graft nephrectomies within 1 year was significantly higher in the study group. The graft survival rates at 1 year and 3, 5, and 10 years were 76%, 67%, 61%, and 47% in the study group versus 94%, 88%, 77%, and 67% ($p<0.001$) in the first control group versus 91%, 86%,78%, and 57% ($p¼0.008$) in the second control group.
Patient survival did not differ significantly between the groups. Kidney retransplantation in ipsilateral iliac fossa is surgically challenging and associated with more vascular complications and graft loss within the first year after transplantation. Whenever feasible, the second renal transplant (first retransplant) should be performed contralateral to the prior failed one.

Comparison of estimated and measured Glomerular Filtration Rate in Longitudinal Follow-up after Living Kidney Donation

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Donor safety requires reliable long term follow-up of renal function after donation. We tested the longitudinal performance of estimated Glomerular Filtration Rate (eGFR) to detect renal function loss after donation by comparison with 125I-iothalamate measured GFR (mGFR), the gold standard.
We compared the slopes of MDRD, CockcroftGault (CG) and CKD-EPI equations with mGFR (125I-iothalamate) to assess renal function loss from 3 months after donation until 5 or 10 years after donation in 146 living kidney donors. We tested eGFR slopes for bias by tertiles of mGFR slopes.
At donation, donors (age 51(10) years, 53% male) had a median [IQR] mGFR of 103 [92;115] mL/min. After donation, mGFR was 65 [59;72], 66 [57;75] and 69 [61;77] mL/min at 3 months, 5 and 10 years, respectively. In donors with decreasing mGFR (n=59/146, slope -0.5 [-1.3;0.0] ml/min/yr), the slope was underestimated by all eGFR equations (CKD-EPI bias -2.4 [-3.8;-1.1] ml/min/1.73m2/yr, p<0.001; MDRD bias -2.6 [-3.7;-1.2] ml/min/1.73m2/yr, p<0.001; and CG/BSA bias -0.6 [-2.2;-0.3] ml/min/1.73m2/yr, p=0.02).
These data show that eGFR equations underestimate the slope of renal function in living donors with pronounced mGFR loss, underlining the value of mGFR in long term follow-up.

Results of the second decade of the Trans-Atlantic Airlift for renal transplantation recipients from the Dutch Antilles: an unique program comes of age

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Background: the prevalence of end-stage renal disease in the Dutch Caribbean is twice as high compared to the Netherlands. In 1998, the St. Elisabeth Hospital and in 2003 the Dr. Horacio E. Oduber Hospital in Aruba, started a unique trans-Atlantic collaboration with the Academic Medical Center in Amsterdam, the Netherlands, and the Eurotransplant Foundation. This study is an analysis of the early renal outcome of this trans-Atlantic program from April 2007 until August 2016. From April 2007 two measures were taken: 1) all patients received induction therapy with basiliximab, and 2) only brain-death donors in case of deceased donors were accepted.

Methods: in 88 consecutive transplantations performed between April 2007 and August 2016, 3 month graft survival, primary non function and rejection rate at 3 months were studied. These were compared with 39 transplantation between April 1997 and end of March 2007.

Results: sixty patients received a first and 3 received a second deceased donor transplant, and 24 patients received a first and 1 a second living donor transplantation. Mean recipient age of deceased and living donors was 52 years (SD 13) and 48 years (SD 15) respectively. Original disease was hypertension (22%), diabetes 17%, glomerulonephritis (6.3%) cystic kidney disease (6.3%). Dialysis vintage of deceased and living donors was 72 months (SD 30) and 40 months (SD 23) respectively. Donor age was 52 years (SD 12) and 52 years (SD 14) for deceased and living donors respectively. Median cumulative HLA mismatches were 3 (IQR 2-4) in deceased and 3 (IQR 3-4) in living donors. Cold Ischemic time was 24.2 hours (SD 8.6) in deceased and 2.9 (0.6) hours in living donors. Primary non-function rate and delayed graft function was 3.2% and 31% in deceased, and 0% and 12% in living donors respectively. Rejection rate at 3 months was 12.7% in deceased, and 12% in living donors. Mean eGFR of deceased donor kidneys-with-function at 3 months was 51 (SD 25), and eGFR was 51 (SD 14) in living donor kidneys. Graft survival in deceased kidneys after April 2007 was higher (93.7% *vs.* 82.1%, p=0.063). Graft survival in living donor kidneys was 100% in both eras. In deceased donor kidneys, primary non-function rate declined after April 2007 (10.5% to 3.2%, p=0.194), delayed graft function was similar, and rejection rate within 3 months declined (23% to 13%, p=0.184).

Conclusion: these data outline the success of the Trans-Atlantic program. This success is achieved despite prolonged cold ischemia times. Routine machine perfusion of all deceased donor kidneys might have a role. Although not significantly, primary non-function and rejection rates seem to have decreased. Long-term follow up results of the program are currently under investigation.

A single-center retrospective study of kidney graft survival after transplantation with a DCD-II donor kidney

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Because of a shortage of kidney donors in the Netherlands, kidneys of donors after circulatory death with a witnessed cardiac arrest but unsuccessful resuscitation (Maastricht type II donor) are sometimes used to enlarge the donor pool. Not many data exist about the long-term graft survival.
The aim of this study was to evaluate the results of DCD-II kidney donors used between 1968 till June 2014 in a university hospital in the Netherlands. Data were collected from two different databases, the National Organ Transplant Registry (NOTR) and Eurotransplant (ET), and from patient files. 21 patients were identified as recipient of a DCD-II kidney transplant. The first transplantation with a DCD-II donor took place in July 1982. The median follow-up time is 5.1 years (range 0.1-19)
Median age of the donor was 30 years (range 13-66) and causes of death were trauma (n=12), myocardial infarction (n=4) and CVA (n=5). Median first warm ischemia time was 37 min (range 10-75), median cold ischemia time was 23.9 h (range 12.9-29.2), median second warm ischemia time was 37 min (range 16-164) and median total ischemia time was 25.2 h (range 15.3-30.5).
Median age of the recipients at the time of transplantation was 59 years (range 32 to 70). The most important causes of end-stage renal disease were polycystic kidney disease (n=6) and glomerulonephritis (n=6). 7 recipients were treated with peritoneal dialysis and 13 with hemodialysis before transplantation, 1 recipient was not treated with dialysis.
The 1-year, 5-year and 10-year graft survival rates were 76%, 60%, and 37%, respectively. The respective 1-year, 5-year and 10-year graft survival rates for DCD-III donor kidneys in the same period were 87%, 66%, and 48%.
Primary non function and delayed graft function occurred in 2 and 16 cases (9,5% and 76,2%).. The median duration of dialysis treatment during delayed graft function was 11 days (6-39). Acute graft rejection occurred in 8 cases (38%). The median eGFR after 3 months, 1 year, 5 years and 10 years was 44 (19-84)(n=17), 41 (23-78)(n=16), 42 (18-108)(n=12) and 47 (23-116)(n=7), respectively.
In the period between 1968 and June 2014 in 0.5% of the kidney transplantations a kidney from a DCD-II donor was used. Primary non function rate is high, however long term graft survival seems almost comparable to graft survival of DCD-III donor kidneys. We should continue to consider DCD-II donors as acceptable kidney donors as long as there is a shortage of donor organs.

Conversion from tacrolimus-based to everolimus-based immune-suppressive therapy 3 months after living-donor kidney trans-plantation: A randomized-controlled clinical trial

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While conversion from ciclosporin to everolimus is well documented, conversion from tacrolimus has been poorly studied.
In this randomized-controlled trial the safety and tolerability of switching from tacrolimus to everolimus with glucocorticoid withdrawal after living-donor kidney transplantation was studied. 194 patients were planned to be randomized 1:1 to either continue tacrolimus or to convert to everolimus at month 3 after transplantation.
At randomization, all patients received tacrolimus, mycophenolate mofetil and prednisolone. Everolimus was started in a dose of 1.5 mg bid, aiming for predose concentrations of 4-7 ng/mL. Prednisolone was gradually withdrawn in both groups. The trial was stopped prematurely after the inclusion of 60 patients. The interim analysis showed an unacceptably high rejection rate in the everolimus group as compared to the control group: 30.0% vs. 6.7% (95%-CI: 0.047-0.420; p = 0.045). An additional 8 patients stopped everolimus because of toxicity. At the end of follow-up (month 12) only 12 (40%) patients assigned to everolimus were still on study drug.
Conversion from tacrolimus to everolimus-based immunosuppression with with-drawal of prednisolone 3 months after kidney transplantation results in an unacceptably high risk of acute rejection and causes considerable toxicity. Based on our findings, such a switch strategy cannot be recommended.

The effectiveness of non-surgical interventions in biliary duct complications after liver transplantation

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Biliary duct complications, consisting of bile duct leakage and bile duct strictures, remain the Achilles' heel of orthotopic liver transplantation (OLT), with a reported incidence of up to 40%. Treatments of first choice are endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) with a reported wide range ofeffectiveness of 50 till 100%. We performed a single-center retrospective cohort study to evaluate the success rate of non-surgical interventions in liver transplant recipients with biliary complications. Additionally, we looked for risk factors for failure of this mode of therapy.

Study period was between January 2006 and December 2015. Graft-, recipient- and treatment characteristics were collected. Treatment was defined a success, if radiologic imaging showed resolving of bile duct complication without additional intervention in six months thereafter. A multivariate analysis was performed to identify risk factors for failure of therapy.

Overall 451 transplants were included in this study. Biliary duct complications developed in 35.5 percent of liver grafts (n=160). Anastomotic bile duct stricture (AS) was the most common complication (n=100), followed by non-anastomotic bile duct strictures (NAS) (n=39) and bile duct leakage (n=14). ERCP was the primary choice of treatment in 115 cases and PTC in 34. Overall success rate was 80%. AS could be successfully treated with non-surgical interventions in 84%, bile duct leakage in 88% and NAS in 45% of the cases, respectively. No differences between ERCP and PTC were observed in relapse rate of bile duct complication, treatment related complications and duration of treatment. Prolonged warm ischemia time (WIT) in minutes (HR. 1.06, 95%CI 1.02-1.10; $p<0.01$) and diagnosis of NAS (HR. 1.92, 95%CI 1.24-2.96; $p<0.001$) were associated with failure of treatment.

Conclusion: Biliary duct complications after OLT are common. Non-surgical interventions, independently of type of procedure, are successful for management of AS and bile duct leakage. NAS and prolonged WIT are associated with less successful therapy outcome.

Overweight kidney transplant recipients are at risk of being overdosed following standard bodyweight-based tacrolimus dosing

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Bodyweight-based dosing of tacrolimus (Tac) is considered standard care, even though the available evidence is thin. An increasing proportion of transplant recipients is overweight, prompting the question if the starting dose should always be based on bodyweight.

The aim of this study was to investigate whether a Tac starting dose based on bodyweight leads to the achievement of Tac target whole-blood predose concentrations (C_0) in overweight patients on day 3 after transplantation. This was defined as the first steady state concentration attained after five unaltered Tac doses.

This is a *post-hoc* analysis of a randomized-controlled trial investigating whether adaptation of the Tac starting dose according to *CYP3A5* genotype increases the proportion of kidney transplant recipients reaching the target Tac predose concentration. In this trial, patients were randomized to receive Tac in either the standard, bodyweight-based dose of 0.20 mg/kg/day according to the package insert, or to a dose based on their *CYP3A5* genotype. For the analysis, the data were divided into three groups: the standard-dose group, the genotype-based group, and all patients scaled to the standard bodyweight dose. The correlation between Tac C_0 and bodyweight (or BMI) was investigated by calculating the goodness of fit. Dosing guidelines were calculated using linear regression lines.

Data was available for 203 kidney transplant recipients with a median BMI of 25.6 (range 17.2-42.2) and bodyweight of 78.9 kg (range 37.6-123.1). More than 50% of the overweight or obese patients had a tacrolimus predose concentration above the target range of 10-15 ng/mL. The CYP3A5 non-expressers tended to be above target when they weighed more than 67.5 kg or had a BMI of 24.5 or higher. If the BMI is 25-30, only 85% of the standard dose (0.2 mg/kg/day) should be prescribed to reach the target concentration, and if the BMI is 30-35 we propose 75% of the standard dose. The dosing guideline for patients with an unknown genotype was validated using the FDCC dataset.

This study demonstrates that dosing tacrolimus solely on bodyweight results in overexposure in more than half of overweight or obese patients.

Opposite Acute Potassium and Sodium Shifts During Transplantation of Machine Perfused Human Liver Grafts

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Background: acute rise of serum potassium levels during orthotopic liver transplantation (OLT) is mainly explained by the systemic entry of the high potassium-containing preservation fluid upon reperfusion, in which the donor graft is immersed during static cold storage (SCS). During end-ischemic hypothermic oxygenated machine perfusion (HMP), livers are flushed and perfused with a low potassium content solution prior to transplantation. The aim of this study was to examine the effect of end-ischemic oxygenated HMP on both *in vivo* and *ex vivo* cation shifts.

Methods: during OLT, we compared serum potassium levels before and after reperfusion of the liver graft. Livers were transplanted either directly after SCS preservation (n=20) or after additional preservation for two hours via end-ischemic oxygenated HMP (n=10). All potassium levels were determined during both machine perfusion and transplantation. Additionally, potassium levels were determined in perfusate samples of livers that were discarded for transplantation. Discarded livers underwent normothermic perfusion (NMP) either directly after SCS preservation (n=16) or after additional preservation for two hours via end-ischemic oxygenated HMP (n=6). Potassium administrations in any form as well as interventions that could have affected hyperkalemia were recorded.

Results: in recipients who received a graft directly after SCS, the mean±SE potassium level rose by 0.27 mmol/L (from 4.43±0.12 to 4.70±0.17 mmol/L; P=0.174), while potassium level decreased by 0.76 mmol/L in the HMP recipients (4.65±0.17 to 3.89±0.31 mmol/L; P=0.003) during reperfusion. Acute potassium administration was required in 0 (0%) and 3 (30%) patients (p=0.030) respectively. Antihyperkalemic measures were performed in 8 (40%) SCS alone and 9 (90%) HMP patients (p=0.017). During HMP, potassium level increased during the first 30 minutes and remained stable thereafter. Balance measurements confirmed considerable hepatic potassium release and sodium uptake during HMP. Similar potassium shifts were seen during both HMP and NMP of discarded livers.

Conclusion: whereas hyperkalemia is anticipated directly after reperfusion during transplantation with conventionally preserved livers, HMP preservation induces *ex vivo* potassium release and frequently leads to hypokalemia after reperfusion. Anesthesiologists should be prepared for an unexpected potassium and sodium response in patients who receive a liver graft after HMP.

Coagulatory state in renal transplants recipients. Is there a differrence between dialysis patients and pre-emptively transplanted patients?

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To prevent renal graft thrombosis different per- and postoperative anticoagulation strategies are used among centers, ranging from no therapy at all to unfractioned heparine for several days post transplantation. In our center preemptively transplanted patients receive 5000 IU of heparin before arterial clamping while dialysis patients do not. This difference is based on the historical assumption that patients on dialysis, and especially hemodialysis (HD), have a prolonged bleeding time compared to patients with end stage renal disease (ESRD). We hypothesized whether these assumptions are valid since HD is able to partially correct the uremic thrombopathy. Also, the impact of ESRD on the coagulation system is complex and both prolonged bleeding time, as well as enhanced thrombi formation are seen. In this study we compare the coagulatory state of dialysis patients with preemptively transplanted patients before and after renal transplantation. Stored plasma samples of patients participating in the VAPOR-1 trial were used. Fifty-seven recipients were included of which 28 were transplanted preemptively (preemptive group, PG) and 29 were on dialysis (dialysis group, DG). A control group (CG) of 37 healthy donors was included (CG). Sample points consisted of start surgery (T1), 5 minutes after reperfusion (T2) and 2 hours post-surgery (T3). Patients in the PG were given 5000 IE of heparin before clamping of the vessels. The following hemostatic and fibrinolytic parameters were analysed: PF4 and sP-selectin as specific platelet activation markers, vWf and F1+2 for coagulation activation and D-dimer for clot breakdown. Plasma potential was studied by thrombin generation (TGA) and clot lysis time (CLT) assays. At T1, PG and DG showed comparable increased platelet and coagulation activation as evidenced by elevated levels of PF4, F1+2 and D-dimer compared to CG as well as a decreased plasma fibrinolytic potential reflected by a prolonged CLT. At T2 increased levels of PF4 showed enhanced platelet activation in DG, compared to PG, in absence of concomitant coagulation activation. At T3, F1+2, PF4 and CLT were substantially higher in DG compared to PG. Compared to CG, prolonged CLT, but comparable levels of PF4 and D-dimer were seen in DG. Prior to transplantation, dialysis and pre-emptively transplanted patients show a comparable but enhanced coagulatory state. So, post-transplantation, dialysis patients show more activation of coagulation and inhibition of fibrinolysis, compared to the preemptive patients. This probably due to the use of heparin in the last group. Inhibition of fibrinolysis is also seen in dialysis patients compared to the control group.

Hair matters: underrated side effect of immunosuppressive therapy in children

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Background: early steroid withdrawal (ESW) after renal transplantation (rtx) in children improves growth and reduces metabolic risks without increasing the number of acute rejections. Hair loss is reported as a non-frequent (1-10%) side effect of tacrolimus (Tac) and mycophenolate mofetil (MMF). Since we switched to an immunosuppressive regimen of ESW combined with Tac, MMF and basiliximab (ESW protocol) we encountered an increased number of children with hair loss, varying from mild to severe. To assess this observation we compared hair loss in children receiving the ESW protocol with children receiving the previous non-ESW schedule.
Methods: the number of children with hair loss receiving the ESW protocol was compared with those receiving the previous non-ESW schedule (basiliximab plus steroids; plus MMF or azathioprine; plus cyclosporine which is switched to Tac 6 months after rtx). Fisher-exact test was used to compare frequencies.
Results: five of 16 (31%) ESW children (median age 11.5 yrs, range 1.7-16,4) and 3 of 13 (23%) non-ESW children (median age 10.7, range 3.2-16.6 yrs) developed hair loss (ns). The onset of hair loss in ESW children was 14,8 (5,3-22,6) months after renal transplantation compared to 30 (9-58) months in non-ESW children. Ten of 16 ESW-children (63%) remained off steroids. 40% (4/10) of children that maintained ESW therapy developed hair loss, which cannot be put aside as a minor nuisance. As an example, a 12-year old girl received a living-related kidney transplant following the ESW-regimen according to TWIST (1). One year after rtx she developed near-total hair loss of the scalp, eyebrows and eyelashes. Other causes such as infection, zinc- and iron deficiency and thyroid disorder were excluded. Prednisolone was reintroduced and Tac tapered to a trough level of around 3 ug/L. MMF dosage was maintained at 600 mg/m^2 with a trough level around 2 ug/L. Hair growth recovered but remained thin.
Conclusion: the number of patients in this study is too small to show significant differences, but ESW treatment might give more hair loss than steroid-based therapy. Hair loss after renal transplantation in children is an underrated problem with a significant cosmetic impact, especially for teen-agers, and is a risk for non-compliance. The cause can be multifactorial and needs more exploration.
[1]Grenda R et al. A randomized trial to assess the impact of early steroid withdrawal on growth in pediatric renal transplantation: the TWIST study. Am J of Tx 2010;10:828-836

"What if this is my chance to save my life?" The patient perspective on public solicitation of living kidney donors

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A small but increasing number of patients use public solicitation (PS) to find a living kidney donor. This qualitative study explores the decision-making and experiences of these patients. Semistructured interviews were conducted with Dutch 20 public solicitors who had publicly solicited between 2011 and 2015. Interviews were transcribed and analyzed for general themes. Most patients used multiple channels for PS including social media and more traditional media such as newspapers. Before considering PS participants had not been able to find an eligible donor in their social network. They also rejected the option of paid donation. Participants were motivated to engage in PS by the ease of social media, encouragement by others, patient/donor autonomy, and despair, but feared public disclosure of vulnerability and feared being (perveiced to be) selfish. During PS participants experienced hope, support, and positive (potential) donor contact. However, PS was also a time and energy-consuming process which was experienced as emotionally taxing. Participants had to manage unequal relationships and take on the roll of health professionals, for example screening donor motives and providing education on living donation. During PS they experienced limited cooperation from health professionals and had to rely on their skills and/or personality to manage their donor search. At the time of the interview 4 patients had received a living donor kidney transplant through the PS route, 5 from another type of donor and 11 were still waiting. These results call for improved communication about the new Dutch policy on PS with patients who are considering engaging in PS, and the development of better support systems to relieve patients of their screening and educating role during the PS process. Greater openness by professionals about this topic may encourage patients to discuss their donor search prior to undertaking PS and create an opportunity for education and counseling during the process.

Niet harder maar slimmer werken

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Inleiding: Vanaf 2010 zien we een jaarlijkse toename van 10-15% van het aantal aanmeldingen van potentiële nierdonoren. Hierdoor ontstaan wachttijden in de procedure wat onzekerheid geeft bij donoren. Zij willen namelijk zo spoedig mogelijk weten of zij kunnen doneren. We hebben daarom gezocht naar mogelijkheden om deze procedure te versnellen binnen de huidige bezetting.

Vraagstelling: Kunnen we het donortraject, vanuit het uitgangspunt van de donor, efficiënter laten verlopen?

Methode: We hebben gekozen voor de Lean-methode, om het hele donortraject in kaart te brengen. Lean is een verbeterfilosofie, waarmee je processen continu kunt verbeteren. Lean is niet harder maar slimmer werken! Belangrijke aandachtspunten hierbij zijn: waar hebben we zelf invloed op en waar kunnen we winst behalen? Met klantvriendelijkheid en efficiëntie als 2 belangrijke pijlers. Stapsgewijs hebben we de huidige situatie van de donorprocedure in kaart gebracht. We hebben bepaalde processtappen verder geanalyseerd om vervolgens verbeterideeën te testen. Wanneer een test de gewenste uitkomst had, hebben we de verbetering geïmplementeerd in het donortraject. Er is ook een verbeterbord geïntroduceerd, dit is een centrale plek om verbetervoorstellen te delen. De voorwaarden hierbij zijn dat de verbetering binnen een maand afgerond kan worden en minimale middelen kost.

Resultaten: We hebben inzicht gekregen in het eerste deel van het donorproces met bijbehorende knelpunten en verbeterpunten. Ook is er meer begrip ten aanzien van elkaars werkzaamheden ontstaan en is er een open sfeer gecreëerd binnen het donorteam. De procedure rond de aanmelding van de donor en de eerste stappen die genomen worden in de donorscreening zijn verbeterd en protocollair vastgelegd. Zodra een donor zich aanmeldt worden diens huisartsgegevens opgevraagd. Ook wordt er standaard navraag gedaan naar de transplantabiliteit van de ontvanger bij diens behandelend arts. Dit laatste is van belang om vast te stellen hoeveel haast er is om desgewenst het donortraject te versnellen. Of dit daadwerkelijk tijdswinst oplevert voor de donor zal moeten blijken zodra de hele procedure is geoptimaliseerd. Door het verbeterbord hebben we al op korte termijn de nodige verbeterpunten kunnen invoeren in onze dagelijkse praktijk.

Conclusie: de Lean filosofie is toepasbaar ter verbetering van het levende nierdonor screeningstraject

The influence of surgical site infections on quality of life in live kidney donors

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Live kidney donors are healthy individuals who underwent donor nephrectomy without benefits. In our hospital we observed an increase in surgical site infections (SSI) in donors. Literature of SSI in donors and its risk factors are scarce. Besides little is known about the effect of SSI on daily life of donors.
The aim of this study is to identify risk factors for SSI in donors and examine the effect of SSI on Quality of Life (QoL).
Baseline characteristics, intra- and postoperative findings were measured. No prophylactic antibiotics were given perioperatively. QoL was recorded preoperatively and 1 and 3 months postoperatively. SSI influence on daily life was measured using the SF-36 questionnaire. The study population was divided into 2 groups; donors with and without SSI.
All donors (N=399) between January 2012 and December 2015 were included. No significant characteristics differences between both groups were found. Donors with SSI (N=35) underwent a hand-assisted approach ($p=0.020$) and had significant higher postoperative pain at day 2 ($p=0.017$). Hospitalization time was longer (5 vs. 3 days) in donors with SSI ($p<0.001$). Small significant differences in QoL 4 weeks postoperatively, between both groups were detected. After 3 months, QoL did not differ between donors with SSI and donors without SSI. Not all donors (N=6) with SSI had returned to work after 3 months.
Hand-assisted donor nephrectomy is a risk factor for developing SSI. Four weeks postoperatively donors with SSI had lowers scores in 2 dimensions of the SF-36 (physical functioning and social role functioning). After 3 months no differences in QoL were found between both donor groups.

Intimiteit, seksualiteit en veilig vrijen na transplantatie

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Zeventig procent van patiënten die een orgaantransplantatie ondergaan ontvangen geen voorlichting betreft intimiteit, seksualiteit en veilig vrijen. Voorlichting over deze onderwerpen is essentieel, omdat uit literatuur blijkt dat 30-50% van de patiënten problemen ondervinden. Deze problemen ontstaan door de verwerking van ziekte en transplantatie, bijwerkingen van medicatie, verminderd zelfvertrouwen door een veranderd lichaamsbeeld en gewijzigde rolverdelingen en relaties.
Er bestaat een online brochure met informatie over dit onderwerp. Echter wezen professionals de patiënten niet op deze brochure en werd in de ontslaginformatie niet verwezen naar de website betreft het onderwerp.
Dit heeft geresulteerd in een brochure die wordt overhandigd tijdens iedere transplantatie opname. Deze brochure kan patiënten en professionals helpen een conversatie aan te gaan over intimiteit, seksualiteit, veilig vrijen en kinderwens na transplantatie.
Feedback op deze brochure van patiënten gaf aan dat deze naast seksualiteit ook informatie bevatte over kinderwens na transplantatie, terwijl die niet op iedere patiënt van toepassing is. De patiënten gaven aan dat zij het zouden waarderen een brochure over seksualiteit en zwangerschap apart te ontvangen. Met de feedback van de patiënten hebben we nu een nieuwe brochure ontwikkeld, betreffende intimiteit, seksualiteit en veilig vrijen na transplantatie.
De brochure geeft onder meer aan hoe je het onderwerp bespreekbaar maakt zowel met partner als professional. Verder bevat het informatie over wanneer de patiënt na transplantatie weer seksueel actief kan zijn, welke invloed medicatie heeft, lichaamsveranderingen en veilig vrijen.
De brochure kan uitgereikt worden door de verpleegkundige tijdens de transplantatie opname. Het onderwerp kinderwens wordt opgenomen in de informatie die op langer termijn na transplantatie gegeven kan worden op de polikliniek. De ontwikkelde brochure speelt op de wensen en behoeften van patiënten. Tevens geeft de brochure professionals handvaten om het onderwerp met iedere patiënt bespreekbaar te maken.
Voor de implementatie van de brochure hebben regionaal transplantatie centrum en een landelijke werkgroep van verpleegkundigen nauwlettend samengewerkt met als resultaat het bereiken van alle transplantatie centra in Nederland.

SIEB: suikers in eigen beheer

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Achtergrond: na niertransplantatie wordt gestart met immunosuppressieve medicatie, zoals tacrolimus en prednison. Een bekende bijwerking van deze medicatie is het ontstaan van diabetes mellitus. Daarnaast speelt gewicht een belangrijke rol. Soms is er voor transplantatie al sprake van overgewicht. Na transplantatie is een gewichtstoename van vele kilo's geen uitzondering

Probleem: diabetes mellitus wordt in de polikliniek onvoldoende snel onderkend. Glucose waardes lopen aan het eind van de dag op terwijl de polibezoeken 's morgen op de poli plaats vinden. Vanwege de (veelvoorkomende) anemie, in de eerste maanden na transplantatie, is de HbA1c waarde niet altijd betrouwbaar

Doel: vroege detectie van diabetes mellitus door thuismetingen van de patiënt

Acties: tijdens de opname voor transplantatie krijgt patiënt uitleg over diabetes mellitus en instructie over het meten van de glucose waardes door een diabetes verpleegkundige. Daarnaast krijgt patiënt uitleg over een gezonde leefstijl. Er wordt advies gegeven over gezonde voeding, bewegen en stoppen met roken.

Patiënten wordt gevraagd wekelijks een 4-punts dagcurve te meten: nuchter en 1,5 uur na de maaltijd en voor de nacht. Uitslagen worden genoteerd in mijnRadboud (het digitale patiënten dossier) of in een dagboekje. Op de afdeling krijgt de patiënt een glucose meter en voldoende strips mee om gedurende de eerste drie maanden na transplantatie te meten. De uitslagen worden tijdens het polibezoek besproken met de verpleegkundig specialist of de nefroloog. Indien insuline behandeling noodzakelijk wordt krijgt de patiënt hiervoor begeleiding van een diabetes verpleegkundige.

Resultaten tot nu toe: vrijwel alle patiënten krijgen instructie ten aanzien van het meten en volgen de adviezen op. 1 patiënt weigerde omdat zij al jaren prednison gebruikt en het niet nodig vindt om te meten. 1 patiënt is blind. Er wordt nu onderzocht in welke mate SIEB vroege detectie van diabetes post-transplantatie versnelt en of er een meer waarde is tov HbA1c en random gemeten glucose waardes tijdens het polibezoek.

Vitamine D suppletie bij Cystic Fibrosis patiënten na longtransplantatie

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Bij Cystic Fibrosis (CF) patiënten na longtransplantatie komen lage vitamine D spiegels voor door malabsorptie bij pancreasinsufficiëntie en een tekort aan UV licht. De gevolgen van vitamine D insufficiënties (25(OH)D<50 nmol/l) en deficiënties (25(OH)D<20 nmol/l) bij longtransplantatiepatiënten kunnen van invloed zijn op het ontstaan van osteoporose en psychische problematiek. Veel patiënten gebruikten de noodzakelijke vitamine D suppletie niet omdat deze niet vergoed werd. Sinds 2016 wordt vitamine D suppletie betaald voor CF patiënten.
Het doel was het meten van het effect van vitamine D suppletie bij CF patiënten met pancreasinsufficiëntie na longtransplantatie na starten van de vergoeding.
Bij CF patiënten na longtransplantatie met een pancreasinsufficiëntie werden de 25(OH)D concentraties in serum uit 2015 vergeleken met de 25(OH)D concentraties in serum uit 2016. Na suppletie (1200 IE/dag) met vitaminecombinatie preparaat ADEK werd na een jaar de concentratie opnieuw gemeten.
Er waren 40 patiënten met CF met pancreasinsufficiëntie na longtransplantatie (19 mannen, leeftijd mediaan: 32,5 jaar; range: 23 tot 55 jaar). De vitamine D spiegels voor suppletie waren, mediaan: 46,5 nmol/l (range: <20 tot 91 nmol/l). Hiervan hadden 21 patiënten (52.5%) insufficiënte spiegels (25(OH)D<50nmol/l), 2 spiegels (5%) waren niet meetbaar.
Na suppletie namen de vitamine D spiegels toe, mediaan: 53,0 nmol/l (range: <20 tot 105 nmol/l). (Wilcoxon Signed Rank test P=0.02). Bij 6 patiënten nam de vitamine D spiegel toe tot sufficiënte waarden (25(OH)D>50 nmol/l). Van 19 patiënten (47,5%) waren de spiegels insufficiënt.
Na verstrekken van suppletie heeft de vitamine D spiegel bij 2 patiënten (5%) geleid tot een insufficiëntie.
Het verstrekken en vergoeden van vitamine D suppletie heeft geleid tot stijging van de vitamine D spiegels. Bij de meeste patiënten stegen de spiegels echter niet binnen de norm. Het niet vergoeden van vitamine D suppletie leidde mogelijk tot onderdosering.

PRISM: A Fast, Compact, In-line, High Yield, Human Pancreatic Islet Isolation Method

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Islet isolations are technically complex, lengthy, expensive, and require a high expertise level from its operators. A low islet yield and/or poor islet quality that is frequently observed result in a high risk that the isolated islets will not be transplanted.
A new, closed method of tissue collection, washing, buffer change and islet purification termed PRISM (PancReatic Islet Separation Method) was developed. Briefly, digested pancreatic tissue is pumped (200 ml/min) through a Medtronic Biotherm heat exchanger, cooling the tissue to 4°C. Mixed with human serum (6 ml/min), the tissue is then continuously concentrated and washed in an air cooled 225 ml Latham centrifugation bowl at 1400 RPM, kept at 4°C. After increasing centrifugation speed to 1500 RPM, UW solution is pumped (30 ml/min) into the bowl while tissue is retained in the bowl. Next, the UW solution containing the digested tissue is transferred from the bowl into a transfusion bag. Two speed controlled Masterflex pumps subsequently mix Iopromide 370 mg I/ml (density 1.409 g/ml) with the digest (suspended in UW) into the bowl until the heaviest tissue has exited the bowl. Microspheres of a similar size, shape and density as digested pancreas tissue, as well as islet depleted tissue (IDP) were used in initial testing of the system. Ten human pancreata, not suitable for clinical use, were used for islet isolation using PRISM. Yield (IEQ), viability (FDA/PI staining) and function (dynamic glucose stimulated insulin secretion test, dGSIS) were evaluated after one day of culture.
Pure fractions of microspheres could be separated in isopycnic centrifugation using the bowl. Microspheres could be concentrated and retained in the bowl without loss at 1400 RPM and pump speed at 200 ml/min. IDP could also be retained in this fashion. Merely one operator can perform PRISM in one flow cabinet. Using this procedure with human pancreata resulted in a higher islet yield when compared to historical controls (431,234±292,833 vs. 285,276±197,392 IEQ, p=0.05). PRISM islets were as functional as historical controls in dGSIS tests (stimulation index of 4.5 vs 4.6 and AUC 351.1 vs. 398.7, respectively; p=ns). Islet viability was 86%. Isolated islets were of similar diameter and shape as historical controls.
PRISM is a novel islet isolation technique that represents a significant improvement in islet isolation efficiency.

Bacterial translocation after liver transplantation is associated with biliary complications

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Introduction: The intestinal microbiome and the translocation of intestinal bacteria to the portal circulation are more and more recognized as an important pathogenic factor in liver diseases like alcoholic and non-alcoholic liver diseases. The role of microbiota translocation in liver transplantation outcomes, including biliary complications, has not been established. Therefore, the aim of this study is to investigate the incidence of bacteremia after liver transplantation and explore a link with biliary complications.
Methods: From 1989 – 2010 all liver transplants were analyzed retrospectively for donor and recipient characteristics and positive bacterial cultures in blood. Overall 365 patients were included. Biliary complications comprised of anastomotic strictures (AS), non-anastomotic strictures (NAS) and recurrence of primary sclerosing cholangitis (PSC).
Results: Of 365 transplants, 68 patients had positive blood cultures (18.6%). Prevalent microbes were Enterococcus faecalis, Staphylococcus aureus and Pseudomonas aeruginosa (33.3%, 20.8% and 16.7%). PSC recurrence was diagnosed in 13 patients out of 66 PSC patients. Positive cultures were 37% in non-recurrent PSC patients and 61% in the recurrence group (p=0.001). NAS was diagnosed in 43 patients of which 25 patients (58%) had positive cultures. In the non-NAS group (n=322), only 43 had positive cultures (13%, p=0.001). Multivariate analysis showed positive blood cultures, re-transplantation and the longer warm ischemia times as independent risk factors for NAS. AS was not associated with positive cultures after transplantation, suggesting a different etiology.
Conclusion: Bacterial translocation occurs in approximate 20% of recipients after liver transplantation and is associated with an increased risk of biliary complications. No association between AS and positive blood cultures was found, suggesting a difference in etiology between anastomotic strictures and NAS or recurrence of PSC.

Bile Duct Strictures after Liver Transplantation are Associated with a Donor Glypican-6 Polymorphism Linked to the Biliary Stem Cell Niche

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Introduction: bile duct strictures (ischemia type biliary lesions and anastomotic strictures) are one of the most common complications after liver transplantation, with an incidence of approximately 30%. The origin of these strictures seems multi-factorial, but damage to bile duct stem cell niche is found to play an important role. Glypican-6 (GPC-6) has recently been identified as an stem cell niche factor important for stimulation of the Wnt-signaling pathway and linked to primary sclerosing cholangitis (PSC). However, the role of GPC-6 in bile duct strictures post transplantation has not been established.
Methods: a retrospective PCR-based SNP analysis was performed for GPC-6 status of liver donors and recipients transplanted between 1989 and 2010. PSC recipients were excluded from analysis.
Results: overall, GPC-6 status could be identified in 309 recipients, 241 donors and 201 paired donor-recipient combinations. Of the 309 transplantation recipients, biliary strictures occurred in 87 grafts (37.2%). Distribution of the GPC-6 polymorphism did not differ between the recipient (AA (n=40) vs AG/GG (n=269)) and donor (AA (n=40) vs AG/GG (n=201)) ($p = 0.818$). Donor GPC-6 AA genotype was associated with the development of biliary strictures ($p = 0.024$). Multivariate analysis with other known risk factors for bile duct strictures showed GPC-6 AA genotype as an independent risk factor for biliary strictures ($p=0.050$).
Conclusions: donor GPC-6 AA genotype is an independent risk factor for the development of bile duct strictures after liver transplantation in non-PSC recipients. The exact relationship of GPC-6 and bile duct injury may be based on decreased Wnt-activation of epithelial stem cells in the peribiliary glands or other stem cell niches. Investigation of the role of GPC-6 genotypes in Wnt-activation is currently on going in organoid cultures of biliary stem cells.

Effective delivery of Mesenchymal Stromal cells during isolated liver machine perfusion to promote graft repair on the pump

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Faced with current organ shortages more donor with compromised graft quality are being used. These grafts have less favorable outcome after transplantation due to increased graft damage. Currently machine preservation provides new opportunities, not only to improve graft preservation, but moreover to apply regenerative medicine strategies to repair damaged organs. Mesenchymal Stromal cells (MSCs) represent a potential new therapeutic strategy to stimulate liver regeneration. The aim of the current study is to investigate whether MSCs can be effectively delivered during hypothermic oxygenated machine perfusion of porcine liver grafts.
Livers from Yorkshire mini pigs (n=9, age 2-3 months, female, 20-30 kg) were procured according to standard methods and cannulated, cooled and flushed with cold preservation before infusion with human bone marrow-derived MSCs. MSCs (10 to 15 million per infusion) were genetically labeled with a luciferase reporter gene to visualize the distribution of cells after infused using bioluminescence imaging. The livers were perfused for 1h at 10˚C with oxygenated preservation fluid before warm, oxygenated reperfusion was done with the pig's own blood. The infused MSCs were identified in biopsies using human specific q-PCR and immunohistochemistry for CK19. Cytokine production of the infused MSC after 4h of warm reperfusion was measured using the Luminex Multiplex platform.
MSCs were clearly visualized directly after infusion (t=0) and following 30 min of cold, oxygenated perfusion. Whole organ imaging showed an even distribution of cells throughout the liver graft, when infused in the hepatic artery and an even spread throughout the liver after 30 min of perfusion. The delivery of human MSC to the graft was confirmed by human specific q-PCR of multiple biopsy samples and by CK19 staining. After 4 h of warm reperfusion with the pigs blood, human-specific cytokines IL-6 and IL-8 were detected in the pig serum, demonstrating that the infused MSC were functionally active during the warm reperfusion.

Conclusion: human MSCs can be effectively delivered to ischemic liver grafts during hypothermic oxygenated machine perfusion. This study shows feasibility of MSC-based therapies for repair of damaged organs on the pump, which is currently investigated with human livers discarded for transplantation.

Treating ischemically damaged porcine kidneys with mesenchymal stromal cells during normothermic machine perfusion

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Donor kidneys of inferior quality are increasingly being accepted to decrease waiting time for a transplant. Normothermic machine perfusion (NMP) could provide superior organ preservation, compared to cold preservation methods and may also be a tool for pre-transplant quality assessment of such marginal grafts. In addition, NMP offers the unique opportunity for active interventions to an isolated organ under near-physiological conditions prior to transplantation. There is increasing evidence that mesenchymal stromal cells (MSCs) could have a positive effect on ischaemia-reperfusion (IR) injury. However, in most studies MSCs are administered to recipients after transplantation, which exposes the whole patient to circulating allogeneic cells. Moreover, administering MSCs earlier in the IR cascade might create better opportunities for beneficial effects. The purpose of this study was to determine whether administering MSCs during NMP is technically feasible, if MSCs reach the kidney and remain viable, to which structures they home and which cytokines are secreted by MSCs during NMP.

Porcine kidneys and autologous blood were obtained from two slaughterhouses. Warm ischaemia time was standardised at 30 min and cold ischaemia time was 3.5-5 hours. Kidneys were machine perfused in a recirculating circuit with 350 ml washed autologous red blood cells, 500 ml Williams' Medium E, albumin, creatinine and Augmentin during 6 hours at 37°C. After 1 hour of perfusion either 0, 10^5, 10^6 or 10^7 cultured human adipose tissue derived MSCs were added (n=3 per group). Vital parameters were monitored and perfusate and urine samples were taken regularly. Biopsies were taken to assess renal histology and to locate MSCs with immunohistochemistry. Luminex analysis was used to determine secretion products of MSCs.

After NMP vital MSCs were detected in the lumen of glomerular capillaries in the 10^7 MSC group, but not in the other groups. MSCs secreted pro-inflammatory cytokines IL-6, IL-8 and MCP-1 in response to the ischemically damaged kidney during NMP, in a dose-dependent fashion.

In conclusion, adding MSCs during pre-transplant renal NMP proved to be feasible. MSCs remained viable and detectable and secreted various pro-inflammatory cytokines. It remains to be studied if this leads to beneficial or harmful processes for the organ, which molecular pathways are activated by exposure to MSCs and whether MSC pre-treatment will indeed enhance renal function post-transplant.

Tacrolimus-based immunosuppression only marginally affects monocyte activation after kidney transplantation

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Monocytes significantly contribute to ischemia reperfusion injury and allograft rejection after kidney transplantation. However, the knowledge about the effects of immunosuppressive drugs on monocyte activation is limited. Here, the phosphorylation profile of 3 signaling proteins was measured to determine the effects of immunosuppression on monocyte activation in kidney transplant patients.

Peripheral blood samples (n=20 patients) were studied before and 4, 30, 90, 180 and 360 days after kidney transplantation. Patients received maintenance therapy consisting of tacrolimus, mycophenolate mofetil and prednisolone in combination with basiliximab induction therapy. Phosphorylation (median fluorescence intensity) of p38MAPK, ERK and Akt was measured by phospho-specific flowcytometry on whole blood samples. Isotype controls were used as negative controls.

After transplantation, in *ex vivo* whole blood samples, p38MAPK phosphorylation was inhibited after transplantation compared to pre-transplantation (mean inhibition ±30%; $p < 0.05$). The other MAPK family member, ERK, showed a predominant decrease in phosphorylation in the first month after transplantation (mean inhibition 35% and 45% at day 4 and 30; $p < 0.05$ and $p < 0.001$, respectively). Finally, p-Akt was also inhibited at all time points after transplantation (mean inhibition ±20%; $p < 0.05$). Interestingly, maximal inhibition was 45% for the tested signalling proteins. At day 4 after transplantation, when the highest whole blood trough levels were measured, p38MAPK and p-Akt inversely correlated with tacrolimus concentrations ($r_s = -0.65$; $p = 0.012$ and $r_s = -0.58$; $p = 0.030$, respectively). This correlation was not found for p-ERK.

In conclusion, phospho-specific flowcytometry is a novel technique to pharmacodynamically monitor immunosuppressive drug effects on monocytes. The currently prescribed immunosuppressive drugs only partially inhibit monocyte activation pathways in kidney transplant recipients, explaining the active contribution of these cells to rejection processes.

The effect of tacrolimus and mycophenolic acid on CD14+ monocyte activation and function

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Monocytes and macrophages play key roles in cellular and humoral rejection after solid organ transplantation. Little is, however, known about the effects of the immunosuppressive drugs tacrolimus and mycophenolic acid (MPA) on monocyte activation and function. Here, the influence of these immunosuppressants on monocytes was investigated by measuring the phosphorylation of 3 intracellular signaling proteins upon exogenous stimulation in the presence or absence of immunosuppressive drugs.

Blood samples from healthy volunteers (n=5) were spiked with 0, 10 50 or 200 ng/ml tacrolimus and 0 or 10 μg/ml MPA, to determine the individual effects of these drugs on CD14+ monocytes, stimulated with PMA/ionomycin. Phosphorylation of the intracellular signaling proteins p38MAPK, ERK and Akt was measured with phospho-specific flowcytometry in peripheral blood monocytes. In addition, biological functions downstream of these signaling pathways were studied, including IL-1β production, phagocytosis and polarization into different types of activated macrophages (stimulated with IFN-γ, IL-4 and IL-10).

Tacrolimus, only at 50 and 200 ng/ml, inhibited phosphorylation of p38MAPK ($p < 0.05$ and $p < 0.01$, respectively) more than p-Akt ($p = 0.11$ and $p < 0.05$, respectively) with a maximum of 35%. MPA, at a therapeutic concentration, showed the strongest inhibition of p-Akt (30%; $p < 0.01$). p-ERK was inhibited with a maximum of 15% after spiking with either 200 ng/ml tacrolimus or 10 μg/ml MPA ($p < 0.05$ and $p < 0.01$, respectively).

The production of IL-1β by monocytes was not affected by tacrolimus, while MPA inhibited IL-1β production by 48% ($p < 0.05$). Phagocytosis by monocytes was not influenced by either drug. Monocyte/macrophage polarization was shifted to an M2-like phenotype in the presence of tacrolimus, seen as the increase in the M2 markers CD200R and CD16 (both $p < 0.05$).

Tacrolimus and MPA suppress monocyte signaling pathway activation only to a limited extent. The residual phosphorylation of signaling proteins probably explains the limited effect of both immunosuppressive drugs on cytokine production and phagocytosis, apart from monocyte differentiation. This suggests that innate immune responses mediated by monocytes after transplantation might still occur under immunosuppression.

Variations in DNA methylation of interferon gamma and programmed death 1 in allograft rejection after kidney transplantation

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The role of DNA methylation in the regulation of the anti-donor directed immune response after organ transplantation is unknown. Here, we studied the methylation of two mediators of the immune response: the pro-inflammatory cytokine *interferon γ* (*IFNγ*) and the inhibitory receptor *programmed death 1* (*PD1*) in CD8+ T-cell subsets in kidney transplant recipients.
Using pyrosequencing, the DNA methylation of regulatory CpGs in the promoter region of either *IFNγ* or *PD1* was determined in FACS sorted naïve (CD27+CD45RA+), CD27+ memory (CD27+CD45RA-), CD27- memory (CD27-CD45RA-) and differentiated effector memory (EMRA; CD27-CD45RA+) CD8+ T-cell subsets before and 3 and 12 months after kidney transplantation. Both kidney transplant recipients experiencing an episode of acute allograft rejection (rejectors) as well as recipients without rejection (non-rejectors) were included.
Both *IFNγ* and *PD1* were significantly ($p<0.001$) higher methylated in the naïve CD8+ T cells compared to the memory T-cell subsets. The methylation status of both *IFNγ* and *PD1* inversely correlated with the % of IFNγ or PD1 producing cells. At 3 months after transplantation, irrespective of rejection and subsequent anti-rejection therapy, the *IFNγ* methylation was significantly higher in the EMRA CD8+ T cells ($p=0.01$) whereas the PD1 methylation was significantly higher in all memory CD8+ T-cell subsets (CD27+ memory; $p=0.02$: CD27- memory; $p=0.02$: EMRA; $p=0.002$). Comparing the increase in methylation in the first 3 months after transplantation between rejectors and non-rejectors demonstrated a significantly more prominent increase in the *PD1* methylation in the CD27- memory CD8+ T cells in rejectors (increase in rejectors: 14%, increase in non-rejectors: 1.9%, $p=0.04$). The increase in DNA methylation in the other memory CD8+ T cells was not significantly different between rejectors and non-rejectors. At 12 months after transplantation the methylation of both *IFNγ* and *PD1* returned to pre transplantation levels.
The DNA methylation of both *IFNγ* and *PD1* increases the first 3 months after transplantation in memory CD8+ T cells in kidney transplant recipients. This increase was present in both rejectors and non-rejectors indicating that general factors of the kidney transplantation procedure, including the use of immunosuppressive medication, contribute to these variations in DNA methylation.

In Vivo Anti-microRNA Treatment In a Humanized Mouse Model for Allograft Vasculopathy

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A limitation in the field of heart transplantation is cardiac allograft vasculopathy which is a diffuse concentric proliferation of the intima of coronary arteries leading to graft failure. An up regulation of several microRNAs (miRs), especially miR-21 and miR-146b-5p, is found in cardiac allograft vasculopathy patients. These miRs might act as potential therapeutic targets. Our aim is to investigate whether intimal proliferation can be reduced by targeting miR-21 and miR-146b-5p in a huSCID/bg-RAG1-/-mouse model.

Immune deficient huSCID/bg-RAG1$^{-/-}$ mice were transplanted with a human coronary arterial graft, injected with allogeneic human peripheral blood mononuclear cells and are intraperitoneally treated with anti-miR therapy. The (systemic) inhibition of miR-21 and miR-146b-5p expression was determined by performing quantitative polymerase chain reaction and the effect of miR inhibition on intimal size was investigated by histologic studies. The composition of cell populations in the intimal layer after treatment was studied by immunohistochemistry (CD45RO, CD68, CD20). To determine downstream effects of the anti-miR treatment messenger RNA targets were measured by quantitative polymerase chain reaction.

Injection with anti-miRs resulted not in reduced miR-21 and miR-146b-5p expression levels in the graft tissue but did in kidney and partly in heart tissue. We did not find significantly smaller intimal areas after systemic anti-miR therapy. Decreased levels of activated T cells and macrophages were found in the intimal layer of the treated mice. Due to a large variance in each of the above measurements no statistical differences were found. Subtle changes in messenger RNA expression levels were found in the graft. Interestingly, expression levels of TGFβ significantly correlated to both miR-21 and miR-146b-5p expression in the graft.

These data show that anti-miRs can affect influx of inflammatory cells into the intimal layer, but have little effect on intimal size in a humanized mouse model for allograft vasculopathy. Overall downstream messenger RNA levels show subtle changes, where specifically TGFβ correlates to levels of both miRs. The data suggest that the anti-miR treatment did change systemic effects, but the penetration at the site of the coronary artery was minimal, causing a limited effect on the intima proliferation.

Healthcare law analyses of the Donor Registry in the Netherlands: Is registered consent to organ donation legally binding after death?

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Introduction: According to the EU Directive 2010/45/EU several models of consent to donation can coexist in the Union. In order to enable individuals to express their wishes within in the different models, some countries developed specific registries where citizens record them. The Netherlands is one of the countries with such a registry. The Organ Donation Act, which is based on an opt-in system, is supported by a national Donor Registry (DR). The legal status of such register is not described in the EU Directive, thus Member States are free in choosing the status. In The Netherlands the DR is not considered to be a will and therefore not legally binding after death. So what is the legal purpose of a registration?

Argumentation: In healthcare law the basic principle is informed consent: a process for getting permission before conducting a healthcare intervention on a person. The EU Directive states that the procurement of organs shall be carried out only after all requirements relating to consent, authorization or absence of any objection have been met. Following from this, a registered consent in the DR is legally a justification in the form of informed consent for organ procurement. Because in The Netherlands the DR is not the same as a will, a registered consent makes the decision to be an organ/tissue donor not legally binding after death of the donor. This has several consequences, one of which is the possibility of the donor's family to overrule the registered decision.

Conclusion: The legal status of a register within the several models of consent to donation is an important issue which has to be taken into consideration before organ procurement. It does not seem very meaningful to have a register which is not legally binding after death of the donor. Therefore a discussion on this subject is necessary even if it is just to bring awareness to the people involved in the field of organ donation and transplantation.

CD4+CD28null T Cells Require Exogenous Cytokines to Become Alloreactive

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Ageing and a pro-inflammatory environment, such as present in patients with end-stage renal disease, are important drivers of increased T-cell differentiation, which is accompanied by loss of the co-stimulatory molecule CD28. $CD4^+CD28^{null}$ T cells have a highly cytotoxic, inflammatory profile and respond to IL-15 and IL-21 in particular. These cells have been associated with an increased as well as a decreased risk for rejection after renal transplantation. Therefore, we wanted to investigate the alloreactive potential of $CD4^+CD28^{null}$ T cells in detail.
FACS-sorted $CD4^+CD28^{null}$ and $CD4^+CD28^+$ T cells were stimulated with HLA-mismatched CD3-depleted cells in the absence or presence of exogenous cytokines. The alloreactive potential was evaluated by measuring proliferation, degranulation (CD107a expression), content of cytotoxic molecules and cytokine production.
Compared with $CD4^+CD28^+$ T cells, the $CD4^+CD28^{null}$ T cells showed an almost absent proliferation, degranulation and cytokine production in response to allogeneic stimulation. Addition of IL-15 (with/without IL-21) to the cell culture increased the frequency of proliferating $CD4^+CD28^{null}$ T cells significantly up to 30% ($p<0.001$) without altering CD28 expression. Next to this, the combination of IL-15 and IL-21 also increased CD107a expression within the $CD4^+CD28^{null}$ T cells ($p<0.05$). Furthermore, granzyme B and perforin positivity seemed to be higher when IL-15 and IL-21 were added to the allogeneic condition within $CD4^+CD28^{null}$ T cells, compared to the allogeneic condition without these cytokines. Also, allogeneic-expanded $CD4^+CD28^{null}$ T cells were capable to lyse allogeneic target cells in a specific lysis assay. Finally $CD4^+CD28^{null}$ T cells, after alloantigen stimulation in the presence of IL-15 +/- IL-21, produced more IFN-γ and TNF-α ($p<0.05$ for IFN-γ and $p<0.01$ for TNF-α).
$CD4^+CD28^{null}$ T cells need exogenous cytokines, in particular IL-15, to proliferate and secrete inflammatory cytokines in response to allogeneic stimulation.

Taking the HLA-specific memory B cell elispot to the next level: assaying the full donor HLA repertoire

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Pre-existing or de-novo donor-specific antibodies (DSA) represent an important risk factor affecting transplant outcome. Patients with a history of immunization, but lacking serum DSA may harbor dormant memory B cells which can rapidly produce DSA upon antigen re-encounter. Current methods to detect memory B cells mainly utilize synthetic monomeric/tetrameric HLA molecules which generally do not represent the complete HLA repertoire of an individual. Here, we present a donor-specific HLA-ELISPOT assay enabling the screening for HLA-specific memory B cells in peripheral blood of immunized individuals using cell lysates as a natural source of both HLA class I and II antigens. Peripheral blood mononuclear cells (PBMC) or splenocytes were treated with non-ionic detergents to obtain HLA-containing lysates. Human B cell hybridomas producing monoclonal HLA antibodies were tested against these lysates for validation purposes. Next, polyclonally activated peripheral blood B cells from women with a history of pregnancy were tested for the presence of HLA-specific memory B cells against paternal PBMC or autologous lysates as the source of HLA (women with serum anti-HLA n=10; women without serum anti-HLA n=10). Non-immunized individuals served as negative controls (n=10). For all hybridomas tested, we detected spot formation against the lysates that contain the corresponding HLA antigens whereas no spots were observed against lysates with irrelevant HLA, indicating the specificity of the assay. Comparable number of spots in total IgG and HLA-ELISPOT assays assured that all antibody-secreting cells were detected. Using this ELISPOT assay, we found significantly higher HLA class I-specific memory B cells (median frequency: 202, range: 0-802) in women with serum HLA class I antibodies compared to those without serum HLA class I antibodies (median frequency:0, range:0-8) and non-immunized males (median: 0, range: 0-25) ($p<0.0001$). Similarly, HLA class II-specific memory B cell frequencies were significantly higher in group of women with serum HLA class II antibodies (median frequency: 91, range: 22-768) compared to women without serum antibodies (median frequency: 3, range: 0-25) and non-immunized males (median frequency: 0, range: 0-22) ($p<0.0001$). HLA-specific memory B cell frequencies did not differ between women without serum HLA antibodies and non-immunized males ($p>0.05$). This novel lysate-based ELISPOT assay allows for the first time to quantify all donor HLA class I and II-specific memory B cells and may serve as a memory B cell crossmatch assay.

Computational approaches to facilitate epitope-based HLA matching in solid organ transplantation

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Epitope-based HLA matching has been emerged over the last few years as an improved method for HLA matching in solid organ transplantation. The epitope-based matching concept has been incorporated both in the PIRCHE-II and the HLAmatchmaker algorithm to find the most suitable donor for a recipient. For these algorithms, high-resolution HLA typing of both donor and recipient is required. Since high-resolution typing is often not available, we developed a computational method which allows epitope-based HLA matching from serological split level HLA typing relying on HLA haplotype frequencies. To validate this method, we simulated a donor-recipient population for which PIRCHE-II and eplet values were calculated when using both high-resolution HLA typing and serological split level HLA typing. The majority of the serological split level HLA-determined *ln(PIRCHE-II)/ln(eplet)* values do not or only slightly deviate from the reference group of high-resolution HLA-determined *ln(PIRCHE-II)/ln(eplet)* values. This deviation was slightly increased when HLA-C or HLA-DQ was omitted from the input and was substantially decreased when using two-field resolution HLA typing of the recipient and serological split level HLA typing of the donor. Thus, our data suggest that our computational approach is a powerful tool to estimate PIRCHE-II/eplet values when high-resolution HLA typing is not available.

Ectopic lymphoid structures are present in type I T-cell mediated kidney transplant rejection

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In renal transplantation, many allograft recipients develop donor-specific antibodies associated with an increased risk for graft rejection. Current immunosuppressive agents are principally aimed at T-cell-mediated alloimmunity, underestimating humoral effectors. Antibody responses are mainly mediated by BCL6+ T follicular helper (Tfh)-cells that activate B-cells predominantly via interleukin-21 (IL-21). Whether this reaction appears in the allograft is still being debated. Here, we investigated if ectopic lymphoid structures (ELSs) are present in T cell mediated rejection (type I and II) and antibody-mediated rejection after renal transplantation.

Fifteen renal transplant biopsies were studied. Primary diagnosis were C4d+ antibody-mediated rejection (ABMR, *n*=5), T-cell mediated rejection type I (TCMRI, *n*=5), and T-cell mediated rejection type II (TCMRII, *n*=5). FFPE sections were stained for T-cells (CD3), B-cells (CD20), and follicular dendritic cells (FDCs, CD23). In addition, double immunofluorescent stainings for IL-21 and BCL6 were performed. Slides were analyzed for the presence and composition of infiltrate.

In all 15 biopsies, infiltrates of CD3+ T cells were detected. In TCMRI, CD20+ B-cells formed aggregates surrounded by T-cells in the tubulo-interstitial compartment. In these aggregates CD23+ FDCs were detected, suggesting the presence ELSs. In contrast, ABMR and TCMRII showed diffuse spread of T cells and B cells and no CD23+ cell aggregates. IL-21 was present in all biopsies, however, co-localization with BCL6 was predominantly observed in TCMRI biopsies.

Nodal lymphoid proliferations with FDC networks and BCL6+IL-21+ cells are mainly found in TCMRI and may suggest a pivotal role for Tfh cell – B cell interaction.

Patients with renal failure have a pERK-dependent defective TCR-mediated activation of CD4+ T cells

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Phenotype and functional aspects of circulating T cells in end-stage renal disease (ESRD) patients resemble that in old healthy individuals (HI). Phosphorylation of extracellular signal-regulated kinase (pERK) is a crucial regulator in augmenting TCR-mediated activation, survival and proliferation of T cells. In naïve $CD4^+$ T cells of HI, an age-associated decline in pERK-levels is observed caused by increased levels of dual specific phosphatase (DUSP) 6, a cytoplasmic phosphatase with substrate specificity to dephosphorylate pERK. Whether the DUSP6/pERK-dependent signaling is affected in ESRD patients is not known. The aim of this study was to assess TCR-mediated induction of pERK and the effect of the DUSP6-inhibitor BCI on pERK-levels in ESRD patients.

PBMCs of young (<45 years) and old (>65 years) ESRD patients (N=24) and age-matched HI (N=24) were pre-incubated with or without BCI prior to stimulation with CD3/CD28 antibodies. Subsequently, median fluorescence intensity (MFI) of pERK was assessed for the different T-cell subsets by flow-cytometry.

An age-associated decline in TCR-induced pERK-levels was observed in the different $CD4^+$ ($CD4^+$ young 658 vs elderly 535, $P<0.05$), but not $CD8^+$, T-cell subsets from HI. Interestingly, pERK-levels of $CD4^+$ T-cell subsets from young ESRD patients were comparable to elderly patients. pERK-levels in both young as well as old ESRD patients were similar to old HI. Differentiation of T cells was associated with a decline in TCR-induced pERK-levels as levels declined when comparing naive to the more differentiated memory $CD4^+$ T cells. Inhibition of DUSP6 significantly increased TCR-induced pERK-levels of $CD4^+$ T cells in young and elderly ESRD patients, as well as in elderly HI.

Young ESRD patients have an impaired TCR-mediated induction of pERK-levels inditcative of premature T cell ageing. A DUSP6-inhibitor is a potential tool to increase TCR-induced activation of $CD4^+$ T-cells in the ESRD patients.

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