NEDERLANDSE **TRANSPLANTATIE** VERENIGING

Bootcongres 2019

Wetenschappelijke voorjaarsvergadering

Nederlandse Transplantatie Vereniging

13 en 14 maart 2019

Koninklijk Instituut voor de Tropen te Amsterdam

georganiseerd in samenwerking met

Amsterdam UMC

Amsterdam UMC
Universitair Medische Centra

Inhoudsopgave

Algemene informatie

Welkom op het Bootcongres in Amsterdam!

Over Uitgekomen Dromen in Mokum

Op 13 februari 2018, met 38 stemmen voor en 36 tegen werd het wetsvoorstel over een actief donorregistratie systeem in de Eerste Kamer aangenomen.
Pia Dijkstra's droom werd werkelijkheid. Zij loodste het wetsvoorstel al in 2016 door de Tweede Kamer. Het afgelopen jaar en nog voor de implementatie van dit wetsvoorstel ging het aantal donoren omhoog met 4%. Maar ook het aantal nee zeggers steeg. Het effect van de donorwet na implementatie blijft gissen. Graag rekenen we ons rijk en hopen op een donortsunami. Zal het aantal donoren per miljoen inwoners de getallen van België en Spanje benaderen? En hoe moeten we ons hierop voorbereiden? Hoe gaan we zo efficiënt en eerlijk mogelijk om met dit gouden goed? Deze vragen en nog veel meer zullen aan bod komen op de donderdagochtend in de sessie "postmortale donatie en allocatie".

Want we hebben nog steeds donoren nodig, het aantal wachtenden op een donororgaan is meer dan 1000 en het afgelopen jaar zelfs iets gegroeid. Graag zouden we al deze wachtenden een vitaal orgaan van topkwaliteit geven. Op woensdag zult u horen over nieuwe wegen om het donororgaan te pimpen door te pompen hetzij warm, hetzij koud met zuurstof, of te vernieuwen en te verjongen met stamcellen. Of door het donororgaan te vervangen door een apparaat: the rise of the machine. Voortschrijdend vernuft maakt kunstharten mogelijk die op de korte termijn niet onderdoen voor een donorhart. In dezelfde sessie hoort u ook welke non-HLA antistoffen van belang zijn voor de overleving van niertransplantaten.
Naast Technologie, biologie en pathologie is er een prominente plaats voor de maatschappelijke aspecten van orgaantransplantatie. Hierbij staan politiek, patiënt, partners/nabestaanden en psychologie prominent op het programma.

Wij sluiten af met het inspirerende verhaal van Paul Iske over briljante mislukkingen, maar beginnen met een briljant succes: de grote uitgekomen droom van die ene Amsterdammer: André Kuipers.

Namens het lokale organisatiecomité,

Frederike Bemelman, Amsterdam UMC

Organisatiecommissie Bootcongres 2019

Vanuit het Amsterdam UMC
Frederike J. Bemelman
Junior Lardy
Neelke van der Weerd
Karlijn van der Pant
Jaap Homan van der Heide
Willy Rensen
Mirza Idu
Tessa de Jong
Azam Nurmohamed
Joost van der Heijden
Frans van Ittersum
Carla Schrauwers
Marjon van Vliet
Arjen Hoksbergen
Jeanique Geest-van Zoest
Anouk Molenaar

Bestuursleden Nederlandse Transplantatie Vereniging
Marlies E.J. Reinders
Martin J. Hoogduijn
Henny G. Otten
Jeroen de Jonge
Niels van der Kaaij
Henri G.D. Leuvenink
Coby H. Annema

Vanuit het secretariaat NTV te Haarlem
Tineke Flietstra
Marie José van Gijtenbeek

Participerende patiëntenorganisaties
Nederlandse Leverpatiënten Vereniging
Nierpatiënten Vereniging Nederland
Patiënten Vereniging Hart- en Longtransplantatie

Accreditatie is aangevraagd bij de volgende verenigingen:

Nederlandse Vereniging voor Heelkunde

Nederlandse Vereniging voor Immunologie

Nederlandse Internisten Vereniging

Nederlandse Vereniging voor Kindergeneeskunde

Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose

Nederlandse Vereniging van Maag-Darm-Leverartsen

Nederlandse vereniging voor Thoraxchirurgie

V&VN, kwaliteitsregister algemeen

V&VN, kwaliteitsregister, deskundigheidsgebied Dialyse

V&VN, verpleegkundig specialisten register

Koninklijk Instituut voor de Tropen

Mauritskade 63
1092 AD Amsterdam
Website: www.kit.nl

Bereikbaarheid met openbaar vervoer

De tramhaltes Alexanderplein en Linnaeusstraat liggen vlak naast ons gebouw en zijn eenvoudig en snel bereikbaar:

- Vanaf Amsterdam Centraal Station: tram 14 – halte Alexanderplein
- Vanaf Amsterdam Sloterdijk: tram 19 – halte Alexanderplein
- Vanaf Diemen: tram 19 – halte Linnaeusstraat 1e van Swindenstraat

Bereikbaarheid met de auto

Neem vanaf ringweg A10 afslag Watergraafsmeer/Diemen (S113). Kies aan het einde van de afrit richting Centrum/Watergraafsmeer en rij door via de Middenweg, die overgaat in de Linnaeusstraat. Het Koninklijk Instituut voor de Tropen ligt aan het einde van deze straat op de hoek met de Mauritskade.

Parkeermogelijkheden

De dichtstbijzijnde parkeergarage is Q-Park Oostpoort (Polderweg 92, 1093 KP Amsterdam). Vanaf de parkeergarage bent u met tramlijn 19 in twee haltes bij het KIT. Een dagkaart kost € 18,00.

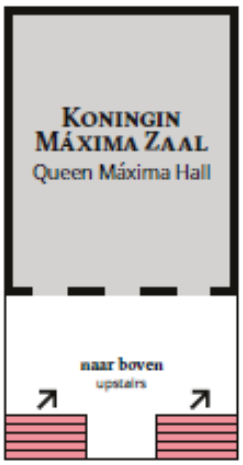
WiFi

In het Koninklijk Instituut voor de Tropen is een openbaar WiFi-netwerk beschikbaar waarop u kunt inloggen:
Netwerk: Conferences & Events
Wachtwoord: welcometokit

Plattegrond zalen

1

Eerste etage
First floor



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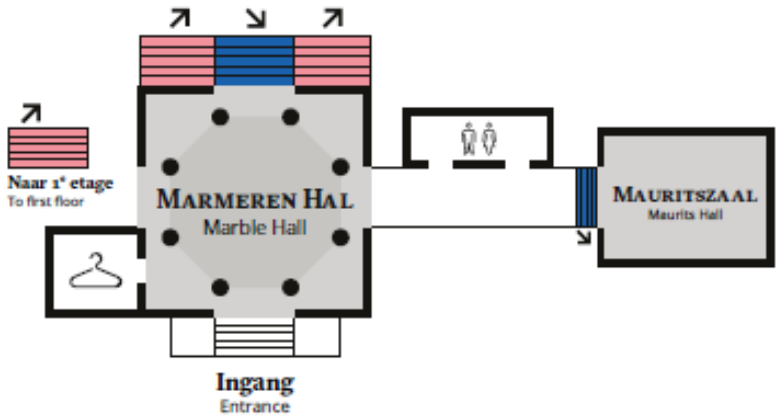
Begane grond
Ground floor



Voor het Bootcongres zijn de volgende congreszalen in gebruik:

1: Koningin Máximazaal, 1ste etage
2: Mauritszaal, begane grond
3: Tropentheater, begane grond*

* *niet op de plattegrond zichtbaar: wordt ter plaatse met bewegwijzering aangegeven.*

Inleveren presentaties

Wij verzoeken sprekers zo spoedig mogelijk na aankomst de presentatie in te leveren in de ter plaatse aangegeven ruimte.

Ophangen posters

De posters graag ophangen op de gereed staande (en genummerde) posterborden. Deelnemers worden verzocht de posters pas te verwijderen na de laatste pauze op donderdag 14 maart.

Tijdstip en locatie van de maaltijden

Woensdag

Lunch	13.00 – 14.00 uur Marmeren Hal *(deelnemers aan de onderwijssessie ontvangen bij de zaal een lunchpakket)*
Walking dinner	19.30 – 23.30 uur Café-Restaurant de Kroon, Rembrandtplein www.dekroon.nl
Afterparty	23.30 Club YOLO *(op eigen gelegenheid, voor eigen rekening)* www.clubyolo.nl *om de hoek bij Café-Restaurant de Kroon*

Donderdag

Lunch:	12.15 – 13.15 uur Marmeren Hal

Bijeenkomsten voorafgaand en tijdens Bootcongres

Dinsdag 12 maart 2019

Locatie: Koninklijk Instituut voor de Tropen *(zaal volgt)*

Landelijk Overleg Regionale Uitname Teams	09.30 uur
TC Nefrologen	14.00 uur
Landelijk Overleg Nier Transplantatie	16.00 uur
Landelijke Werkgroep Transplantatie Verpleegkunde	18.00 uur

Woensdag 13 maart 2019

Ledenvergadering Nederlandse Transplantatie Vereniging 17.30 – 18.30
Locatie: Tropentheater

Schematisch overzicht programma
Woensdag 13 maart 2019

Woensdagochtend	**Koningin Máximazaal**
09.00 – 09.30	Ontvangst met koffie
09.30 – 11.10	Opening congres door voorzitter LOC en NTV introductie programma **Plenaire sessie I** (voorzitters: Frederike Bemelman en Marlies Reinders) 09.40-10.40 André Kuipers **Prijsuitreikingen** Chiesiprijs 2019 – Beste Idee in Transplantatie Astellas Trans(p)la(n)t(at)ionele Researchprijs 2019, gevolgd door presentatie 2018 Novartis Transplantation Awards 2019 Prijs voor Innovatie in transplantatie onderwijs 2019, gevolgd door presentatie 2018
11.10 – 11.30	Koffiepauze
11.30 – 13.00	**Plenaire sessie II** *Thema: Spannende ontwikkelingen: van mens tot machine* Henny Otten, UMC Utrecht - Non-HLA antistoffen bij niertransplantatie: een nieuwe speler om rekening mee te houden Ton Rabelink, LUMC - Laatste ontwikkelingen van stamcel onderzoek in de nierziekten Steven Tsui, Cambridge - Cardiac Replacement Therapy – *The rise of the machine*
13.00 – 14.00	Lunch en onderwijssessie

Schematisch overzicht programma
Woensdag 13 maart 2019

Woensdagmiddag	Koningin Máximazaal	Mauritszaal	Tropentheater
14.00 – 15.30	**Parallelle sessie III – Basaal I** *Voorzitters: Carla Baan en Jan Stephan Sanders*	**Parallelle sessie IV - Klinisch I** *Voorzitters: Maarten Christiaans en Marije Baas*	**Parallelle sessie V - Actuele Klinische trials** *Voorzitters: Joost v.d. Heijden en Karlijn v.d. Pant*
15.30 – 16.00	Koffiepauze		
16.00 – 17.15	**Parallelle sessie VI - Best Abstracts I** *Voorzitters: Aiko de Vries en Frans van Ittersum*	**Parallelle sessie VII - YTP: Nederlanders in het buitenland** *Voorzitters: Dorottya de Vries en Martin Hoogduijn*	**Parallelle sessie VIII - Best Abstracts 2** *Voorzitters: Nouaf Ajubi en Junior Lardy*
17.30 – 18.30	Ledenvergadering in het Tropentheater		
19.30 – 23:30	Walking dinner Café de Kroon, Rembrandtplein		
23:30	Afterparty in club YOLO *(op eigen gelegenheid)*		

Schematisch overzicht programma
Donderdag 14 maart 2019

Donderdagochtend	**Koningin Máximazaal**		
08.30 – 09.00	Ontvangst en registratie, koffie		
09.00 – 10.30	**Plenaire sessie IX** *Voorzitters: Hans Bart en Jaap Homan van der Heijde* Bas van den Dungen, directeur-generaal Curatieve Zorg, Ministerie van Volksgezondheid, Welzijn en Sport: Nieuwe donorwet Uwe Heemann, Germany: Allocation in ET, problems and solutions Lisa Mumford, UK: The new British allocation system, what can we learn from the UK?		
10.30 – 11.00	Koffiepauze		
	Koningin Máximazaal	**Mauritszaal**	**Tropentheater**
11.00 – 12.15	**Parallelle sessie X** *Thema: Cognitie en coping bij chronische ziekte en transplantatie* *Voorzitters: Franka van Reekum / Lid patiëntenorg.* Sophie Lijdsman Marit van Sandwijk	**Parallelle sessie XI** *Patiënten sessie* *Voorzitters: Tessa de Jong / Stefan Berger* Donatie: de kijk van een altruïstist en een nabestaande versus de medisch professional, met gefilmde interviews. Dirk Ubbink: Shared Decision Making	**Parallelle sessie XII - Best abstracts 3** *Voorzitters: Joke Roodnat / Volkert Huurman*
12.15 – 13.15 12.45 – 13.10	Lunch Gemodereerde Postersessies		

Schematisch overzicht programma
Donderdag 14 maart 2019

Donderdagmiddag	Koningin Máximazaal	Mauritszaal	Tropentheater
13.15 – 15.00	**Parallelle sessie XIII - Leefstijl sessie** *Voorzitters: Eddie van Breukelen en Jacqueline v.d. Wetering* Adilson da Silva: Blijf in beweging, blijf fit Andrea Evers: Benefit for all: de rol van zelfmanage-ment en gezonde leefstijl bij chronische nierziektes Gerjan Navis: Time to ACT! Hanno Pijl: Leefstijlgeneeskunde, waarom de zorg anders moet	**Parallelle sessie XIV** *Voorzitters: Carla Schrauwers en Willy Rensen* Dilemma's bij donatie Annemarie Roelofs: Leverdonatie bij leven Postmortem donoren, casuïstiekbespreking.	**Parallelle sessie XV - Klinisch / Basaal 2** *Voorzitters: Luuk Hilbrands en Michiel Betjes*
15.00-15.30	Koffiepauze		
	Koningin Máximazaal		
15.30 16.15	**Plenaire sessie XIV** *Voorzitters: Frederike Bemelman en Marlies Reinders* Paul Louis Iske: Briljante mislukkingen **Prijsuitreikingen** LWTV Innovatie-Kwaliteitsprijs 2019, gevolgd door voordracht winnaar 2018 Distinguished Research Award 2019 Gauke Kootstraprijs 2019, gevolgd door voordracht		
16.45	Sluiting congres		

Woensdag 13 maart 2019

Sessie I – Plenair **Koningin Máximazaal**

09.00 Ontvangst en registratie

09.30 Opening

Voorzitters: Prof. dr. Frederike J. Bemelman, voorzitter LOC, nefroloog, A'dam UMC (AMC)
Prof. dr. Marlies E.J. Reinders, voorzitter NTV, internist-nefroloog, LUMC

09.40 **Medische aspecten van de ruimtevaart**
André Kuipers

10.40 Chiesi-prijs Beste Idee in Transplantatie 2019
Uitgereikt door Niels van Dijk

10.50 Astellas Trans(p)la(n)t(at)ionele Research Prijs 2019
Uitgereikt door Leon Commissaris

DHOPE – COR – NMP trial - A Single Center Clinical Trial to Assess Viability of High Risk Donor Livers Using Hypothermic and Normothermic Machine Perfusion with Rewarming Phase Prior to Transplantation
Yvonne de Vries, prijswinnaar Astellas Trans(p)la(n)t(at)ionele Research Prijs 2018

10.55 Novartis Transplantation Awards 2019
Uitgereikt door Dr. Arjan D. van Zuilen, internist-nefroloog UMC Utrecht voorzitter Novartis Transplant Advisory Board (NTAB)

11.00 Prijs voor Innovatie in transplantatie onderwijs 2019
Uitgereikt door Dr. M.J. Hoogduijn, secretaris NTV

11.05 Demonstratie winnaar Innovatie in transplantatie onderwijs 2018
Prof. dr. T. van Gelder, internist-nefroloog, Erasmus MC, Rotterdam

11.10 Koffiepauze

Woensdag 13 maart 2019

Sessie II – Plenair **Koningin Máximazaal**

Voorzitters: *Dr. Azam Nurmohamed, nefroloog, Amsterdam UMC (VUmc)*
Dr. Mirza Idu, chirurg, Amsterdam UMC (AMC)

Thema **Spannende ontwikkelingen: van mens tot machine**

11.30 Non-HLA antistoffen bij niertransplantatie: een nieuwe speler om rekening mee te houden
Dr. Henny G. Otten, medisch immunoloog, UMCU

12.00 Laatste ontwikkelingen van stamcel onderzoek in de nierziekten
Prof. dr. Ton Rabelink, hoofd afdeling nierziekten, LUMC

12.30 Cardiac Replacement Therapy – ***The rise of the machine***
Dr. S. Tsui, Consultant Cardiothoracic Surgeon, Royal Papworth Hospital NHS Foundation Trust, Papworth Everard | Cambridge

Onderwijssessie **Mauritszaal**

Voorzitters: *Dr. Coby H. Annema-de Jong, senior researcher, UMC Groningen*
Prof. dr. Henry Leuvenink, scientist, UMC Groningen

13.00 **Frailty en transplantatie**
Dr. R.A. Pol, vaat- en transplantatiechirurg UMC Groningen

Zelf management na transplantatie
Dr. Emma Massey, universitair hoofddocent, Erasmus MC, Rotterdam

14.00 Sluiting onderwijssessie

Woensdag 13 maart 2019

Parallelsessie III – Basaal 1 — Koningin Máximazaal

Voorzitters: *Prof. dr. Carla C. Baan, hoofd transplantatie laboratorium, Erasmus MC*
Dr. Jan-Stephan F. Sanders, internist-nefroloog, UMCG

Voordrachten in het Engels, 16 pitches van 2 minuten en 8 presentaties van 5 minuten

14.00 Mucosal associated invariant T-cells in renal transplant recipients before- and 12 months after transplantation (p.45)
M.L. Terpstra[1], M.J. Sinnige[2], M.C. van Aalderen[2], E.B.M. Remmerswaal[2], J. Kers[3], S.E. Geerlings[4], F.J. Bemelman[5]. [1]Dept. of Internal Medicine, division of Nephrology, Renal Transplant Unit, Amsterdam UMC (loc. AMC), Amsterdam. [2]Dept. of Experimental Immunology, Amsterdam UMC (loc. AMC), Amsterdam. [3]Dept. of Pathology, Amsterdam Infection & Immunity Institute (AI&II), Amsterdam. [4]Dept. of Internal Medicine, division of Infectious Diseases, Amsterdam UMC (loc. AMC), Amsterdam. [5]Dept. of Internal Medicine, division of Nephrology, Renal Transplant Unit, Amsterdam, The Netherlands.

14.02 Natural killer cells express significantly more CD16 during chronic-active antibody mediated rejection which is not caused by a single nucleotide polymorphism within the CD16 gene (p.46)
K.A. Sablik[1], N.H.R. Litjens[1], A. Peeters[1], M.C. Clahsen-van Groningen[2], M. Klepper[1], M.G.H. Betjes[1]. [1]Dept. of Internal Medicine, division Nephrology and Transplantation, [2]Dept. of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.04 Characterization of the immunogenicity of ipsc-derived kidney organoids (p.47)
A.S. Shankar[1], S.S. Korevaar[1,2], T.P.P. van den Bosch[3], M. Clahsen-van Groningen[3], J. Gribnau[4], C.C. Baan[2], E.J. Hoorn[2], M.J. Hoogduijn[2]. [1]Division of Nephrology and Transplantation, [2]Dept. of Internal Medicine, [3]Dept. of Pathology, [4]Dept. of Developmental Biology, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.06 Near-infrared fluorescence imaging with ZW800-1 dye to assess donor kidneys while on ex-vivo normothermic machine perfusion (p.48)
A.S. Arykbaeva[1], K.M. Rozenberg[2], M.L. Lo Faro[2], J. Hunter[2], J.B. Doppenberg[3], A.R.P.M. Valentijn[4], A.G.T. Terwisscha van Scheltinga[4], H. Putter[5], I.P.J. Alwayn[6], J.V. Frangioni[7], J. Burggraaf[8], A.L. Vahrmeijer[3], R.J. Ploeg[2], V.A.L. Huurman[3]. [1]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands.

[2]Nuffield Dept. of Surgical Sciences, University of Oxford, United Kingdom. [3]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [4]Dept. of Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, The Netherlands. [5]Dept. of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands. [6]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [7]Curadel, LLC, Marlborough, United States of America. [8]Centre for Human Drug Research, Leiden, The Netherlands.

14.08 Recombinant human monoclonal HLA antibodies of different IgG subclasses with the same epitope specificity: excellent tools to study the differential effect of donor specific antibodies in transplantation. (p.49)

C.S.M. Kramer[1], M.E.I. Franke-van Dijk[1], A.J. Priddey[2], H. Car[1], E. Gnudi[1], G.E. Karahan[1], E. van Beelen[1], C.C.C. Zilvold-van den Oever[3], H.J. Rademaker[3], P.W.H.I. Parren[1], V. Kosmoliaptsis[2], A. Mulder[1], D.L. Roelen[1], F.H.J. Claas[1], S. Heidt[1]. [1]Dept. of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Surgery, University of Cambridge, United Kingdom, [3]Genmab, Utrecht, The Netherlands.

14.10 Tolerance-associated circulating T-cells in immunologically tolerant liver transplant recipients (p.50)

A.A. Duizendstra[1], R.J. de Knegt[1], M.G.H. Betjes[2], M.P. Peppelenbosch[1], J. Kwekkeboom[1], N.H.R. Litjens[2]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.12 Delivery of mesenchymal stromal cell therapy via renal intra-arterial infusion (p.51)

J.M. Sierra Parraga[1], C. Andersen[2], A. Munk[2], S. Lohmann[3], C. Moers[4], C.C. Baan[1], R.J. Ploeg[5], A. Keller[2], B.K. Møller[6], M.J. Hoogduijn[1], B. Jespersen[7], M. Eijken[2]. [1]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark. [3]Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark. [4]Dept. of Surgery - Organ Donation and Transplantation, University Medical Center Groningen, Groningen, The Netherlands. [5]Nuffield Dept. of Surgical Sciences and Oxford Biomedical Research Centre, University of Oxford, Oxford, United Kingdom. [6]Dept. of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark. [7]Dept. of Renal Medicine, Aarhus University Hospital, Aarhus, Denmark.

14.14 Complement C4 is an important mediator of brain-death induced lung injury (p.52)

J.E. van Zanden[1], N.M. Jager[1], F. Poppelaars[2], Z.J. Veldhuis[1], M.E. Erasmus[3], H.G.D. Leuvenink[1], M.A. Seelen[2]. [1]Dept. of Surgery, [2]Dept. of Internal Medicine, [3]Dept. of Cardiothoracic Surgery, University Medical Center Groningen, Groningen, The Netherlands.

14.16 Ex vivo magnetic resonance imaging during normothermic machine perfusion - developing a novel non-invasive tool to assess donor kidney quality (p.53)

R. Schutter[1], O.C. van Varsseveld[1], V.A. Lantinga[1], H.G.D. Leuvenink[1], R.J.H. Borra[2], C. Moers[1]. [1]Dept. of Surgery, [2]Dept of Radiology, University Medical Center Groningen, Groningen, The Netherlands.

14.18 The effect of ischemia on protein degradation during renal transplantation (p.54)

L.L. van Leeuwen[1], B.M. Kessler[2], R.J. Ploeg[3], H.G.D. Leuvenink[1]. [1]Dept. of Experimental Surgery, University Medical Center Groningen, Groningen, The Netherlands. [2]Target Discovery Institute, University of Oxford, Oxford, United Kingdom. [3]Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, United Kingdom.

14.20 Effect of normothermic machine perfusion conditions on mesenchymal stromal cells (p.55)

J.M. Sierra Parraga[1], K. Rozenberg[2], M. Eijken[3], H. Leuvenink[4], J. Hunter[2], A.M. Merino[1], C. Moers[4], B.K. Møller[5], R.J. Ploeg[2], C.C. Baan[1], B. Jespersen[6], M.J. Hoogduijn[1]. [1]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Nuffield Dept. of Surgical Sciences and Oxford Biomedical Research Centre, University of Oxford, Oxford, United Kingdom. [3]Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark. [4]Dept. of Surgery - Organ Donation and Transplantation, University Medical Center Groningen, Groningen, The Netherlands. [5]Dept. of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark. [6]Dept. of Renal Medicine, Aarhus University Hospital, Aarhus, Denmark.

14.22 Factors Influencing Access to kidney Transplantation (FIAT): a protocol of a qualitative study on stakeholders' perspectives (p.56)

A. Luchtenburg[1], K. Kloss[1], S. Redeker[1], J. van Busschbach[1], J. van de Wetering[2], S. Ismail[1]. [1]Dept. of Psychiatry, section Medical Psychology and Psychotherapy, [2]Dept. of Internal Medicine, section Nephrology & Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.24 Donor postoperative outcome and quality of life after living donor liver transplantation (p.57)

J. van Son[1], G.J.A. Hegeman[1], F.M. Heikamp[1], H.J.L. Quaedvlieg[1], J.H. Annema[2], M.T. de Boer[1]. [1]Dept. of Surgery, [2]Nursing research, University Medical Center Groningen, Groningen, The Netherlands.

14.26 Human kidneys contain tissue-resident mucosal associated invariant T-cells (p.58)

M.L. Terpstra[1], M.J. Sinnige[2], E.B.M. Remmerswaal[2], M.C. van Aalderen[2], J. Kers[3], S.E. Geerlings[4], F.J. Bemelman[1]. [1]Dept. of Internal Medicine, division of Nephrology, Renal Transplant Unit, Amsterdam UMC (loc. AMC), Amsterdam. [2]Dept. of Experimental Immunology, Amsterdam UMC (loc. AMC), Amsterdam. [3]Dept. of Pathology, Amsterdam Infection & Immunity Institute (AI&II), Amsterdam. [4]Dept. of Internal Medicine, division of Infectious Diseases, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

14.28 Hypothermic oxygenated machine perfusion enables 24-hour ex situ preservation of porcine donation after circulatory death livers (p.59)

I.M.A. Brüggenwirth[1], O.B. van Leeuwen[1], Y. de Vries[1], J. Adelmeijer[2], J.J. Wiersema-Buist[2], T. Lisman[2], P.N. Martins[3], R.J. Porte[1]. [1]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands. [2]Surgical Research Lab, University Medical Center Groningen, Groningen, The Netherlands. [3]Dept. of Surgery, University of Massachusetts Medical School, Worcester, United States of America.

14.30 Factors associated with the acceptance of livers for liver transplantation: validation of the Discard Risk Index in the Eurotransplant region. (p.60)

J.D. de Boer[1], H. Putter[2], J.J. Blok[3], N. Cambridge[4], S. van den Berg[4], U. Samuel[5], G. Berlakovich[6], M. Guba[7], A.E. Braat[8]. [1]Dept. of Transplantation Surgery, Eurotransplant/ Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Medical Statistics, Leiden University Medical Center, Leiden, The Netherlands. [3]Dept. of Surgery, Haaglanden Medical Center, The Hague, The Netherlands. [4]Allocation Eurotransplant, Leiden, The Netherlands. [5]Eurotransplant, Leiden, The Netherlands. [6]Dept. of Surgery, Vienna, Austria. [7]Dept. of Surgery, Munich, Germany. [8]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands.

14.32 8 beste pitches (5 minuten spreektijd en 1 minuut discussietijd)

15.30 Koffiepauze

Woensdag 13 maart 2019

Parallelsessie IV – Klinisch 1 — Mauritszaal

Voorzitter: *Dr. Maarten H.L. Christiaans, nefroloog, MUMC*
Dr. Marije C. Baas, nefroloog, Radboudumc

Voordrachten in Nederlands of Engels, 16 pitches van 2 minuten en 8 presentaties van 5 minuten.

14.00 Evaluation of the current post-transplantation Human Leukocyte Antigen antibody screening in paediatric renal transplant recipients (p.61)
A. Demirok[1], C. Ranzijn[2], N.M. Lardy[2], S. Florquin[3], A.H.M. Bouts[4]. [1]Amsterdam UMC (loc. AMC), Amsterdam. [2]Dept. of Immunogenetics, Sanquin, Amsterdam. [3]Dept. of Pathology, Amsterdam UMC (loc. AMC), Amsterdam. [4]Dept. of Pediatric Nephrology, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

14.02 Computerised Integration of Alternative kidney Transplantation (CIAT) programs to improve transplants for HI patients: a simulation (p.62)
M. de Klerk[1], J.A. Kal-van Gestel[1], S. Middel-de Sterke[1], J. van de Wetering[1], M.M.L. Kho[1], M.G.H. Betjes[1], W.C. Zuidema[1], D.L. Roelen[2], K.M. Glorie[3], J.I. Roodnat[1]. [1]Dept. of Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam. [2]Dept. of Immunology, Leiden University Medical Center, Leiden. [3]Dept. of Econometrics, Erasmus Q-Intelligence, Rotterdam, The Netherlands.

14.04 High numbers of differentiated CD8+CD28- T cells are associated with a substantially lowered risk for late rejection and graft loss after kidney transplantation (p.63)
M.G.H. Betjes[1], A.W. Langerak[2], M. Klepper[1], N.H.R. Litjens[1]. [1]Dept. of Nephrology & Transplantation, [2]Dept. of Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.06 Efficacy of deep versus moderate neuromuscular blockade in enhancing intra-operative safety and post-operative recovery after laparoscopic donor nephrectomy: a randomised controlled trial (p.64)
M.H.D. Bruintjes[1], P. Krijtenburg[2], C.H. Martini[3], P.P. Poyck[4], F.C.H. d' Ancona[1], V.A.L. Huurman[5], M. van der Jagt[4], J.F. Langenhuijsen[1], W.N. Nijboer[5], C.J.H.M. van Laarhoven[4], A. Dahan[3], M.C. Warlé[4]. [1]Dept. of Urology, Radboud University Medical Center, Nijmegen. [2]Dept. of Anesthesiology, Radboud University Medical Center, Nijmegen. [3]Dept. of Anesthesiology, Leiden University Medical Center, Leiden. [4]Dept. of Surgery, Radboud University Medical Center, Nijmegen. [5]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands.

Woensdag 13 maart 2019

14.08 Pre-transplant donor-specific B cell memory for prediction of antibody mediated rejection - a pilot study (p.65)

G.E. Karahan[1], C. Wehmeier[1], J. Krop[1], Y. de Vaal[1], J. Langerak-Langerak[1], D.L. Roelen[1], N.M. Lardy[2], F.J. Bemelman[3], I. ten Berge[3], M.E.J. Reinders[4], C. van Kooten[4], S. Schaub[5], F.H.J. Claas[1], S. Heidt[1]. [1]Dept. of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands. [2]Dept. of Immunogenetics, Sanquin Diagnostic Services, Amsterdam, The Netherlands. [3]Renal Transplantation Unit, Dept. of Nephrology, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands. [4]Dept. of Nephrology, Leiden University Medical Center, Leiden, The Netherlands. [5]Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland.

14.10 Comparison of long-term outcomes between alemtuzumab and rabbit anti-thymocyte globulin for acute kidney allograft rejection (p.66)

M. van der Zwan[1], M.C. Clahsen-Van Groningen[2], D.L. Roelen[3], M.W.F. van den Hoogen[4], M. van Agteren[4], J.I. Roodnat[4], M.G.H. Betjes[4], C.C. Baan[1], D.A. Hesselink[1]. [1]Dept. of Internal Medicine, Division of Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam. [2]Dept. of Pathology, Erasmus University Medical Center, Rotterdam. [3]Dept. of Immunology, Leiden University Medical Center, Leiden. [4]Dept. of Nephrology, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.12 Therapeutic drug monitoring of tacrolimus and mycophenolic acid in outpatient renal transplant recipients using a volumetric dried blood spot sampling device (p.67)

T.C. Zwart[1], S.R.M. Gokoel[2], P.J.M. van der Boog[2], J.W. de Fijter[2], D.M. Kweekel[1], J.J. Swen[1], H.J. Guchelaar[1], D.J.A.R. Moes[1]. [1]Dept. of Clinical Pharmacy and Toxicology, [2]Dept. of Nephrology, Leiden University Medical Center, Leiden, The Netherlands.

14.14 Detection, treatment and clinical outcome of graft thrombosis following pancreas transplantation (p.68)

W.H. Kopp, C.A.T. van Leeuwen, H.D. Lam, V.A.L. Huurman, A.F. Schaapherder, A.G. Baranski, A.E. Braat. Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands.

14.16 Implementation of Normothermic Regional Perfusion in the Netherlands (p.69)

V.A.L. Huurman[1], D.E.M.A. Detillon[2], L.J.M. Habets[1], F.E.M. van de Leemkolk[1], I.J. Schurink[2], M. van der Hoeven[3], J. de Jonge[2]. [1]Dept. of Surgery, Leiden University Medical Center, Leiden. [2]Dept. of Surgery, Erasmus University Medical Center, Rotterdam. [3]Transplantation Center, Leiden University Medical Center, Leiden, The Netherlands.

14.18 Advanced immunological T-cell ageing defined by a very low thymic function identifies patients with substantial increased risk for long-term mortality after kidney transplantation (p.70)

M.G.H. Betjes[1], A.W. Langerak[2], M. Klepper[1], N.H.R. Litjens[1]. [1]Dept. of Nephrology & Transplantation, [2]Dept. of Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.20 The national HLA-incompatible kidney transplantation program: two years onwards (p.71)

A.E. de Weerd[1], D.L. Roelen[2], M.G.H. Betjes[1], M.M.L. Kho[1], J.I. Roodnat[1], J. van de Wetering[1]. [1]Dept. of Nephrology and Kidney Transplantation, Erasmus University Medical Center, Rotterdam. [2]Dept. of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands.

14.22 Outcome after liver transplantation for hilar cholangiocarcinoma in the Netherlands after implementation of a nationwide protocol (p.72)

F.J.H. Hoogwater[1], V.E. de Meijer[1], B. van Hoek[2], W. Polak[3], I.P.J. Alwayn[4], A.P. van den Berg[5], S. Darwish Murad[6], R.J. Porte[7]. [1]Dept. of Surgery, HPB & Liver Transplantation, University Medical Center Groningen, Groningen. [2]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden. [3]Dept. of Surgery, Erasmus University Medical Center, Rotterdam. [4]Dept. of Surgery, Leiden University Medical Center, Leiden. [5]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen. [6]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam. [7]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands.

14.24 Especially 'elderly' patients should receive a living donor kidney transplant (p.73)

M. Laging, J.A. Kal-van Gestel, W. Weimar, J.I. Roodnat. Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands.

14.26 Macroscopic arteriosclerosis of the renal artery is associated with organ discard and primary non-function, but not with graft function or long term survival of 50+ deceased donor kidneys (p.74)

C. Moers[1], A. Keijbeck[2], R. Veenstra[1], R. Pol[1], C. Konijn[3], N. Jansen[3], H. van Goor[4], C. Peutz-Kootstra[2], A. Hoitsma[3], C. Moers[1]. [1]Dept. of Surgery - Organ Donation and Transplantation, University Medical Center Groningen, Groningen. [2]Dept. of Pathology, Maastricht University Medical Center, Maastricht. [3]NTS, Dutch Transplantation Foundation, Leiden. [4]Dept. of Pathology, University Medical Center Groningen, Groningen, The Netherlands.

14.28 Increased and safe utilization of high-risk donor livers for transplantation after ex situ resuscitation and assessment using sequential hypo- and normothermic machine perfusion (p.75)

O.B. van Leeuwen[1], Y. de Vries[1], M. Fujiyoshi[1], R. Ubbink[2], G.J. Pelgrim[2], M.J.M. Werner[1], K. Reyntjens[3], A.P. van den Berg[4], M.T. de Boer[1], R.H.J. de Kleine[1], V.E. de Meijer[1], R.J. Porte[1]. [1]Dept. of Surgery, [2]Groningen Transplant Center, [3]Dept. of Anesthesiology, [4]Dept. of Internal Medicine, division of Hepatology, University Medical Center Groningen, Groningen, The Netherlands.

14.30 First experience with ex-vivo lung perfusion for initially discarded donor lungs in The Netherlands. a single center study (p.76)

Z.L. Zhang[1], V. van Suylen[1], J.E. van Zanden[1], C. van de Wauwer[1], E.A.M. Verschuuren[2], W. van der Bij[2], M.E. Erasmus[1]. [1]Dept. of Cardio-Thoracic Surgery, [2]Dept. of Respiratory Medicine, University Medical Center Groningen, Groningen, The Netherlands.

14.32 8 beste pitches (5 minuten spreektijd en 1 minuut discussietijd)

15.30 Theepauze

Woensdag 13 maart 2019

Parallelsessie V **Tropentheater**

Voorzitters: *Dr. Joost van der Heijde, nefroloog, Amsterdam UMC (VUmc)*
Drs. Karlijn A.M.I. van der Pant, nefroloog, Amsterdam UMC (AMC)

Thema: ***Actuele klinische trials: 'The Future is Now'***

14.00 Overzicht van de actuele transplantatie gerelateerde studies in de UMC's

Amsterdam UMC, loc AMC
Frederike Bemelman

Amsterdam UMC, loc. VUmc
Joost van der Heijden en Azam Nurmohamed

Erasmus MC
Dennis Hesselink en Robert Minnee

Leids Universitair Medisch Centrum
Cees van Kooten en Volkert Huurman

Radboudumc
Marije Baas

UMC Groningen
Cyril Moers en Stefan Berger

UMC Utrecht
Arjan van Zuilen en Niels van der Kaaij

15.30 Theepauze

Parallelsessie VI – Best abstracts 1 — Koningin Máximazaal

Voorzitter: *Dr. Aiko P.J. de Vries, nefroloog, LUMC*
Dr. Frans J. van Ittersum, internist-nefroloog, Amsterdam UMC (VUmc)

Voordrachten in het Engels, 7 minuten presentatie en 3 minuten discussie.

16.00 CD40 inhibition with CFZ533 - a fully human, non-depleting, Fc silent mAB - improves renal allograft function while demonstrating comparable efficacy vs tacrolimus after kidney transplantation (p.77)
M.W.F. van den Hoogen[1], B. Nashan[2], H. Tedesco[2], S. Berger[2], D. Cibrik[2], S. Mulgaonkar[2], D. Leeser[2], R. Alloway[2], A. Patel[2], J. Pratschke[2], C. Sommerer[2], A. Wiseman[2], A. van Zuilen[2], U. Laessing[3], J. Rush[3], B. Haraldsson[3]. [1]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]CFZ533 Study group, The Netherlands. [3]Novartis, Basel, Switzerland.

16.10 Luminal preservation of the human small bowel graft reduces mucosal damage during cold storage (p.78)
A.M.S. de Jong[1], G. Trentadue[1], J. van Praagh[2], J. Pirenne[3], L.J. Ceulemans[4], J.W. Haveman[5], K.N. Faber[6], G. Dijkstra[1]. [1]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Pharmacy, Pharmaceutical Technology and Biopharmacy, University Medical Center Groningen, Groningen, The Netherlands. [3]Dept. of Abdominal Transplant Surgery, Microbiology and Immunology, University Hospitals Leuven, Leuven, Belgium. [4]Dept. of Abdominal Transplant Surgery, Thoracic Surgery, University Hospitals Leuven, Belgium. [5]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands. [6]Dept. of Laboratory Medicine, University Medical Center Groningen, Groningen, The Netherlands.

16.20 Oxygenated hypothermic machine perfusion of kidneys donated after circulatory death: an international randomised controlled trial (p.79)
Hofker[1], I. Jochmans[2], A. Brat[1], F. Leemkolk[3], L. Davies[3], S. Knight[3], J. Pirenne[2], R.J. Ploeg[3]. [1]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Surgery, University Hospitals Leuven, KU Leuven, Leuven, Belgium. [3]Dept. of Surgery, Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, United Kingdom.

Woensdag 13 maart 2019

16.30 Prevalence of psychological distress and the correlation with medication non-adherence among lung transplant patients (p.80)
M.J.C. Wessels-Bakker[1], E.A. van de Graaf[1], J.M. Kwakkel-van Erp[2], H.G. Heijerman[2], W. Cahn[3], R. Schappin[4]. [1]Dept. of Lung Transplantation, [2]Dept. of Respiratory Medicine, [3]Dept. of Psychiatry, [4]Dept. of Medical Psychology and Social Work, division Children, Utrecht University Medical Center, Utrecht, The Netherlands.

16.40 Hypothermic machine perfusion as a national standard preservation method for deceased donor kidneys (p.81)
A. Brat[1], L.W.E. van Heurn[2], V.A.L. Huurman[3], W. de Jongh[4], H.G.D. Leuvenink[1], K.M. Ooms - de Vries[5], A.D. van Zuilen[6], J. de Jonge[7], B.J.J.M. Haase - Kromwijk[5], S.P. Berger[8], H.S. Hofker[1]. [1]Dept. of Surgery, University Medical Center Groningen, Groningen. [2]Dept. of Surgery, Amsterdam UMC (loc. AMC), Amsterdam, [3]Dept. of Surgery, Leiden University Medical Center, Leiden. [4]Dept. of Surgery, Maastricht University Medical Center, Maastricht. [5]Dutch Transplant Foundation, Leiden. [6]Dept. of Nephrology, University Medical Center Utrecht, Utrecht. [7]Dept. of Surgery, Erasmus University Medical Center, Rotterdam. [8]Dept. of Nephrology, University Medical Center Groningen, Groningen, The Netherlands.

16.50 Tacrolimus monotherapy in immunologically low-risk kidney transplant recipients: a randomized controlled trial (p.82)
A.E. de Weerd[1], M.J. Verschragen[2], J.A. van Gestel[2], M.G.H. Betjes[2]. [1]Dept. of Nephrology and Kidney Transplantation, [2]Dept. of Nephrology, Erasmus Medical Center, Rotterdam, The Netherlands.

17.00 Pneumococcal and tetanus vaccination in tacrolimus treated kidney transplant recipients with and without mycophenolate mofetil: a randomized controlled trial (p.83)
A.E. de Weerd[1], M.J. Verschragen[2], J.A. van Gestel[2], W.A. Dik[3], M.G.H. Betjes[1]. [1]Dept. of Nephrology and Kidney Transplantation, [2]Dept. of Nephrology, [3]Dept. of Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands.

17.30 Ledenvergadering in Tropentheater

19.30 Walking dinner Café-Restaurant de Kroon, Rembrandtplein

Woensdag 13 maart 2019

Parallelsessie VII – Young Professionals — Mauritszaal

Voorzitters: *Dr. Dorottya K. de Vries, chirurg, LUMC*
Dr. Martin J. Hoogduijn, universitair docent, Erasmus MC

Thema: **Nederlanders in het buitenland**

16.00 Wat brengt het jou persoonlijk?

16.30 Wat brengt het professioneel?

17.00 Paneldiscussie en quiz

17.30 Ledenvergadering in Tropentheater

19.30 Walking dinner Café de Kroon, Rembrandtplein

Parallelsessie VIII – Best abstracts 2 — Tropentheater

Voorzitter: *Dr. Nouaf Ajubi, internist-nefroloog, Curaçao*
Dr. Junior Lardy, manager Sanquin

Voordrachten in het Engels, 7 minuten presentatie en 3 minuten discussie.

16.00 A decade of ABO-incompatible kidney transplantation in the Netherlands (p.84)
A.E. de Weerd[1], J.A.J.G. van den Brand[2], H. Bouwsma[3], A.P.J. de Vries[3], P.M.M. Dooper[2], J.S.F. Sanders[4], M. van Dijk[4], M.H.L. Christiaans[5], F.E. van Reekum[5], A.D. van Zuilen[6], F.J. Bemelman[7], M.S. van Sandwijk[7], A. Nurmohamed[8], M. van Agteren[1], M.G.H. Betjes[1], M.F.C. de Jong[4], M.C. Baas[2]. [1]Dept. of Nephrology and Kidney Transplantation, Erasmus Medical Center, Rotterdam. [2]Dept. of Nephrology, Radboudumc, Nijmegen. [3]Dept. of Nephrology, Leiden University Medical Center, Leiden. [4]Dept. of Nephrology, University Medical Center Groningen, Groningen. [5]Dept. of Nephrology, University Medical Center Maastricht, Maastricht. [6]Dept. of Nephrology, University Medical Center Utrecht, Utrecht. [7]Dept. of Nephrology, Amsterdam UMC (loc. AMC), Amsterdam. [8]Dept. of Nephrology, Amsterdam UMC (loc. VUmc), Amsterdam, The Netherlands.

16.10 Predictors for graft survival after pregnancy in kidney transplant recipients (p.85)

M.C. van Buren[1], A.T. Lely[2], J. van de Wetering[1]. [1]Dept. of Nephrology & Transplantation, Erasmus University Medical Center, Rotterdam. [2]Dept. of Gynaecologie & Obstetrics, University Medical Center Utrecht, Wilhelmina Children Hospital, Utrecht. Pregnancy after Renal Transplantation OUTcomes.

16.20 Identification of new drug targets to prevent ischemia-induced bile toxicity using a human biliary organoid model (p.86)

F.J.M. Roos[1], M. Bijvelds[2], H. de Jonge[2], H.J. Metselaar[2], K. Burka[1], J.N.M. IJzermans[1], M.M.A. Verstegen[1], L.J.W. van der Laan[1]. [1]Dept. of Sugery, [2]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands.

16.30 Immunologically tolerant liver transplant recipients are characterized by donor-specific hypo responsiveness of circulating T-cells (p.87)

A.A. Duizendstra[1], R.J. de Knegt[1], M.G.H. Betjes[2], M.P. Peppelenbosch[1], N.H.R. Litjens[2], J. Kwekkeboom[1]. [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands.

16.40 The potential of donation after circulatory death heart transplantations in the Netherlands (p.88)

S. Roest[1], N.P. van der Kaaij[2], K. Damman[3], L.W. van Laake[4], J.A. Bekkers[5], M.E. Erasmus[6], O.C. Manintveld[1]. [1]Dept. of Cardiology, Thoraxcenter, Erasmus University Medical Center, Rotterdam. [2]Dept. of Cardiothoracic Surgery, University Medical Center Utrecht, Utrecht. [3]Dept. of Cardiology, University Medical Center Groningen, Groningen. [4]Dept. of Cardiology, University Medical Center Utrecht, Utrecht. [5]Dept. of Cardiothoracic Surgery, Thoraxcenter, Erasmus University Medical Center, Rotterdam. [6]Dept. of Cardiothoracic Surgery, University Medical Center Groningen, Groningen, The Netherlands.

16.50 Bile as a non-invasive source of cholangiocyte organoids for develping patient-specific disease modelling and personalized regenerative medicine (p.89)

F.J.M. Roos[1], M.M.A. Verstegen[1], J.W. Poley[2], M. Bruno[2], G.W.M. Tetteroo[3], J.N.M. IJzermans[1], L.J.W. van der Laan[1]. [1]Dept. of Surgery, Erasmus University Medical Center, Rotterdam. [2]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam. [3]Dept. of Surgery, IJsselland Hospital, Capelle aan de IJssel, The Netherlands.

Woensdag 13 maart 2019

17.00 10 years of islet transplantation in the Netherlands (p.90)
M.F. Nijhoff. Dept. of Nephrology, Leiden University Medical Center, Leiden, The Netherlands.

17.30 Ledenvergadering in Tropentheater

19.30 Walking dinner en feest Café de Kroon, Rembrandtplein

Donderdag 14 maart 2019

Sessie IX – Plenair — Koningin Máximazaal

Voorzitters: *Hans Bart, Nierpatiënten Vereniging Nederland*
Prof. dr. Jaap. J. Homan van der Heijde, nefroloog, Amsterdam UMC (AMC)

09.00 Nieuwe donorwet
Drs. Bas van den Dungen, directeur-generaal Curatieve Zorg
Ministerie van Volksgezondheid, Welzijn en Sport

09.30 Allocation in ET problems and solutions
Prof. dr. Uwe Heemann, nephrologist
Technische Universität München, TUM, Abteilung für Nephrologie

10.00 The new British allocation system, what can we learn from the UK?
Dr. Lisa Mumford, Head of ODT Studies, Statistics and Clinical Studies
NHS Blood and Transplant

10.30 Koffiepauze

Parallelsessie X — Koningin Máximazaal

Voorzitters: *Franka van Reekum, internist-nefroloog UMC Utrecht*
Tony de Ronde, afgevaardigde NVN

Thema: ***Cognitie en arbeidsparticipatie na transplantatie***

11.00 Nierziekte en werk
Annemieke Visser, andragoog en onderzoeker,
afdeling Toegepast Gezondheidsonderzoek, UMCG

11.30 Severe chronic kidney disease in children, adolescents and adults: the impact on neurocognition and brain white matter microstructure.
Sophie Lijdsman, Neuropsycholoog/onderzoeker INPACT studie
Psychosociale afdeling - Emma Kinderziekenhuis/AMC, Amsterdam

Donderdag 14 maart 2019

11.50 Cognitive Improvement in Kidney Transplant Recipients Exceeds Improvement in Kidney Donors and is Associated with Structural and Functional Changes on MRI (p.91)
M.S. van Sandwijk[1], I.J.M. ten Berge[1], M.W.A. Caan[2], W.A. van Gool[3], C.B.L.M. Majoie[2], H.J. Mutsaerts[2], B.A. Schmand[4], A. Schrantee[2], L.M.J. de Sonneville[5], F.J. Bemelman[1]. [1]Nefrologie, [2]Radiologie, [3]Neurologie, Amsterdam UMC (loc. AMC), Amsterdam. [4]Psychologie, Universiteit van Amsterdam, Amsterdam. [5]Faculteit der Sociale Wetenschappen, Universiteit Leiden, Leiden.

12.15 Lunch en postersessies

Parallelsessie XI — Mauritszaal

Voorzitters: Tessa de Jong, verpleegkundig specialist, Amsterdam UMC (AMC)
Stefan Berger, nefroloog, UMCG, Groningen

Patiëntensessie

11.00 Donatie: de kijk van een altruïstist en een nabestaande versus de medisch professional - *met gefilmde interviews*

11.45 Shared Decision making
Prof. dr. Dirk Ubbink, hoogleraar Evidence-Based Medicine and Shared Decision-Making (AMC-UvA).

12.15 Lunch en postersessies

Parallelsessie XII – Best abstracts 3 — Tropentheater

Voorzitter: Dr. Joke I. Roodnat, internist-nefroloog, Erasmus MC
Dr. Volkert A.L. Huurman, chirurg, LUMC

Voordrachten in het Engels, 7 minuten presentatie en 3 minuten discussie.

11.00 Disrupted regulation of serpinB9 in circulating T cells is associated with an increased risk for post-transplant skin cancer (p.92)

K. Boer, F.S. Peters, A.M.A. Peeters, J. van de Wetering, M.G.H. Betjes, C.C. Baan. Dept. of Internal Medicine, section Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands.

11.10 Inhibitory monoclonal antibody to factor B attenuates brain death-induced renal injury and inflammation (p.93)

N.M. Jager[1], F. Poppelaars[2], M. Subías[3], H.G.D. Leuvenink[4], M.R. Daha[2], S.R. de Córdoba[3], M.A. Seelen[2]. [1]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Internal Medicine, University Medical Center Groningen, Groningen, The Netherlands. [3]Centro de Investigaciones Biologicas, Madrid, Spain. [4]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands.

11.20 The renin-angiotensin system is present and functional in ipsc-derived kidney organoids (p.94)

A.S. Shankar[1], S.S. Korevaar[1], I.M. van den Berg-Garrelds[2], J. Gribnau[3], C.C. Baan[1], A.H.J. Danser[2], E.J. Hoorn[1], M.J. Hoogduijn[1]. [1]Dept. of Internal Medicine, Division of Nephrology and Transplantation, [2]Dept. of Internal Medicine, Division of Pharmacology and Vascular Medicine, [3]Dept. of Developmental Biology, Erasmus University Medical Center, Rotterdam, The Netherlands.

11.30 Targeted proteomic analysis detects acute T cell-mediated kidney allograft rejection in belatacept-treated patients (p.95)

M. van der Zwan[1], D.A. Hesselink[1], M.C. Clahsen-van Groningen[2], C.C. Baan[1]. [1]Dept. of Internal Medicine, Division of Nephrology and Transplantation, [2]Dept. of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands.

11.40 Donor-specific memory T cell responsiveness decreases after kidney transplantation (p.96)

A. Mendoza[1], D. Reijerkerk[1], R. de Kuiper[1], T. van Gelder[2], D.A. Hesselink[1], C.C. Baan[1], N.M. van Besouw[1]. [1]Dept. of Internal medicine, Nephrology & Transplantation, [2]Dept. of Internal Medicine, Nephrology & Transplantation & Clinical Pharmacology Unit, Erasmus University Medical Center, Rotterdam.

11.50 A single nucleotide donor C3 polymorphism associates with clinical outcome after lung transplantation (p.97)

T. Kardol-Hoefnagel[1], K. Budding[1], E.A. van de Graaf[2], J. van Setten[3], O.A. van Rossum[1], E.J.D. Oudijk[4], H.G. Otten[1]. [1]Laboratory of Translational Immunology, UMC Utrecht, Utrecht. [2]Dept. of Respiratory Medicine, UMC Utrecht, Utrecht. [3]Dept. of Cardiology, University Medical Center Utrecht, Utrecht. [4]Center of Interstitial Lung Diseases, St. Antonius Hospital, Nieuwegein, The Netherlands.

Donderdag 14 maart 2019

12.00 Organ resilience contributes to different impact of delayed graft function on graft survival in kidneys donated by brain death and circulatory death donors (p.98)
M.J.C. de Kok[1], A.F.M. Schaapherder[1], L.G.M. Wijermars[1], D.K. de Vries[1], L. Verschuren[2], J.H.N. Lindeman[1]. [1]Dept. of Transplant Surgery, Leiden University Medical Center, Leiden. [2]Dept. of Microbiology and Systems Biology, The Netherlands Organization for Applied Scientific Research (TNO), Leiden, The Netherlands.

12.15 Lunch en postersessies

Postersessies 1 - Nursing

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

12.30-12.45

Moderator: Jeanique van de Geest-van Zoest

1. Expanding the donor pool by extended DCD lung donation (p.99)
E.M.M. Koffeman[1], J.M. Droogh[2], A. Veen[1], M.E. Erasmus[3], C.T. Gan[4], H.A.M. Kerstjens[4], M. Mariani[3], E.A.M. Verschuuren[4]. [1]Dept. of Surgery,. [2]Dept. of Critical Care, [3]Dept. of Cardiothoracic Surgery, [4]Dept. of Pulmonary Diseases and Tuberculosis, University Medical Center Groningen, Groningen, The Netherlands.

2. Anti-hypertensive drug adherence in lung transplant recipients (p.100)
I. van Ewijk, E.A. van de Graaf. Dept. of Pulmonary Transplantation, University Medical Center Utrecht, Utrecht, The Netherlands.

3. Leverdonatie bij leven ten behoeve van een kind, een update van ons programma en de rol van de verpleegkundig specialist leverdonatie. (p.101)
A.M.S. Roelofs. Dept. of Gastroenterology & Hepatology, University Medical Center Groningen, Groningen, The Netherlands.

4. Moet ambulante bloeddrukmeting onderdeel zijn van screening nierdonatie bij leven? (p.102)
J.M. Wierdsma, F.E. van Reekum, A.D. van Zuilen. Dept. of Nephrology, University Medical Center Utrecht, Utrecht, The Netherlands.

5. AB0 incompatibele niertransplantatie anno 2018 in het UMCG, 10 jaar ervaring (p.103)
D.P. Jansen. Dept. of Kidney Transplantation, University Medical Center Groningen, Groningen, The Netherlands.

Postersessies 2 - Clinical

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

12.45-13.00

Moderator: Nienke Manson

6. High intra-patient variability in tacrolimus exposure is not associated with immune-mediated graft injury after liver transplantation (p.104)
M.A.A. van der Veer[1], N. Nangrahary[2], D.A. Hesselink[3], N.S. Erler[4], H.J. Metselaar[1], T. van Gelder[3], S. Darwish Murad[1]. [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam. [2]Dept. of Hospital Pharmacy, Erasmus University Medical Center, Rotterdam. [3]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam. [4]Dept. of Biostatistics, Erasmus University Medical Center, Rotterdam, The Netherlands.

7. Personalized screening schedules to monitor the development of chronic renal allograft failure (p.105)
H. Peters-Sengers[1], A. Tomer[2], S. Florquin[3], J.J.T.H. Roelofs[3], E.W. Steyerberg[4], F.J. Bemelman[5], D. Rizopoulos[6], J. Kers[3]. [1]Dept. of Infectious diseases, Amsterdam UMC, locatie AMC, Amsterdam. [2]Dept. of Biostatistics, Erasmus University Medical Center, Rotterdam. [3]Dept. of Pathology, Amsterdam UMC, locatie AMC, Amsterdam. [4]Dept. of Public Health, Erasmus University Medical Center, Rotterdam. [5]Dept. of Nephrology, Renal Transplantation Unit, Amsterdam UMC, locatie AMC, Amsterdam. [6]Dept. of Biostatistics, Erasmus University Medical Center, Rotterdam, The Netherlands.

8. Reducing hepatectomy times in all Dutch organ procurement teams (p.106)
K.M. Ooms-de Vries. Nederlandse Transplantatie Stichting, Leiden, The Netherlands.

9. Using a Massive Open Online Course on Clinical Kidney, Prancreas and Islet Transplantion in different settings of transplant education (p.107)
P.G.M. de Jong[1], F. Luk[2]. [1]Dept. of Education, [2]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands.

10. New ways of reporting on Dutch lung transplant waiting list and outcomes (p.108)
E.T.M. Schiks. Nederlandse Transplantatie Stichting, Leiden, Nederland.

Postersessies 3 - Clinical

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

13.00-13.15

Moderator: Matty Terpstra

11. Long term graft function and graft loss following pregnancy in kidney transplant recipients: a systematic review and meta-analysis. (p.109)
A.H. Schellekens[1], M.C. van Buren[2], J. van de Wetering[2], F. van Reekum[3], N.D. Paauw[4], T.K.J. Groenhof[5], A.T. Lely[4]. [1]Dept. of Gynaecology & Obstetrics, St. Antonius Hospital, Nieuwegein. [2]Dept. of Internal Medicine, Nephrology & Kidney transplantation, Erasmus University Medical Center, Rotterdam. [3]Dept. of Nephrology, University Medical Center Utrecht, Utrecht. [4]Dept. of Obstetrics, University Medical Center Utrecht - Wilhelmina Children's Hospital, Utrecht. [5]Dept. of Cardiovascular Epidemiology, Julius Center, Utrecht, The Netherlands.

12. Pancreas donation after euthanasia - a suitable islet source for transplantation? (p.110)
A. Steffen[1], J.B. Doppenberg[1], M.A.J. Hanegraaf[1], D.J.C. Alders[2], V.A.L. Huurman[3], M.A. Engelse[1], E.J.P. de Koning[1]. [1]Dept. of Internal Medicine, [2]Dept. of Anesthesiology, [3]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands.

13. A comparison of the BAR, DRM, DRI, sRRI, ET-DRI, D-MELD and SOFT score to predict outcome after liver transplantation in the SRTR database (p.111)
J.D. de Boer[1], H. Putter[2], J.J. Blok[3], I.P.J. Alwayn[4], B. van Hoek[5], A.E. Braat[4]. [1]Dept. of Transplant Surgery, Eurotransplant, Leiden. [2]Dept. of Medical Statistics, Leiden University Medical Center, Leiden. [3]Dept. of Surgery, Haaglanden Medical Center, Den Haag. [4]Dept. of Transplant Surgery, Leiden University Medical Center, Leiden. [5]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands.

14. Donor hematocrit is an independent predictor for the development of non-anastomotic biliary strictures after donation after circulatory death liver transplantation (p.112)

O.B. van Leeuwen[1], M. van Reeven[2], J.N.M. IJzermans[2], V.E. de Meijer[1], W.G. Polak[2], R.J. Porte[1]. [1]Dept. of Surgery, University Medical Center Groningen, Groningen. [2]Dept. of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands.

15. Post-operative Duplex ultrasound predicts early complications and renal function after kidney transplantation. (p.113)
A. van de Kuit[1], S. Benjamens[1], S.P. Berger[2], J.S.F. Sanders[2], D. Yakar[3], R.A. Pol[1]. [1]Dept. of Transplant Surgery, [2]Dept. of Internal Medicine, [3]Medical Imaging Center, University Medical Center Groningen, The Netherlands.

Postersessies 4 - Clinical

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

12.30-12.45

Moderator: Julia Houtzager

16. Aorto-iliac calcification is a risk factor for inferior patient and graft survival in kidney transplant recipients; a systematic review and meta-analysis (p.114)
A.A. Rijkse, J.L. van Dam, H.J.A.N. Kimenai, J.N.M. IJzermans, R.C. Minnee. Dept. of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands.

17. Parainfluenza infections in lung transplant recipients; from bedside to bench and back (p.115)
A.E.S. de Zwart[1], A. Riezebos-Brilman[2], D. Jochmans[3], H.A.M. Kerstjens[1], J.W.C. Alffenaar[4], J. Neyts[3], E.A.M. Verschuuren[1]. [1]Dept. of Pulmonary Diseases and Tuberculosis, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Medical Microbiology and Virology, University Medical Center Utrecht, Utrecht, The Netherlands. [3]Dept. of Microbiology and Immunology, University of Leuven, Rega Institute, Leuven, Belgium. [4]Dept. of Clinical Pharmacy & Pharmacology, University Medical Center Groningen, Groningen, The Netherlands.

18. Graft failure by rejection in adolescent kidney transplant recipients (p.116)
F.H.M. Vrieling-Prince[1], J.I. Roodnat[2], M.C. Clahsen-van Groningen[3], H. de Jong[1], K. Cransberg[1]. [1]Dept. of Paediatric Nephrology, Erasmus MC - Sophia Children's Hospital, Rotterdam, The Netherlands. [2]Dept. of Nephrology & Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands. [3]Dept. of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands.

19. Clinical outcomes of DCD type V liver transplantation: donation after euthanasia (p.117)
M. van Reeven[1], O.B. van Leeuwen[2], D. van der Helm[3], S. Darwish Murad[4],

J. Blokzijl[5], B. van Hoek[3], I. Alwayn[6], R.J. Porte[2], J.N.M. IJzermans[1], W.G. Polak[1]. [1]Dept. of Surgery, Division of Hepatopancreatobiliary and Transplant Surgery, Erasmus University Medical Center, Rotterdam. [2]Dept. of Surgery, Section of Hepatobiliary Surgery & Liver Transplantation, University Medical Center Groningen, Groningen. [3]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden. [4]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam. [5]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen. [6]Dept. of Surgery, division of Hepatopancreatobiliary and Transplant Surgery, Leiden University Medical Center, Leiden, The Netherlands.

20. Liver donors with metabolic disturbances can extend the donor pool (p.118)
M. van Reeven[1], I. Vasiliauskaite[1], S. Darwish Murad[2], W.G. Polak[1], R.W.F. de Bruin[3], J.N.M. IJzermans[1]. [1]Dept. of Surgery, Division of Hepatopancreatobiliary and Transplant Surgery, [2]Dept. of Gastroenterology and Hepatology, [3]Dept. of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands.

Postersessies 5 - Clinical

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

12.45-13.00

Moderator: Karin Britsemmer

21. Broadly profiling the activation status of circulating immune cells in c-aABMR reveals increased CD38 and CD16 expression on monocytes and NK cells (p.119)
K.A. Sablik, N.H.R. Litjens, M. Klepper, M.G.H. Betjes. Dept. of Internal Medicine, Division of Nephrology and Kidney Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands.

22. Using a cardiac-output guided hemodynamic therapy algorithm reduces intraoperative fluid administration in LDKT with large donor-recipient size mismatch (p.120)
E.A.M. Cornelissen[1], M. Voet[2], A. Nusmeier[3], J. Lemson[3]. [1]Amalia Children's Hospital, Radboud University Medical Center, Nijmegen. [2]Dept. of Ped Anesthesiology, [3]Dept. of

Ped Intensive Care, Radboud University Medical Center, Nijmegen, The Netherlands.

23. Transplanting kidneys from hepatitis C virus positive donors: new possibilities (p.121)
K.M. van Dijk, R.C. van Riet, M.W.F. van den Hoogen. Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands.

24. Timing of ureteric stent removal and occurrence of urological complications after kidney transplantation: A systematic review and meta-analysis (p.122)
I.J. Visser, J.P.T. van der Staaij, J.A. Lafranca, J.M.F. Dor. Imperial College Renal and Transplant Centre, Imperial College NHS Healthcare, London, United Kingdom.

25. Increased number of intragraft FOXP3+ T cells is strongly correlated with decreased graft survival in chronic-active antibody-mediated rejection (p.123)
K.A. Sablik[1], E.S. Jordanova[2], M.C. Clahsen-van Groningen[3], M.G.H. Betjes[1]. [1]Dept. of Internal Medicine, Division of Nephrology and Kidney Transplantation, [2]Dept. of Oncological Gynaecology, [3]Dept. of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands.

Postersessies 6 - Clinical

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

13.00-13.15

Moderator: Jivika Sewraising

26. Management of portal vein anastomotic stenosis after pediatric liver transplantation: evaluation of single center experience (p.124)
H.P.J. van der Doef[1], R.H.J. de Kleine[2], R.P.H. Bokkers[3], R.J. Porte[2], R. Dikkers[3], R.J. de Haas[3], M. Kater[3], F.A.J.A. Bodewes[1]. [1]Dept. of Paediatric Gastroenterology & Hepatology, University Medical Center Groningen, Groningen. [2]Dept. of Hepato-pancreato-biliary Surgery, University Medical Center Groningen, Groningen. [3]Dept. of Radiology, University Medical Center Groningen, Groningen, The Netherlands.

27. A temporary portocaval shunt and initial arterial perfusion in orthotopic liver transplantation (p.125)
L.C. Pietersen[1], E. Sarton[2], I. Alwayn[1], H.D. Lam[3], H. Putter[4], B. van Hoek[5], A.E. Braat[1]. [1]Dept. of Surgery, Leiden University Medical Center, Leiden. [2]Dept. of Anesthesiology, Leiden University Medical Center, Leiden. [3]Dept. of Surgery, Leiden

University Medical Center, Leiden. [4]Dept. of Medical Statistics, Leiden University Medical Center, Leiden. [5]Dept. of Gastroenterology & Hepatology, Leiden University Medical Center, Leiden, The Netherlands.

28. Risk Predictive Strategy to Optimize Pancreas Donor Selection (p.126)
J.W. Mensink[1], K.M. Ooms - de Vries[2], V.A.L. Huurman[1], R.A. Pol[3], I.P.J. Alwayn[1], A.E. Braat[1]. [1]Dept. of Surgery, Division of Transplantation, Leiden University Medical Center, Leiden. [2]Dept. of Quality, Dutch Transplant Foundation, Leiden. [3]Dept. of Surgery, Division of Transplantation, University Medical Center Groningen, Groningen, The Netherlands.

29. Risk Factors for Thrombosis and Bleeding in Pediatric Liver Transplantation in an Era of Routine Postoperative Antithrombotic Therapy (p.127)
M.J.M. Werner[1], R.H.J. de Kleine[1], M.T. de Boer[1], V.E. de Meijer[1], R. Scheenstra[2], H.J. Verkade[3], F.A.J.A. Bodewes[3], S.T.H. Bontemps[4], K.M.E.M. Reyntjens[5], R. Dikkers[6], T. Lisman[7], R.J. Porte[1]. [1]Dept. of Hepatobiliary Surgery and Liver Transplantation, [2]Dept. of Pediatric Gastroenterology and Hepatology, [3]Dept. of Pediatric Gastroenterology and Hepatology, [4]Dept. of Pediatric Intensive Care, [5]Dept. of Anesthesiology, [6]Dept. of Pediatric Radiology, [7]Dept. of Surgery, Section Surgical Research Laboratory, University Medical Center Groningen, Groningen, The Netherlands.

30. Elevated plasma levels of cell-free DNA during orthotopic liver transplantation are associated with activation of coagulation (p.128)
F.A. von Meijenfeldt[1], L.C. Burlage[2], S. Bos[3], J. Adelmeijer[4], R.J. Porte[1], J.A. Lisman[1]. [1]Dept. of Surgery, HPB & Livertransplantation, [2]Dept. of Surgery, [3]Dept. of Internal Medicine, [4]Surgical Researchlab, University Medical Center Groningen, Groningen, The Netherlands.

Parallelsessie XIII — Koningin Máximazaal

Voorzitters: Eddie van Breukelen, scale-up ondernemer
Dr. Jacqueline van der Wetering, nefroloog, Erasmus MC

Thema: Leefstijl sessie

13.15 Blijf in beweging, blijf fit
Adilson da Silva, medisch maatschappelijk werker, Erasmus MC
Mevr. B. Diaby (patiënt)

Donderdag 14 maart 2019

13.40 Benefit for all: de rol van zelfmanagement en een gezonde leefstijl bij chronische nierziektes
Prof. dr. Andrea Evers, hoogleraar gezondheidspsychologie Universiteit Leiden, hoofd afdeling Gezondheids-, Medische en Neuropsychologie.

14.00 Time to ACT!
Prof. dr. Gerjan Navis, internist-nefroloog, UMCG

14.30 Leefstijl geneeskunde, waarom de zorg anders moet.
Prof. dr. Hanno Pijl, internist, LUMC

15.00 Koffiepauze

Parallelsessie XIV — Mauritszaal

Voorzitters: Carla M.M. Schrauwers, verpleegkundig specialist, Amsterdam UMC (VUmc)
Willy T.M. Rensen, transplantatie coördinator, Amsterdam UMC (AMC)

Thema: Dilemma's bij donatie

13.15 Leverdonatie bij leven
Annemarie Roelofs en lever/nierdonor

14.00 Postmortem donoren
Casuïstiekbespreking door Karin Beer, Robert Klaasen, Janneke Vervelde en Laura Bruinenberg.

15.00 Koffiepauze

Parallelsessie XV – Basaal / Klinisch 2 — Tropentheater

Voorzitter: Prof. dr. Luuk Hilbrands, internist-nefroloog, Radboudumc
Michiel Betjes, internist-nefroloog, Erasmus MC

Voordrachten in het Engels, 17 pitches van 2 minuten en presentaties van 6 minuten.

13.15 Recall of living kidney donors for long-term follow-up is worthwhile (p.129)

H.J. Kloke, A. Rasing, P.h.M.M. Dooper, D.B. Pilzecker, C.W. Hooghof, E.M. van Ommen, A.J. Hoitsma. Dept. of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands.

13.17 Ex-vivo normothermic perfusion of a porcine kidney with three different perfusion solutions (p.130)

M.B.F. Pool[1], T.L. Hamelink[2], H.G.D. Leuvenink[2], C. Moers[2]. [1]Surgical Research-lab, BA44, University Medical Center Groningen, Groningen. [2]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands.

13.19 Mucosal associated invariant T cells in patients with recurrent urinary tract infection exhibit an activated and cytotoxic profile (p.131)

M.L. Terpstra[1], J.J. Wever[1], M.J. Sinnige[2], E.B.M. Remmerswaal[2], M.C. van Aalderen[2], S.E. Geerlings[3], F.J. Bemelman[1]. [1]Dept. of Internal Medicine, division of Nephrology, Renal Transplant Unit, [2]Dept. of Experimental Immunology, [3]Dept. of Internal Medicine, division of Infectious Diseases, Amsterdam UMC (loc. AMC), Amsterdam, The Netherlands.

13.21 The effect of preceding respiratory viral infection towards bronchiolitis obliterans syndrome development in lung transplant recipients (p.132)

A. Rasoul. Dept. of Respiratory Medicine, University Medical Center Utrecht, Utrecht, The Netherlands.

13.23 How reliable are HLA antibody detection assays under immunosuppressive regimen? (p.133)

B. Duygu, M.H. van Tuijl, C. van Groesen, L. Wieten, C.E.M. Voorter. Dept. of Transplantation Immunology, Tissue Typing Laboratory, Maastricht University Medical Center, Maastricht, The Netherlands.

13.25 Lower urinary tract dysfunction is still underestimated in pediatric kidney transplants despite underlying cause of renal failure (p.134)

C.M.H.H.T Bootsma-Robroeks[1], L.L. de Wall[2], W. Feitz[2], E.A.M. Cornelissen[1]. [1]Dept. of Pediatrics, [2]Dept. of Urology, Amalia Childrens Hospital, Radboud University Medical Center, Nijmegen, The Netherlands.

13.27 The effects of an IL-21 receptor antagonist on the alloimmune response in a humanized skin transplant mouse model (p.135)

K. de Leur[1], F. Luk[1], T.P.P. van den Bosch[2], M. Dieterich[1], L.J.W. van der Laan[3], R.W. Hendriks[4], M.C. Clahsen-van Groningen[2], F. Issa[5], C.C. Baan[1], M.J. Hoogduijn[1]. [1]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Pathology, Erasmus University Medical

Center, Rotterdam, The Netherlands. [3]Dept. of Surgery, division of HPB and Transplant Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands. [4]Dept. of Pulmonary Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands. [5]Transplantation Research Immunology Group, Nuffield Dept. of Surgical Sciences, Oxford, United Kingdom.

13.29 Predictors of symptomatic lymphocele after kidney transplantation (p.136)

M. Joosten[1], F.C. D'Ancona[2], W.A.G. van der Meijden[3], P.P. Poyck[1]. [1]Dept. of Vascular Surgery, [2]Dept. of Urology, [3]Dept. of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands.

13.31 Whole body CT imaging in post-mortem donor screening (p.137)

J.W. Mensink[1], R.A. Pol[2], W.N. Nijboer[1], J. de Jonge[3], K.M. Ooms - de Vries[4], M.F. van der Jagt[5], M.C.G. van de Poll[6], I.P.J. Alwayn[1], A.E. Braat[1]. [1]Dept. of Surgery, Division of Transplantation, Leiden University Medical Center / Dutch Transplant Foundation, Leiden. [2]Dept. of Surgery, Division of Transplantation, University Medical Center Groningen, Groningen. [3]Dept. of Surgery, Division of Transplantation, Erasmus Medical Center, Rotterdam. [4]Quality, Dutch Transplant Foundation, Leiden. [5]Dept. of Surgery, Division of Vascular and Transplant Surgery, Radboud University Medical Center, Nijmegen. [6]Dept. of Surgery and Dept. of Intensive Care Medicine, Maastricht University Medical Center, Maastricht, The Netherlands.

13.33 Post-transplant obesity is associated with poor long-term survival after liver transplantation (p.138)

J. van Son[1], S.P. Stam[2], A.W. Gomes Neto[2], J. Blokzijl[3], A.P. van den Berg[3], R.J. Porte[1], S.J.L. Bakker[2], V.E. de Meijer[1]. [1]Dept. of Surgery, [2]Dept. of Nephrology, [3]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands.

13.35 The inhibitory effect of tacrolimus and sirolimus on the differentiation of T cells into follicular helper-like T cells (p.139)

R. Kraaijeveld[1], Y. Li[2], L. Yan[2], K. de Leur[1], M. Dieterich[1], A.M.A. Peeters[1], L. Wang[3], Y. Shi[4], C.C. Baan[1]. [1]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands. [2]Dept. of Lab. Medicine, West China Hospital, Chengdu, China. [3]Dept. of Lab. Medicine, Sichuan University, Chengdu, China, [4]Dept. of Nephrology, Sichuan University, Chengdu, China.

13.37 Exploring TTV as a potential biomarker of infection in renal transplant recipients (p.140)

A.L. van Rijn[1], H.F. Wunderink[2], C.S. de Brouwer[1], J.I. Rotmans[3], M.C.W. Feltkamp[1]. [1]Dept. of Medical Microbiology, Leiden University Medical Center, Leiden. [2]Dept. of Medical Microbiology, University Medical Center Utrecht, Utrecht. [3]Dept. of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands.

13.39 Islet allo-autotransplantation: allogeneic pancreas transplantation followed by transplant pancreatectomy and islet transplantation (p.141)
M.F. Nijhoff, Dept. of Nephrology, Leiden University Medical Center, Leiden, The Netherlands.

13.41 Multiple non-HLA antibodies are significantly increased in chronic-active antibody-mediated rejection (p.142)
K.A. Sablik[1], E.G. Kamburova[2], D.L. Roelen[3], H.G. Otten[2], M.G.H. Betjes[1]. [1]Dept. of Internal Medicine, division Nephrology and Transplantation, Erasmus University Medical Center, Rotterdam. [2]Laboratory of Translational Immunology, Radboud University Medical Center, Nijmegen. [3]Dept. of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands.

13.43 Outcome after transplantation of liver grafts from diabetic donors: a national multicenter study (p.143)
I.M.A. Brüggenwirth[1], M. van Reeven[2], I. Vasiliauskaite[2], B. van Hoek[3], A.E. Braat[4], A.P. van Den Berg[5], H.J. Metselaar[6], W.G. Polak[2], R.J. Porte[1]. [1]Dept. of Surgery, University Medical Center Groningen, Groningen. [2]Dept. of Surgery, Erasmus University Medical Center, Rotterdam. [3]Dept. of Gastroenterology and Hepatologie, Leiden University Medical Center, Leiden. [4]Dept. of Surgery, Leiden University Medical Center, Leiden. [5]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen. [6]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands.

13.45 Altruistic liver donation in the Netherlands (p.144)
M.T. de Boer[1], C.I. Buis[1], A.M. Roelofs[2], A.P. van den Berg[2]. [1]Dept. of HPB Surgery and Liver Transplantation, [2]Dept. of Hepatology, University Medical Center Groningen, Groningen, The Netherlands.

13.47 Cost-effectiveness of a home-based educational programme on renal replacement therapies: A proof-of-principle study (p.145)
S. Redeker[1], M. Oppe[2], J.J. van Busschbach[1], W. Weimar[3], E.K. Massey[3], S.Y. Ismail[1]. [1]Dept. of Medical Psychology and Psychotherapy, Erasmus University Medical Center, Rotterdam. [2]Quality of Life, EuroQoL, Rotterdam, [3]Dept. of

Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands.

13.59 8 beste pitches (5 minuten spreektijd en 1 minuut discussietijd)

15.00 Theepauze

Sessie XVI – Plenair — Koningin Máximazaal

Voorzitters: *Prof. dr. Frederike J. Bemelman, voorzitter LOC, nefroloog, Amsterdam UMC (AMC)*
Prof. dr. Marlies E.J. Reinders, voorzitter NTV, internist-nefroloog, LUMC

15.30 Briljante mislukkingen
Paul Iske, hoogleraar Open Innovation & Business Venturing aan de School of Business and Economics van de Universiteit Maastricht.

16.15 LWTV prijs uitreiking winnaar 2019
Marjo van Helden, voorzitter LWTV

Lezing door prijswinnaar 2018: Marion J.C. Wessels en Francis Hollander, UMCU

16.25 Uitreiking Distinguished Research Award 2019
Prof. dr. Marlies E.J. Reinders, voorzitter NTV

16.30 Gauke Kootstraprijs 2019
Uitreiking door Prof. dr. Gauke Kootstra, naamgever van de prijs

Lezing prijswinnaar Gauke Kootstraprijs 2019

16.45 Sluiting congres

Mucosal Associated Invariant T-cells in renal transplant recipients before- and 12 months after transplantation

M.L. Terpstra[1], M.J. Sinnige[2], M.C. van Aalderen[2], E.B.M. Remmerswaal[2], J. Kers[3], S.E. Geerlings[4], F.J. Bemelman[5]. [1]Dept. of Internal Medicine, division of Nephrology, Renal Transplant Unit, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, [2]Dept. of Experimental Immunology, Amsterdam UMC (loc. AMC), Amsterdam, [3]Dept. of Pathology, Amsterdam Infection & Immunity Institute (AI&II), [4]Dept. of Internal Medicine, division of Infectious Diseases, [5]Dept. of Internal Medicine, division of Nephrology, Renal Transplant Unit, The Netherlands.

Background: Mucosal Associated Invariant T (MAIT) cells are innate-like T-cells involved in the antibacterial response by recognizing riboflavin metabolites produced by these organisms and comprise ~ 10% of the T-cell population in human blood. Bacterial infections are common in renal transplant recipients and MAIT cell functions may be impaired in patients with renal disease. Currently, it is unclear how MAIT cell numbers, phenotype and functions evolve after renal transplantation.

Methods: We used a fluorescently-labelled MR1-tetramer in conjunction with 14-color flowcytometry to identify and characterize MAIT cells in blood from renal transplant recipients obtained pre-transplantation and 12 months post transplantation (n=21) and in healthy controls (n=21).

Results: There was no difference in the absolute number of MAIT cells between the renal transplant recipients (both pre- and post-transplantation) and the controls. Within the MAIT cell population, the amount of $CD4^-CD8^+$ cells was lower in both the pre- and post-transplantation samples compared to the controls (respectively 70.9%, 73.2% vs. 79.1% $p<0.05$). However, there was no significant increase in the proportion of $CD4^-CD8^-$, $CD4^+CD8^-$ or $CD4^+CD8^+$ MAIT cells, neither was there a difference between the pre- and post-transplantation samples. The mean percentage of MAIT cells expressing CD161, a marker that was previously used to identify MAIT cells, was respectively 88.7%, 94.1% and 92.7% ($p>0.05$). Thus, without using the MR1 tetramer, about 10% of the MAIT cell population will be missed. Interestingly, $CD161^-$ MAIT cells differed from $CD161^+$ MAIT cells. Among the $CD161^-$ MAIT cell population, the percentage of cells expressing Tbet, Eomes, Helios (transcription factors) and perforin (cytotoxic potential) was significantly lower, whilst a significant higher percentage of cells expressed Ki67 (proliferation marker) and granzyme B (cytotoxic potential) when compared to $CD161^+$ MAIT cells. These differences were observed in each patient group. Furthermore, MAIT cells differed in both pre- and post-transplant samples when compared to the controls with regard to the chemokine receptors CXCR4 and CXCR3, with a higher percentage of MAIT cells expressing CXCR4 (respectively 26.3%, 22.1% vs. 9.5%, $p<0.05$), and a lower expression of CXCR3 (36.9%, 32.0% vs. 50.0% $p<0.05$). This suggests a different homing potential for these cells in renal transplant recipients. There was no difference between the pre- and post-transplantation samples.

Conclusions: In contrast to prior reports, MAIT cell numbers are not decreased in the circulation of renal transplant recipients before- and one year after transplantation. About 10 percent of the MAIT cell population appears to be $CD161^-$ and this $CD161^-$ MAIT cell populations displays distinct features. MAIT cells in renal transplant recipient both pre- and post- transplantation express a different homing profile. Further research is warranted to determine what the cause and consequence is of this altered expression of chemokine receptors.

Natural killer cells express significantly more CD16 during chronic-active antibody mediated rejection which is not caused by a single nucleotide polymorphism within the CD16 gene

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Background: Chronic-active antibody mediated rejection (c-aABMR) is the leading cause of long-term renal allograft loss. Fc-receptor CD16 bearing natural killer (NK) cells may be involved in mediating renal endothelial cell damage in c-aABMR. A single nucleotide polymorphism within CD16 gene, i.e. the GG- but not the GT- or TT-genotype, is associated with increased CD16 expression and function of NK cells. The GG-genotype could therefore be a risk factor for developing c-aABMR. This study investigated NK cells and their CD16 expression in cases of c-aABMR.

Methods: Cases of c-aABMR in renal allografts (N=148) and controls (N=137, kidney transplant recipients without c-aABMR) were genotyped for the G or T allele of the CD16 gene. Frequencies of circulating NK cells and their expression of CD16 were measured in 25 cases of c-aABMR and compared to matched controls of kidney transplant recipients. Furthermore, the presence of NK cells in renal biopsies of 20 c-aABMR cases ($CD3^-CD57^+$ cells) was studied.

Results: The allelic distribution of the GG, GT and TT-genotype within CD16 was respectively, 16%, 41% and 43% for c-aABMR cases and 13%, 39% and 48% for controls (p=0.73).

Individuals with TT had the lowest expression of CD16 on their circulating NK cells (median MFI 3.7 $x10^4$) compared to GT (median MFI 6.3 $x10^4$) and GG (median MFI 5.8 $x10^4$), (p=0.01). In addition, the % of $CD16^+$ NK cells was lowest in the TT group (median 80% vs 93% and 87%, p=0.02).

However, independent of T/G genotype, cases with c-aABMR showed a significantly higher expression of CD16 on their circulating NK compared to the matched controls (p=0.01). Frequencies of NK cells were similar between both groups.

NK cells in renal biopsies of c-aABMR cases were absent in glomeruli in 40% of the cases and present at low numbers in the remaining 60% of cases. NK cells were observed in the interstitium but at low numbers (<5% of infiltrating cells).

Conclusions: Cases of c-aABMR have a significant higher expression of CD16 on circulating NK cells which cannot be explained by a difference in allelic distribution pattern for the T/G variants within the CD16 gene. NK cells are rarely found in kidney biopsies of c- aABMR patients suggesting that an ephemeral interaction between NK cells and renal endothelial cells may explain the increased CD16 expression.

Characterization of the immunogenicity of ipsc-derived kidney organoids

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Background: There is an increasing interest in iPSC-based therapies for kidney regeneration. Recently protocols for the *in vitro* generation of kidney organoids have been developed. For successful implementation into clinical practice, immunological acceptance of the iPSC-derived cells is crucial. Therefore, our aim was to study the immunogenicity of iPSC-derived kidney organoids.
Methods: Three human iPSC lines were grown on Geltrex and treated with CHIR99201 and fibroblast growth factor 9.
Results: The resulting organoids showed a 10- to 40-fold increase in mRNA for kidney-specific markers after 25 days of differentiation. Immunostaining confirmed that organoids contained essential renal structures. The kidney organoids were cultured together with peripheral blood mononuclear cells from two healthy donors for 7 days. Subsequently, a >100-fold increase in the mRNA expression of the leukocyte marker CD45 was observed in the organoids. Immunostaining confirmed the presence of infiltrating CD45+ cells in the organoids. The response appeared to be T-cell mediated as there was a 10-fold mRNA increase in CD4 and CD8, while macrophage marker CD68 was also highly expressed. At the protein level, T-cells predominantly clustered around glomerular structures while macrophages were diffusely distributed throughout the organoid. A mixed pattern of macrophages could be observed, as both pro-inflammatory (M1) and anti-inflammatory (M2) macrophage markers were substantially increased at the mRNA level. Even though a 10-fold mRNA increase of inflammatory factors such as TNFα and Granzyme B was suggestive of a pro-inflammatory response, immunofluorescence showed that the infiltrating cells did not proliferate as observed by the absence of Ki-67+CD45+ cells. The mRNA expression of kidney differentiation markers remained stable throughout the co-culture. Yet, immunohistochemistry revealed that the expression of WT1, a podocyte marker, was decreased 4-fold in comparison to control organoids, indicating that specifically podocytes may be a target of the immune response.
Conclusions: Although further characterization of the immune response to kidney organoids and its influence on differentiation is required, these preliminary results offer novel insights into the *in vitro* interaction of immune cells with iPSC-derived kidney organoids.

Near-infrared fluorescence imaging with ZW800-1 dye to assess donor kidneys while on ex-vivo normothermic machine perfusion

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Background: At present, more older and higher risk donor kidneys are accepted resulting in increased uncertainty about quality. This may result in unjustified discard of donor organs. To increase organ utilisation without compromising outcomes, assessment of real-time perfusion using near-infrared fluorescence (NIRF) imaging prior to transplantation may assist in the decision making. ZW800-1 is a clinical applied non-toxic NIRF dye, which is rapidly and efficiently cleared by the kidney, thus allowing immediate functional testing. Its ability to visualise (cortical) kidney perfusion may be more reliable than the experienced *surgical eye*. In this pilot, we studied the feasibility of NIRF imaging as a technique to measure perfusion and kidney function during normothermic machine perfusion (NMP).

Methods: Slaughterhouse pig kidneys were flushed, underwent 2h hypothermic machine perfusion, and were placed on NMP at 37°C for 7h with oxygenated, leukocyte-depleted autologous whole blood. Dose-escalation experiments (0.125;0.25; 1.0;4.0mg/kg per kidney weight) were conducted to obtain robust and reproducible images. Boluses of ZW800-1 were injected intravenously after 1h and 6h of NMP. Following ZW800-1 injection fluorescent images of kidneys were quantified as signal-to-background ratios (SBRs) using the FLARE imaging system. Urine and perfusate samples were collected to measure ZW800-1 concentration and calculate excretion as a reflection of kidney function.

Results: A series of dosage experiments showed that 1.0 mg/kg of the compound was optimal, allowing reliable assessment of perfusion with a clear differentiation between well perfused and marginally perfused kidneys or areas of the kidneys. The average SBR (n=5) in the 1.0 mg/kg group decreased from 3.42±1.09 to 2.28±0.73, corresponding with a ZW800-1 concentration in the perfusate decreasing from 100±51 µg/ml up to 6.4±36.5 µg/ml, whilst increasing in the urine up to 8.7±14.4 µg/ml throughout the perfusion. The clearance of dye per kidney (median 17%±24%) was directly associated with diminished fluorescence intensity. In kidneys without any urine production, the SBR remained the same.

Conclusions: This pilot study shows that NIRF imaging is feasible during NMP. By assessing the fluorescent intensity of different areas of the kidney and the urine dye excretion, the application of NIRF imaging could provide clinically relevant information concerning perfusion and function, potentially helping the clinical decision in accepting a high risk donor kidney.

Recombinant human monoclonal HLA antibodies of different IgG subclasses with the same epitope specificity: excellent tools to study the differential effect of donor specific antibodies in transplantation.

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Background: The humoral immune response against mismatched HLA antigens in renal transplantation is associated with inferior graft survival, but only in a subpopulation of patients. The various clinical effects may be caused by different IgG subclasses of donor-specific HLA antibodies. IgG subclass antibodies have been associated with either complement dependent or independent graft damage. The mechanism of action of IgG subclass antibodies can be studied in experimental systems using HLA monoclonal antibodies (mAbs). Since currently available human HLA-specific mAbs are mainly of the IgG1 subclass, our aim was to generate human HLA class I and II mAbs of all four IgG subclasses.
Methods: Recombinant HLA class I and II-specific mAbs were generated from established human B cell hybridomas by cloning genes encoding the antibody variable domains into vectors. The antibodies were expressed by transient co-transfection of heavy and light chain vectors and purified using protein G column. IgG subclass cloning was confirmed with modified luminex screening assay using detection antibodies specific for each IgG subclass. Antibody specificity was determined by luminex single antigen bead (SAB) technology, affinity by bio-layer interferometry, and the effector functions were determined by complement dependent cytotoxicity (CDC), as well as antibody dependent cellular cytotoxicity (ADCC) assays.
Results: The IgG subclass cloning was verified with the modified luminex screening. Screening of the recombinant mAbs with luminex SAB assays showed that all four IgG subclasses have identical HLA specificities. Importantly, the four IgG subclasses have similar binding affinity for the immunizing HLA allele. Next, the four IgG subclass mAbs were tested with CDC and cell lysis of target cells was only observed for IgG1 and IgG3 mAbs in a dose-dependent manner. Thus, both IgG1 and IgG3 mAbs are highly cytotoxic and the most cell lysis was observed for IgG1 mAbs. No cytotoxicity was observed for IgG2 and IgG4 mAbs. In addition, both IgG1 and IgG3 mAbs can trigger effector cells to lyse target cells in ADCC. As expected, IgG2 and IgG4 mAbs did not induced specific cell lysis.
Conclusions: It is feasible to generate human HLA class I and II IgG subclass mAbs recognizing the same HLA epitope with the same affinity and with the appropriate functional properties. These mAbs can be used to understand the mechanism of HLA IgG subclass antibodies in renal transplantation and other clinical settings.

Tolerance-associated circulating T-cells in immunologically tolerant liver transplant recipients

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Background: Treatment with immunosuppressive drugs (IS) in liver transplant (LTx) recipients is accompanied by side effects. Some recipients have been withdrawn from IS late after LTx and are immunologically tolerant (TOL) towards their graft. If these TOL LTx recipients are recognized earlier after LTx and withdrawn from IS, side effects may be reversed or avoided. Studies have used circulating T-cells to identify TOL LTx recipients, e.g. Vδ1/Vδ2 γδT-cell ratios and FoxP3+CD25+ T-cells characterizing regulatory T-cells (Tregs). However, the biomarker potential of these markers is limited. Moreover, cytomegalovirus (CMV) influences circulating T-cells. In this study, by matching the study groups for CMV, we characterized circulating T-cells.

Methods: TOL LTx recipients (n=11) withdrawn from IS for on average 4.2 years, and a control group on regular IS regimen (CTRL; n=12) matched for time after LTx (on average 15.2 years), primary disease, age, gender and CMV serostatus were included. In addition, healthy controls (HC; n=12) matched for age, gender and CMV serostatus were included. Circulating T-cells were characterized by flow cytometry. Activated Tregs (aTregs), resting Tregs (rTregs) and activated T-helper (aTh) were characterized by FoxP3 and CD45RA expression. Stimulatory molecule ICOS and inhibitory molecule CTLA4 were assessed.

Results: Vδ1 and Vδ2 γδT-cells and Vδ1/Vδ2 ratios did not differ between TOL and CTRL. In TOL FoxP3+CD25+ T-cells were significantly higher compared to CTRL ($p=0.02$) and HC ($p=0.03$). However, aTregs and rTregs did not differ between groups, whereas aTh was significantly higher in TOL compared to HC ($p=0.02$) and a higher trend was present compared to CTRL ($p=0.07$). ICOS expression on CD4 T-cells was significantly higher in TOL compared to CTRL ($p=0.04$) and HC ($p=0.02$). FoxP3+CTLA4+ T-cells were significantly higher in TOL compared to CTRL ($p=0.01$), but TOL did not differ with HC.

Conclusions: The Vδ1/Vδ2 γδ T-cell ratio could not discriminate TOL from CTRL, most probably because of the matched CMV serostatus. This shows that the Vδ1/Vδ2 γδ T-cell ratio is not influenced by the state of tolerance. Furthermore, our data indicates that FoxP3+CD25+ T-cells discriminate TOL from CTRL, but the higher number of FoxP3+CD25+ T-cells in TOL LTx recipients could possibly reflect a higher number of aTh and not Tregs. Higher expression of CTLA4 in the FoxP3+ T-cell compartment and expression of ICOS could indicate a more enhanced inhibitory immune response in TOL compared to CTRL.

Delivery of mesenchymal stromal cell therapy via renal intra-arterial infusion

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Background: Mesenchymal stromal cell (MSC) therapy has been proposed to treat kidney disease due to their immunoregulatory and regenerative capacities. Intravenous MSC infusion has been associated with off-target engraftment and intra-arterial (IA) delivery could offer a more targeted therapy. Limited knowledge is available regarding the fate and state of MSC after IA infusion. Therefore, we have studied the efficacy of this delivery route.
Methods: MSC were isolated from adipose tissue or male pigs. A female porcine unilateral kidney ischemia-reperfusion model was infused with 10 million fluorescently labeled MSC via the renal artery.
Analysis of blood and or dissociated kidney tissue biopsies by flow cytometry allowed MSC detection. Confocal microscopy analysis of kidney biopsies allowed to identify structures where MSC are retained.
Y-chromosome PCR allowed identification or MSC 2 weeks after infusion.
To elucidate an active or passive mechanism for MSC retention, metabolically inactive MSC were infused and retention was analyzed.
Results: After infusion, low numbers or MSC left the kidney through the renal vein. No MSC were seen in systemic arterial blood. MSC were found in kidney tissue, predominantly in the renal cortex with 80% of MSC alive. Also, MSC were detected in kidney tissue using confocal microcopy 8h after infusion.
Heat-inactivated MSC (HI-MSC) were found in MSC. *In vitro,*regular MSC but not HI-MSC exhibited adherent capacities, suggesting retention was a passive process in the kidney.
Survival after 2 weeks was analyzed by Y chromosome PCR. A reduced but significant percentage of MSC was still detected in kidney tissue, while HI-MSC derived DNA was undetectable.
Conclusions: Summarizing, delivery of MSC therapy through the renal artery is feasible and effective. MSC stay in kidney tissue for 8h with a high survival rate. After 2 weeks, MSC are still found in kidney tissue. Our results suggest that MSC are retained in the kidney through a passive process but the specific interactions remain unclear and require further investigation.

Complement C4 is an important mediator of brain-death induced lung injury

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Background: The process of brain death (BD) in multi-organ donors causes hemodynamic and hormonal dysregulation, leading to pulmonary inflammation. As a result, the quality of the lung graft is deteriorated and only 30% of potential donor lungs are suitable for transplantation. The complement system is known to play an important role in the BD-induced inflammatory response. Therapeutically targeting the complement system in donor grafts seems to be a promising method to improve donor organ quality and thereby graft survival. To do so, the specific role of complement molecules activated in brain-dead donor lungs needs to be elucidated. Our study was designed to identify which complement pathway(s) are involved in BD-induced lung injury.
Methods: In order to dissect contribution of the different complement components in BD-induced inflammation, wildtype (WT) mice were compared to complement deficient mice. The central complement component was studied in C3-/- mice, the classical and lectin pathway in C4-/- mice and the alternative pathway in factor Properdin-/- (P) mice. BD was induced by inflating a Fogarthy catheter in the epidural space, sustained for 3 hours under continuous blood pressure monitoring. Lungs were ventilated with a frequency of 190/min, tidal volume of 225 µl and a PEEP of 1 cmH_2O. Immunohistochemistry was performed to assess lung morphology, neutrophil infiltration and membrane-attack complex deposition as depicted by C9 staining. Gene expression for pro-inflammatory cytokines were measured by qPCR.
Results: Compared to WT mice, absence of C3 prevented C9 deposition, improved lung morphology, decreased neutrophil influx and significantly downregulated pro-inflammatory cytokines and chemokines. Those results suggest a promising role for central complement component blockade in lung grafts derived from brain-dead donors. Regarding the activation pathways, C4 seems mainly involved in BD-related lung injury. Lung morphology, neutrophil influx and pro-inflammatory gene expression levels were ameliorated in C4-/- compared to WT mice, and C9 deposition was diminished to a level comparable to sham-operated mice. P-/- mice showed improved morphology and decreased gene expressions, yet neutrophil influx and C9 deposition were not affected.
Conclusions: Those results suggest primary involvement of the classical/lectin complement pathway in the BD-induced pulmonary immune response, providing insight for future targeted complement blockade in potential donor lungs.

Ex vivo magnetic resonance imaging during normothermic machine perfusion - developing a novel non-invasive tool to assess donor kidney quality

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Background: Pre-transplant prognostic models and diagnostic tools that are currently available for deceased donor kidneys have insufficient independent predictive value to be used in decisions on organ acceptance or discard. As a result, such decisions always have an element of subjectivity. Normothermic machine perfusion (NMP) of renal grafts at 37°C provides an ideal platform for isolated organ imaging prior to transplantation. In recent years, novel magnetic resonance imaging (MRI) sequences have been developed, which can quantify important determinants of allograft quality, such as endothelial integrity, mitochondrial function and tissue stiffness. These parameters are likely to correlate with outcome after transplantation. The overall aim of this project is to provide evidence for the predictive value of ex vivo non-invasive MRI assessment of kidney grafts during normothermic machine perfusion. First, we performed a series of pilot experiments to test feasibility of this approach.
Methods: Five porcine slaughterhouse kidneys were used to optimize the setup and test several sequences for their relevance. NMP was performed with autologous red blood cells in Williams' Medium E with the addition of creatinine, bovine serum albumin and amoxicillin with clavulanic acid. Segmental ischemia/reperfusion injury was induced by inflating and deflating a balloon catheter in one of the main branches of the renal artery. Imaging sequences were performed during different stages of the perfusion. Blood and urine samples were obtained, as well as histological samples at the end of the perfusion.
Results: A stable and reliable NMP setup for isolated kidneys inside a clinical MRI scanner was obtained. Pilot perfusions were mainly performed to develop and optimize the NMP setup. Experience was gained in developing a smooth logistical procedure and technical aspects of MRI sequences applicable to an ex vivo perfused kidney.
Conclusions: This pilot study showed that it is logistically and technically feasible to combine the promising (pre-transplant) evaluation of normothermic machine perfusion with ex vivo magnetic resonance imaging. Several important aspects of allograft quality could be imaged. After finalizing the optimization phase with porcine grafts, human discarded kidneys will be evaluated for allograft quality. Ultimately, we aim to image human donor kidneys that have been accepted for transplantation and correlate outcomes with ex vivo MRI data to develop an unique pre-transplant organ assessment tool.

The effect of ischemia on protein degradation during renal transplantation

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Background: Degradation mechanisms underlying transplant related renal ischemia are still not fully understood, and the proteolytic events causing this protein degradation are still undefined. Proteomic profiling with the use of mass spectrometry has been widely adapted in medical research, including the field of transplantation. *N-terminal amine isotopic labelling of substrates*(TAILS) is a specialized technique that is used for protease substrate discovery and N-terminome analysis. To date, this method has only scarcely been used for clinical research. The main objectives of this study were to test and optimize a TAILS to gain insights in the degradation mechanisms during warm ischemia and static cold storage.
Methods: We used a TMT-TAILS based workflow to characterize the N-terminome during different periods of warm ischemia time (WIT) and cold ischemia time (CIT) of human kidneys.
Results: 1218 peptides and 691 proteins were identified as the WIT N-terminome, and 2511 peptides and 1649 proteins were identified as the CIT N-terminome.We found 29 proteins that were significantly up or downregulated during medium and long warm ischemia compared to short warm ischemia. 19 of these proteins are located in extracellular regions, and 5 of these proteins play a role in the PI3K-Akt signalling pathway.Moreover, our results show that proteins of the extracellular matrix are significantly degraded during warm ischemia. Based on both our findings, and previous findings, these proteins are mostly degraded by proteases that are known for the degradation and remodeling of the extracellular matrix, namely matrix metalloproteinase (MMP) 2 and 9. Nonetheless, we identified that many proteins involved in oxidative phosphorylation, reduction of H_20_2, and many cytoskeletal proteins are degraded during warm and cold ischemia. We also identified cleavage of calpain activity and degradation of its activator calpastatin.
Conclusions: Taken all together, these identified degradation mechanisms and proteolytic events could play an important role in the loss of kidney function caused by ischemia.Thereby offering pharmacological intervention strategies to modulate proteolytic pathways to attenuate proteolytic tissue degradation during renal ischemia, storage and preservation.

Effect of normothermic machine perfusion conditions on mesenchymal stromal cells

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Background: *Ex-situ*normothermic machine perfusion (NMP) may allow better assessment of kidney quality and targeted damage to organs prior to transplantation. Mesenchymal stromal cells (MSC) have bone shown to stimulate kidney repair. Therefore, the combination of NMP and MSC therapy offers potential. NMP conditions concern the infusion of thawed cryopreserved MSC, the fact that they are delivered in suspension and the biochemical composition of the perfusion fluid itself. In this study the effect of NMP on survival, metabolism and function of human (h) MSC and porcine (p) MSC was studied*in vitro*.The effect of NMP on MSCs immediately after culture was compared to frozen-thawed batches or MSCs, the latter being preferred for most clinical applications for practical reasons.
Methods: In this study, the effect of NMP conditions on survival, metabolism and function of human (h) MSC and porcine (p) MSC was studied *in vitro* by flow cytometry.The capacity of MSC to adhere to endothelial cells was tested in a bespoke NMP solution and the effect of NMP conditions on MSCs immediately after culture was compared to frozen-thawed batches or MSCs, the latter being preferred for most clinical applications for practical reasons.
Results: pMSC were found to be very sensitive when compared to hMSC, 40 and 70% respectively. When MSCs were able to survive, survival of the cells was not affected. The perfusion fluid did not affect survival of fresh MSC in suspension compared to the control culture medium. However, the freeze-thawing process is impaired the survival of hMSC; 95% survival of fresh hMSC compared to 70% survival of thawed hMSC. Furthermore, thawed MSC shows increased levels of reactive oxygen species, which indicates elevated levels of oxidative stress, and reduced mitochondrial activity, which implies reduced metabolism. The adherence of human and MSC to endothelial cells (EC) was reduced after the thawing process, an effect that was boosted in the perfusion fluid.
Conclusions: To summarize, we observed that conditions required for machine perfusion are influencing the behavior of MSC. The freeze-thawing process reduces immediate survival and metabolism and increases oxidative stress, whilst their ability to adhere to endothelial cells was diminished. In addition, we found that our hMSC and pMSC behaved differently, which has to be considered before translating results from animal experiments to clinical studies.

Factors influencing access to kidney transplantation (FIAT): a protocol of a qualitative study on stakeholders' perspectives

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Background: Approximately 60% of the kidney patients on dialysis are not waitlisted for transplantation. An unknown part of them might be as well eligible for kidney transplantation but has never been assessed for it. Moreover, increasing disparities in access to kidney transplantation are discussed in literature, like for older patients and patients with a migration background. The present qualitative study aims to explore the factors influencing access to kidney transplantation in the Dutch setting. Based on these factors, targets for potential policy changes will be identified in order to improve access to transplantation in the Netherlands.
Methods: Factors on different levels will be investigated by analyzing interviews held with various stakeholders involved in access to transplantation, namely, patients, dialysis nurses, social workers, nephrologists, health insurers and policy makers. These stakeholders will be approached for focus group or individual interviews nationwide in different settings (e.g. transplant centers, general hospitals, conferences, governmental agencies, community centers). The interviews will be audio-recorded and transcribed verbatim. This qualitative data will be analyzed according the principles of Grounded Theory.
Results: Participants will be interviewed in three phases about their beliefs, opinions and attitudes on access to kidney transplantation. The topic list contains the domains clinical, psychological, ethical, social, economic and policy. In a first phase, stakeholders' perspectives will be explored through individual in-depth or focus group interviews. In a second phase of focus group interviews, stakeholders will be confronted with the outcomes of phase one from the different stakeholder groups in order to create an integrated model of contributing factors. Finally, in the third phase, stakeholders will be invited to focus group discussions about possible solutions for improving access to transplantation based on the results of phase two.
Conclusions: Multi-level factors influencing access to kidney transplantation will be investigated systematically in the Dutch transplant setting by exploring different perspectives of multiple stakeholders, including those perspectives who have rarely been represented in literature (health insurers and policy makers). The final goal is to present a report with national policy recommendations pointing towards a more optimal access to kidney transplantation in The Netherlands.

Donor postoperative outcome and quality of life after living donor liver transplantation

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Background: Living donor liver transplantation (LDLT) is a life-saving procedure for pediatric patients with end stage liver disease. However, living donors are put at risk and studies on the long-term complications and health related quality of life (HRQoL) for living donors after left lateral sectionectomy (LLS) are limited. In this study we aim to describe the postoperative complications, to compare the HRQoL of LDLT donors with the general population and with living donor kidney transplantation (LDKT) donors.
Methods: 45 LDLT donors were included. Complications were prospectively documented in a database. Comprehensive Complication Index (CCI) was calculated. A questionnaire consisting of RAND-36, PGWBI and Carolina's Comfort Scale (CCS) was sent to the donors. Results were compared to the general population and LDKT donors.
Results: Common problems after LDLT were excessive postoperative pain (20.0%) and cardiopulmonary complications (15.6%), although grade 3 complications according to Clavien Dindo were seldom seen (n=2, 5.4%). Median CCI was 0 (IQR 0-12.2). Response rate to the questionnaire was 44%. On the RAND-36, LDLT donors scored higher on physical functioning than LDKT donors ($P< 0.001$) and higher than general population ($P = 0.012$). On social functioning LDLT donors scored lower than the general population ($P = 0.046$). On role limitations emotional problems ($P = 0.004$), mental health ($P = 0.008$) and vitality ($P = 0.032$) LDLT donors scored lower than LDKT donors. On the PGWBI, no significant differences were found. On the CCS, LDLT donors had more movement limitations when coughing or deep breathing ($P = 0.041$) than LDKT donors.
Conclusions: Major complications are rare after LLS liver donation. Although physically the LDLT procedure does not seem to impair HRQoL, negative effects were seen on psychological domains. Furthermore liver donors showed more movement limitations after surgery when compared to kidney donors, which can probably be explained by the extent of the operation. Future studies after the implementation of our long-term HRQoL program in LDLT and LDKT donors are required to make reliable comparisons between groups possible.

Human kidneys contain tissue-resident Mucosal Associated Invariant T-cells

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Background: Mucosal associated invariant T (MAIT) cells are innate-like T-cells involved in the antibacterial response by recognizing bacterial riboflavin metabolites. They are present in human blood but are particularly abundant in the liver, lungs and intestines. Currently it is unclear whether MAIT cells are present in human kidneys.
Methods: We used a fluorescently-labelled MR1-tetramer in conjunction with 14-color flowcytometry to identify and characterize MAIT cells in normal renal tissue (n=5), in renal allografts explanted after allograft failure (n=13) and in peripheral blood mononuclear cells (PBMCs) from healthy donors (n=21). We performed an additional analysis of the allografts that clinically failed due to recurrent urinary tract infections (RUTI) (n=5).
Results: MAIT cells were present in each of the measured renal samples. Both the absolute T-cell counts and the MAIT cell counts were significantly higher in the explanted allografts than in the normal kidneys ($p<0.0001$ and $p=0.004$, respectively). MAIT cells comprised an equal share of the total T-cell population, as defined by live CD3+ events, in the normal kidneys compared to the renal allografts and also the PBMCs, median 0.77 % (range 0.2-1.7), vs 0.20 % (0.01-9.7) and 0.38% (0.07-4.8), respectively. MAIT cell counts in the normal kidneys were too low to perform a phenotypic characterization. The renal allografts comprised a mainly $CD4^{-}CD8^{+}$ MAIT cell population that encompassed a substantial $CD69^{+}$ and $CD69^{+}/CD103^{+}$ 'tissue-resident' subset. MAIT cells in the allografts less often expressed CD161 and displayed a different phenotype consisting of an increased expression of T-bet and granzyme B and a lower expression frequency of CD27 and IL-7Rα than circulatory MAIT cells. Further analyses of MAIT cells in allografts that failed due to RUTI, revealed that these MAIT cells displayed a less cytotoxic phenotype.
Conclusions: MAIT cells are present in human kidneys and comprise a $CD69^{+}CD103^{+}$ tissue-resident population. MAIT cells in renal allografts display a distinct effector profile. Remarkably, in allografts that failed due to RUTI, MAIT cells display a less cytotoxic profile than in allografts that failed for other reasons.

Hypothermic oxygenated machine perfusion enables 24-hour ex situ preservation of porcine donation after circulatory death livers

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Background: End-ischemic hypothermic oxygenated machine perfusion reduces ischemia-reperfusion injury of donor liver grafts during storage and subsequent transplantation. However, it is unknown whether this technique also supports an extension of the *ex situ* preservation time. We aimed to determine whether liver grafts from donation after circulatory death (DCD) porcine donors can be effectively preserved for up to 24-hours using dual hypothermic oxygenated machine perfusion (DHOPE).
Methods: Liver grafts from DCD pig donors were subjected to 2h static cold storage (SCS), followed by 2, 6, or 24 hours DHOPE (n=6 in each group), using Belzer UW machine perfusion solution. Subsequently, hepatocellular and bile duct viability were tested during 4h normothermic *ex situ* reperfusion with autologous whole blood. DCD livers preserved for 24h by SCS (n=2) served as controls.
Results: In all three study groups, portal venous and arterial flows remained stable during DHOPE. After normothermic graft reperfusion, there were no significant differences in lactate clearance, blood pH, glucose and alanine aminotransferase levels among the three groups of DHOPE-preserved livers. All livers produced bile and there were no significant differences in biliary HCO_3^-, pH, and LDH between the three DHOPE groups at 4h after reperfusion. Moreover, levels of malondialdehyde (marker for oxidative stress) and danger associated molecular pattern protein HMGB-1 in serum and liver parenchyma, were similar for all three groups of DHOPE-preserved livers. Levels of cell-free DNA, a marker of cell death, were not different between the thee groups. Histological analyses of bile ducts and liver parenchyma also revealed no differences. In contrast, livers preserved for 24h *ex situ* by SCS did not produce any bile after reperfusion and turned bluish with reducing portal and arterial flows, representative for a dying/non-functional liver. Histology of these livers revealed massive cellular necrosis.
Conclusions: While 24h SCS preservation of porcine DCD liver grafts leads to massive necrosis and primary non-function after warm reperfusion, DHOPE enabled successful *ex situ* preservation of donor livers for up to 24h. If confirmed with human liver grafts, this technique opens new avenues to prolong storage time in case of necessity (e.g. difficult recipient hepatectomy) or to allocate grafts over longer distances.

Factors associated with the acceptance of livers for liver transplantation: validation of the Discard Risk Index in the Eurotransplant region.

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Background: Waiting list mortality remains an important issue although not all available liver allografts are used for transplantation. The utilization of available liver allografts might be further optimized with a better understanding of the reasons why livers are not transplanted. This study aims to analyze factors associated with the discarding of livers and to validate the prognostic ability of the Discard Risk Index (DSRI).
Methods: All donors that were reported to Eurotransplant from 01.01.2010 to 31.12.2015 were included. Liver utilization was defined by transplant status (y/n) and risk factors for discarding were identified. Based on this analysis, the ET-DSRI was developed in a training set. In the validation set, the ET-DSRI's prognostic performance was analyzed and compared to the DSRI. Furthermore, reasons for discarding livers that were procured but not transplanted were analyzed.
Results: In the study period, 9,565 out of 11,670 potential livers (81%) were transplanted. Utilization rate remained stable throughout the study period although significant differences were observed between countries. Highest percentage of livers were used from donors from Croatia, while this percentage was lower in the Netherlands. Multivariable analysis identified the following risk factors for non-utilization: diabetes, history of a malignancy, vasopressors, history of drug abuse, male sex, BMI, age, DCD donor and higher laboratory values of sodium, INR, transaminases, bilirubin, gamma-glutamyl-transpeptidase (GGT) and a lower CRP. The newly developed ET-DSRI achieved a c-statistic of 0.77 in the training set compared to a c-statistic of 0.73 for the DSRI. In the validation set the ET-DSRI and DSRI achieved c-statistics of 0.75 and 0.72, respectively.
Conclusions: The ET-DSRI has the highest prognostic ability to predict liver utilization in a European setting. This model can provide a valuable tool to identify livers at high risk of not being transplanted in an early phase in the allocation process. This information might be useful for surgeons to evaluate an organ offer and offers opportunities to avoid organ loss. Allocation might be modified for these high-risk organs to minimize ischemic times and they represent a group of livers that would benefit most from advanced preservation techniques.

Evaluation of the current post-transplantation Human Leukocyte Antigen antibody screening in paediatric renal transplant recipients

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Background: The necessity of post-transplant monitoring for donor specific antibodies (DSA) is unclear. This study evaluates the clinical relevance of post-transplantation donor specific HLA antibodies in pediatric renal transplant recipients, aiming at better stratification of patients at risk of graft dysfunction, and better recommendations for post-transplant monitoring.
Methods: A cohort of 68 pediatric kidney recipients, involving 76 transplantations between 2004 and 2014, was studied retrospectively. All patients were screened for HLA antibodies at 1, 3, 6 and 12 months after transplantation, and yearly thereafter. Samples testing positive were further analyzed to detect DSA. A biopsy was performed on clinical indication. We studied the baseline characteristics of the patients with biopsy, with DSA, and with rejection. We assessed the effect of post-transplant DSA on clinical outcome, including antibody-mediated acute rejection and GFR decrease.
Results: In our cohort the prevalence of DSA was 19% (13/68 transplantations). Most patients with HLA antibodies after transplantation were DSA-positive (76%; 13/17). A clear association between DSA and subsequent rejection was found. At the end of the study period, a significant lower GFR was found in patients with biopsy, DSA or rejection.
Conclusions: Based on our observations we recommend routine post-transplantation screening for HLA and DSA. The presence of DSA justifies a renal biopsy even in the absence of clinical signs of rejection.

Computerised Integration of Alternative kidney Transplantation (CIAT) programs to improve transplants for HI patients: a simulation

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Background: A selected group of highly immunised patients (sHI), participates unsuccessfully in transplant programs while donor specific antibody levels (DSA) are too high for desensitisation. In 2016, in an extremely laborious procedure, one couple with an sHI recipient had been matched using domino-paired, kidney-exchange, ABOi and desensitisation programs at the time for this one transplantation. The unacceptables of the new donor were fewer and had lower MFI's compared to the original donor. Our experience with this patient eventually led to the initiation of CIAT (Computer program for Integration of Alternative Transplantation programs). CIAT was developed to integrate kidney-exchange, altruistic donation, ABO incompatible and desensitization programs. sHI patients were prioritized and ABOi and HLAi combinations were allowed for them.
Methods: In collaboration with Erasmus Q-Intelligence a computer program was developed to integrate all alternative programs. We aimed at prioritizing sHI patients without diminishing the chances of the other patients. To compare CIAT with reality, a simulation was carried out including waitlisted patients, unspecified donors and HLAi and/or ABOi pairs that participated in our programs in 2015-2016. sHI patients were introduced with all their unacceptables and, in order to increase their chances also with reduced number of unacceptables. For reduction of unacceptables MFI<8000 was chosen because in our experience and that of others cdc cross matches of donor-recipient combinations with MFI below 8000 are mostly negative.
Results: In the period studied 40 unspecified donors, 63 exchange pairs and 20 sHI patients were registered. In reality, 90 alternative program transplantations were carried out: 73 compatible, 16 ABOi transplants and 1 ABOi and HLAi combination in a sHI patient (the index patient). In the simulation the CIAT program found 95 matches: 83 compatible (including 1 sHI) and 5 ABOi matches. Eight sHI patients were matched: 1 compatible, 6 HLAi with anti donor MFI<8000(1 was also ABOi), and 1 ABOi match.
Conclusions: Our simulation showed that computer driven integration leads to 14% more compatible matches. Additionally, 8 times as much matches were found for sHI-patients. These offered them better chances in the desensitisation program because of a more favourable MFI profile against the new donor. Integration of all alternative donation programs and prioritisation of sHI patients not only leads to better transplant opportunities for sHI patients, but also to an increase of the number of compatible matches.

High numbers of differentiated CD8+CD28- T cells are associated with a substantially lowered risk for late rejection and graft loss after kidney transplantation

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Background: Recipients of a kidney transplant have a prematurely aged T-cell system. This is reflected in lowered thymic output, reduced telomere length and more highly differentiated T cells. The latter harbor alloreactive cytotoxic memory T cells and are therefore potentially harmful for a kidney transplant. However, recent studies have found an inverse relation between the number of these cells and acute early rejection. In this study, we tested the hypothesis that parameters of an aged T-cell compartment decrease the risk for late rejection after kidney transplantation.

Methods: Recipients of a kidney transplant in the period 2007-2013 were (N=364) were included. T cell telomere length and thymic output were assessed and T cells were characterized prior to transplantation by flow cytometry as naive ($CD45RO^-CCR7^+$), central-memory ($CD45RO^+CCR7^+$), effector-memory ($CD45RO^-CCR7^-$), terminally differentiated $CD8^+$ Temra ($CD45RO^-/CCR7^-/CD28^-$) and $CD4^+CD28^-$ or $CD8^+CD28^-$ T cells. Follow-up was until September 2018. The date of the first time of biopsy-proven late rejection (>6 months after transplantation) was used to calculate the rejection-free survival time.

Results: The median follow up time was 79 months. Forty-nine cases of biopsy-proven rejection were recorded of which most were c-aABMR (77.5%), followed by TCMR (10.3%) and mixed type rejections (10.2%). Median time to diagnosis of late rejection was 44 months. Immunological T-cell ageing parameters correlated with calendar age of the recipients. Thymic output and T cell telomere length did not associate with late rejection-free survival. However, the percentage and absolute numbers of $CD8^+$Temra and $CD8^+CD28^-$ T cells were significantly lower in patients with late rejection. Specifically, in the highest tertile of percentages of $CD8^+CD28^-$ T cells, the cumulative incidence of late rejection at 5 and 10 years was only 5% and 8% compared to 16% and 20% in the middle to lowest tertile ($p=0.002$). Multivariate proportional hazard analysis, including clinical relevant parameters and age, showed that percentage and absolute number of $CD8^+CD28^-$ T cells remained significantly associated with late rejection ($p=0.009$). In addition, percentage and absolute number of $CD8^+CD28^-$ T cells ($p=0.001$) were inversely associated with rejection-related graft loss.

Conclusions: Recipients with high numbers of differentiated $CD8^+CD28^-$ T cells have a decreased risk for late rejection and rejection-related graft loss after kidney transplantation.

Efficacy of deep versus moderate neuromuscular blockade in enhancing intra-operative safety and post-operative recovery after laparoscopic donor nephrectomy: a randomised controlled trial

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Background: Laparoscopic donor nephrectomy is the gold standard to procure living donor kidneys. Postoperative recovery after laparoscopic donor nephrectomy is largely determined by the consequences of postoperative pain and analgesic consumption. It has been shown that deep neuromuscular blockade reduces postoperative pain scores, when compared to a moderate block. The aim of this study was to compare the effectiveness of deep *versus* moderate neuromuscular blockade during laparoscopic donor nephrectomy in enhancing postoperative recovery.
Methods: We performed a phase IV, multicentre, double-blinded, randomised controlled trial in which ninety-six live kidney donors were randomly allocated to receive deep (PTC 1-2) or moderate (TOF 1-2) neuromuscular block. Our primary outcome was the early quality of recovery at postoperative day 1, measured by the Quality of Recovery-40 questionnaire. The QoR-40 is a validated patient-rated questionnaire, measuring 5 dimensions of recovery after surgery, including comfort, emotions, physical independence, pain, and patient support. Secondary outcome measures were: intra-operative adverse events, the quality of recovery at postoperative day 2, post-operative pain scores, the cumulative use of analgesics and length of hospital stay.
Results: The intention-to-treat analysis did not show a difference with regard to the quality of recovery, pain scores, analgesic consumption and length-of-stay. Significantly less intra-operative adverse events occurred in patients allocated to a deep NMB (1/48 *versus* 6/48). Despite a clear protocol regarding neuromuscular monitoring and rocuronium dosing, we failed to establish and maintain a deep block in 7/48 patients. Therefore, we performed both an intention-to-treat analysis and a per-protocol analysis. The per-protocol analysis revealed that pain scores were significantly lower at 6h, 24h and 48h after surgery. Moreover the quality of recovery was significantly better at postoperative day 2 in patients receiving a deep *versus* moderate block (179.5 ± 13.6 *versus* 172.3 ± 19.2).
Conclusions: Our results show that an adequately maintained deep neuromuscular block improves intra-operative safety, post-operative pain scores and quality of recovery. As the intention-to-treat analysis did not reveal a difference regarding the primary endpoint, future studies should pursue if a thoroughly maintained deep NMB during laparoscopy improves relevant patient outcomes.

Pre-transplant donor-specific B cell memory for prediction of antibody mediated rejection - a pilot study

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Background: Pre-transplant immunological risk assessment is currently based on the evaluation of donor-specific HLA antibodies (DSA) present in serum. While being an excellent source for HLA antibodies produced by bone marrow-residing plasma cells, serum analysis does not provide information on the memory B cell compartment. Therefore, we have developed a highly sensitive method to profile memory B cell-derived HLA antibodies and evaluated the clinical relevance of this novel method in a pilot study.
Methods: Peripheral blood mononuclear cells (PBMC) and paired serum samples were obtained from transplant candidates with serum HLA antibodies (n=13) and alloantigen non-exposed individuals (n=10). Culture supernatants from polyclonally activated PBMC were either 10-fold concentrated or IgG was isolated from culture supernatants (eluates) using a protein G affinity purification method. Clinical utility of detecting donor HLA-specific memory B cell-derived antibodies (DSA-M) in eluates were investigated in a separate cohort of 20 patients transplanted across a luminex single antigen bead (SAB)-defined serum DSA with negative complement-dependent cytotoxic crossmatches. All patients had at least two allograft biopsies (indication and/or surveillance) within the first year post-transplant. Serum samples as well as processed culture supernatants were tested using luminex SAB assays.
Results: Utilization of eluates enabled detection of HLA-specific B cell memory in 82% of immunized individuals in comparison 64% in 10-fold concentrated supernatants. No B cell memory was detected in eluates of individuals without history of alloantigen exposure, confirming the specificity of the assay. Using this novel, highly sensitive method, DSA-M was detected in 9 patients (45%) with pre-transplant DSA. Patients with concurrent DSA and DSA-M had a higher incidence of of (sub)clinical antibody-mediated rejection ($p=0.032$) and a higher extent ($g\geq1+ptc\geq1$) of microvascular inflammation (67% versus 9%, $p=0.02$).
Conclusions: The current highly sensitive and easy to apply method for the detection of HLA-specific memory B cells allows for donor-specific memory B cell analyses in clinical settings. Results of our pilot study suggest that analysis of memory B cell-derived HLA antibodies can serve as a novel tool supplementary to serum HLA antibody analysis in pre-transplant risk assessment.

Comparison of long-term outcomes between alemtuzumab and rabbit anti-thymocyte globulin for acute kidney allograft rejection

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Background: T cell-depleting antibody therapy with rabbit anti-thymocyte globulin (rATG) is the treatment of choice for glucocorticoid-resistant, recurrent and/or severe acute kidney allograft rejection (AR). Although effective, the use of rATG is associated with serious infusion-related side effects. Alemtuzumab, a humanized rat monoclonal antibody against CD52, is incidentally used as off-label treatment for AR. Following satisfactory results in a pilot study, alemtuzumab has become the first line T-cell depleting agent in our center. Here, the long-term outcomes (patient- and allograft outcomes, and adverse events) were compared of patients treated with either alemtuzumab or rATG for AR.
Methods: Between 2012 to 2017, we identified 113 patients, treated with alemtuzumab (30 mg, subcutaneously) for biopsy-proven glucocorticoid-resistant, recurrent or severe AR (Banff acute T cell-mediated rejection grade IIA or more). Long-term outcome was compared with the outcome of a retrospective cohort of 108 patients treated with rATG for AR between 2002 and 2012.
Results: Patient survival between patients treated with alemtuzumab or rATG was similar (p=0.05, hazard ratio (HR) 2.08, 95%-confidence interval (CI) 0.99-4.34). Death-censored allograft survival after AR was comparable between both groups (p=0.87, HR 0.96, 95%-CI 0.62-1.50). A multivariate Cox regression analysis of alemtuzumab-treated patients showed 4 variables that influenced allograft survival negatively: no maintenance immunosuppressive therapy with glucocorticoids, actual panel reactive antibodies above 6%, estimated glomerular filtration rate (eGFR) drop of more than 50% between baseline eGFR and eGFR at time of AR, and remarkably, a lower HLA mismatch. Infusion-related adverse events occurred less often after alemtuzumab treatment: No patients developed cytokine release syndrome or serum sickness. Infection-free survival in the first year after alemtuzumab treatment was superior compared with the infection-free survival of rATG-treated patients (p=0.002, HR 0.54, 95%-CI 0.37-0.84). After alemtuzumab (median follow-up 2.63 years [interquartile range 1.3-3.6]), 7 solid tumors occurred.
Conclusions: Patient- and allograft survival were comparable between patients treated for severe AR with either alemtuzumab and rATG. However, in the alemtuzumab-treated patients, fewer infusion-related side effects and less infections occurred. Alemtuzumab therapy is a good alternative therapy for glucocorticoid-resistant, recurrent and/or severe AR.

Therapeutic drug monitoring of tacrolimus and mycophenolic acid in outpatient renal transplant recipients using a volumetric dried blood spot sampling device

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Background: Tacrolimus and mycophenolic acid dosing after renal transplantation is individualized through therapeutic drug monitoring (TDM). Home-based dried blood spot (DBS) sampling has the potential to replace conventional TDM sampling at the clinic. A liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay was developed to quantify tacrolimus and mycophenolic acid in DBS and clinically validated for abbreviated area under the concentration-time curve (AUC) monitoring using an innovative volumetric DBS sampling device.
Methods: Clinical validation was performed by direct comparison of paired DBS and whole blood (WB) (tacrolimus) and plasma (mycophenolic acid) concentrations and AUCs. Agreement was evaluated using Passing-Bablok regression, Bland-Altman analysis and DBS-to-WB predictive performance. TDM dosing recommendations based on both methods were compared to assess clinical impact.
Results: Paired tacrolimus (n = 200) and mycophenolic acid (n = 192) DBS and WB samples were collected from 65 kidney(-pancreas) transplant recipients. Differences for tacrolimus and mycophenolic acid were within ±20% for 84.5% and 76.6% of concentrations and 90.5% and 90.7% of AUCs, respectively. Tacrolimus and mycophenolic acid dosing recommendation differences occurred on 44.4% and 4.7% of occasions. Tacrolimus DBS dosing recommendations were 0.35 ± 0.14 mg higher than for WB and 8 ± 3% of the initial dose. Mycophenolic acid DBS dosing recommendations were 23.3 ± 31.9 mg lower than for plasma and 2 ± 3.5% of the initial dose.
Conclusions: Tacrolimus and mycophenolic acid TDM for outpatient renal transplant recipients, based on abbreviated AUC collected with a DBS sampling device, is comparable to conventional TDM based on WB sampling. Patient training and guidance on good blood-spotting practices is essential to ensure method feasibility.

Detection, treatment and clinical outcome of graft thrombosis following pancreas transplantation

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Background: Complete graft thrombosis is the leading cause of early graft loss following pancreas transplantation. Partial thrombosis is usually subclinical and discovered on routine imaging. Treatment options may vary in such cases. We describe the incidence and relevance of partial graft thrombosis in a large transplant center.
Methods: All consecutive pancreas transplantation at our center (2004-2015) were included in this study. Standard clinical follow up includes computed tomography. Radiological follow-up, type and quantity of thrombosis prophylaxis, complications and graft and patient survival were collected. Partial thrombosis and follow-up were also studied.
Results: All 230 pancreas transplantations were included in the analysis. Computed tomography was performed in most cases (89.1%). Early graft failure occurred in 23 patients (13/23 due to graft thrombosis, 3/23 bleeding, 1/23 anastomotic leakage, 6/23 secondary to antibody mediated rejection). There was evidence of partial thrombosis in 59 cases (26%), of which the majority was treated with heparin and a vitamin K antagonist with graft preservation in 57/59 patients (97%). When CT imaging was performed per protocol (n=122), in 30 cases (25%), partial thrombosis was found.
Conclusions: Thrombosis is the leading cause of early graft loss following pancreas transplantation. Computed tomography allows for early detection of partial thrombosis, which is usually subclinical. Partial graft thrombosis occurs in about 25% of all cases. In this series, treatment with anticoagulant therapy (heparin and vitamin K antagonist) resulted in graft preservation in almost all cases.

Implementation of Normothermic Regional Perfusion in The Netherlands

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Background: Organ shortage still causes waiting list morbidity and mortality in the Netherlands. Increasing donor utilisation and donor organ quality may lead to a decrease in waiting lists. Normothermic Regional Perfusion (NRP) of abdominal organs may achieve this, by allowing macroscopic and laboratory value assessment of extended criteria donation after circulatory death (DCD) organs during perfusion. A program for NRP was initiated in the western part of The Netherlands.
Methods: A project organization was established by the combined Erasmus MC and LUMC procurement teams, supported by the Ministry of Health and the Dutch Transplant Foundation. Necessary legal and logistic arrangements were made. Four organ perfusion specialists were trained by clinical perfusionists in the Netherlands and at expert centres abroad. Animal experiments and training programs were performed for training of procurement teams. A perfusion and assessment protocol was developed and implemented in a selected group of extended criteria DCD donors.
Results: Since the start of the project on October 1st 2018, multiple potential NRP donors were identified, of which three could be effectively included in the protocol. From these donors, six kidneys were successfully transplanted. One liver, which was not accepted for regular transplantation, was positively assessed during NRP and successfully transplanted. Two other livers were negatively assessed and declined for transplantation. One pancreas was retrieved for islet isolation. No adverse events were noted. The duration of the procedures was comparable to regular donation after brain death (DBD) procedures. All recipients have good clinical function of the organ transplanted.
Conclusions: Establishment of a NRP protocol by the combined Erasmus MC/LUMC procurement teams was successful. In the first procedures, no adverse events were noted. Despite the short duration of the project, already one liver was transplanted that otherwise would not have been used for transplantation. These promising first results may ultimately lead to an increase in donor utilisation and less waiting list mortality.

Advanced immunological T-cell ageing defined by a very low thymic function identifies patients with substantial increased risk for long-term mortality after kidney transplantation

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Background: End-stage renal disease is associated with premature ageing of the T-cell immune system. At the time of kidney transplantation the average biological age of the circulating T cell system is increased by 15-20 years over the calendar age, but inter-individual variation is substantial. The hypothesis was tested that advanced immunological T-cell ageing increases the long-term mortality risk after kidney transplantation.
Methods: Patients from a well-defined cohort (N=210), transplanted with a kidney from a living donor between 2010-2013, were included. All recipients received induction therapy with basiliximab and prednisone/MMF/tacrolimus. Circulating T cells were analyzed before, at 3, 6 and 12 months after transplantation. The number of CD31 expressing naive T cells (identifying recent thymic emigrants, a marker for thymic function), telomere length of $CD4^+$ and $CD8^+$ T cells and T-cell differentiation status were assessed by flow cytometry. The results were validated in a cohort of 180 kidney transplant recipients transplanted between 2007-2010.
Results: Thirty recipients (median age 63 year, range 26-78) died during follow-up until sept 2018. The absolute numbers of naive $CD4^+$ (living:258 cells/ul vs. deceased:101 cells/ul, p=0.001) and naive $CD8^+$ T cells (living:97 cell/ul vs. deceased:37 cells/ul, p=0.001) were significantly lower in the deceased group prior to transplantation. Numbers of naive $CD31^+$ T cells were inversely related with increasing age (r=0.56, p<0.001). However, the average numbers of naive $CD4^+CD31^+$ and $CD8^+CD31^+$ T cells in the deceased patient group was at the level of patients >75 years. In a multivariate proportional hazard analysis including recipient age, the number of naive $CD4^+$ T cells remained associated with all-cause mortality (HR 0.98, CI 0.98-0.99, p<0.001). The lowered number of naive $CD4^+$ T cells in the deceased patient group was primarily caused by a decreased thymic function (less $CD31^+$ naive T cells). In addition, a compensatory increase in $CD31^-$ naive T cells, which is normally observed with age-related loss of thymic function, was not observed. Within the first year after transplantation, the number and characteristics of naive T cells remained remarkably stable. All other immunological parameters were not related to patient survival after transplantation.
Conclusions: Advanced immunological T-cell ageing at time of transplantation, defined by a severe reduction in thymic function, is highly associated with all-cause mortality after kidney transplantation.

The national HLA-incompatible kidney transplantation program: two years onwards.

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Background: Desensitization for Dutch HLA-incompatible kidney transplant recipients in a national referral center is reimbursed by health insurance since January 2017.
Methods: Highly-immunized patients with an HLA-incompatible donor, who unsuccessfully participated in the national kidney exchange program and the Eurotransplant Acceptable Mismatch program, are eligible. After referral, an immunological assessment of the antibodies against the current (cross-over) donor as well as against former potential donors is made. Desensitization consists of 5 cycles of plasmapheresis (PE) with low-dose IVIG, tacrolimus, mycophenolate mofetil and steroids. If the complement-dependent cytotoxicity test remains positive after one week, this schedule is repeated for at most one more week. rATG is given pre-operatively and during 4 days postoperatively in a cumulative dose of 7 mg/kg. Postoperative care consists of 3 cycles of plasmapheresis/IVIG and the continuation of triple immunosuppressive drugs.
Results: Since 2017 15 patients were referred of whom five have been transplanted with an HLA-incompatible allograft:
Transplanted patients were young (range 29-39 years) and all had multiple previous kidney transplantations (range 3-4). Antibodies against multiple class I and II donor HLA antigens (DSA) were present. Two patients were also ABO-incompatible with their donor. In 4 patients, 5 cycles of PE sufficed to proceed with transplantation, whereas 1 patient needed 10 PE cycles. In patient VI desensitization failed. No clear relationship was observed between height of DSA and successful desensitization.
All recipients but one experienced acute rejection within two weeks, treated with plasmapheresis, pulse steroids and IVIG. Recipients I and III had a steep rise in their DSA intensity during rejection. Patient II and III developed ongoing rejection for which alemtuzumab and currently monthly tocilizumab is administered. None of them lost their graft.
Of the remaining 9 patients, 2 have been transplanted with a cross-over donor, 2 found HLA-compatible donors after interviewing, one was advised to participate in the AM program for a longer period because of a relatively high ETKAS score, 2 are still in analysis and 2 are awaiting desensitization.
Conclusions: Desensitization with the current protocol is successful. Early rejection occurs in the majority of patients, but without graft loss. Treatment of ongoing rejection is challenging and warrants novel treatments, possibly tocilizumab.

Outcome after liver transplantation for hilar cholangiocarcinoma in the Netherlands after implementation of a nationwide protocol

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Background: The introduction of the Mayo Clinic protocol (i.e., neoadjuvant chemoradiation therapy followed by liver transplantation) has achieved 5-year survival rates of 68% for patients with unresectable hilar cholangiocarcinoma (hCCA). The question remains if the favorable results could be attributed to the neoadjuvant therapy or to the adherence to the strict selection criteria. The aim of this study was to evaluate whether liver transplantation for hCCA after implementation of a national protocol solely based on strict selection criteria, could have equivalent results.
Methods: Prospective, multicenter national cohort study from 2011-2018. All patients with unresectable hCCA who fulfilled the inclusion criteria for the Dutch protocol for liver transplantation for hCCA were included. All potential eligible patients underwent a multidisciplinary evaluation by all three transplant centers. Patients received non-standard exception (NSE) points only after approval by all three transplant centers.
Results: A total of 19 patients with unresectable hCCA were enrolled in the transplant screening protocol. After approval by all three centers, 10 patients (53%) received NSE points and underwent orthotopic liver transplantation. In 7 (70%) patients the pathology specimen confirmed cholangiocarcinoma; the other 3 patients were diagnosed with atypical cells or no dysplasia. After a median time of 30 months four patients are still alive and a 57% survival rate is reached.
Conclusions: The survival rate of 57% as reached with the Dutch protocol based on strict selection criteria alone closely approaches the survival rates reported for patients with upfront pathological confirmed hCCA that were transplanted after completion of the chemoradiation protocol at the Mayo Clinic (68%). Although the power of our study is limited by a small number of patients, it does suggest that with strict selection alone a favorable survival after transplantation for hCCA can be achieved.

Especially 'elderly' patients should receive a living donor kidney transplant

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Background: Age criteria for kidney transplantation have been liberalized over the years resulting in more waitlisted elderly patients. However, waiting time may be up to several years, while both age and waiting time are important risk factors for death on the waiting list. In this retrospective cohort study we analyzed how age influenced outflow from the waiting list.
Methods: Between 2000-2013, 2622 patients had been placed on our regional waiting list. Waiting time was defined as the period between start dialysis and being delisted. Patients were categorized according to age at inflow in <25 (N=122), 25-44 (N=600), 45-54 (N=584), 55-64 (N=752), and >64 years (N=564). The influence of ABO blood type and PRA on outflow patterns was studied as well.
Results: At the end of observation (November 2017), 1273 (49%) patients had been transplanted with a living donor kidney, 674 (26%) had been transplanted with a deceased donor kidney, 333 (13%) had been delisted without a transplantation, 271 (10%) had died, and 61 (2%) were still waiting. When comparing the age categories, outflow patterns were completely different. The percentage of patients transplanted decreased with increasing age, while the percentage of patients that had been delisted or had died increased with increasing age, especially in the population without a living donor. After only 2 years, the differences between age categories are clearly visible. While the majority of younger patients had been transplanted, the number of elderly patients that had died or had been delisted increased profoundly in the first years after start dialysis. Although significant, the influence of ABO blood type and PRA on outflow patterns was only modest.
Conclusions: While "elderly" less often receive a living donor kidney transplantation, they cannot bear the waiting time of 3 to 4 years for a deceased donor kidney, resulting in delisting without a transplant in more than half the population of patients over 54 years without a living donor. Age is of paramount importance on outflow from the waiting list. ABO blood type and PRA are less influential when comparing both percentages of patients that had died or had been delisted and percentages of patients that had been transplanted after 6 years. In order to improve their survival, living donor kidney transplantation should be promoted in this "elderly" population.

Macroscopic arteriosclerosis of the renal artery is associated with organ discard and primary non-function, but not with graft function or long term survival of 50+ deceased donor kidneys

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Background: The average deceased donor today is significantly older than donors were a few decades ago. Older donors have more arteriosclerosis of the renal artery. During organ retrieval, surgeons estimate the degree of arteriosclerosis and this plays an important role in decisions on organ acceptance. Our study aimed to elucidate the association between macroscopic renal artery arteriosclerosis, donor kidney discard and transplant outcome. We also investigated whether assessment of macroscopic arteriosclerosis correlated with histological evidence of intrarenal arteriosclerosis.
Methods: We selected all renal transplants between 01-01-2000 and 31-12-2015, from deceased donors aged 50 years and older, carried out in any of the 8 transplant centres in The Netherlands. We included only those for which data on renal artery arteriosclerosis were available (n=2,239). Donors were either DBD (n=1,107) or controlled DCD (n=1,132). The association between arteriosclerosis and kidney discard, the relation between arteriosclerosis and outcome and the correlation between macroscopic and microscopic arteriosclerosis were explored by means of univariable and multivariable analyses.
Results: Median donor age was 60 (range 50-82). Degree of macroscopic arteriosclerosis was either none, mild, moderate, or massive. Macroscopic arteriosclerosis was independently associated with kidney discard (OR 1.36 95% CI 1.02-1.80 p=0.03). Arteriosclerosis was not significantly associated with delayed graft function (OR 1.16 95% CI 0.94-1.43 p=0.16), eGFR 1 year post-transplant (B 0.58 95% CI -2.07-3.22 p=0.67) and long term death censored graft survival (HR 1.07 95% CI 0.86-1.33 p=0.55). There was a significant association between mild arteriosclerosis and primary non-function (OR 2.14 95% CI 1.19-3.84 p=0.01). However, higher degrees of arteriosclerosis were not a risk factor for primary non-function. There was no correlation between macroscopic and histological parameters of arteriosclerosis.
Conclusions: Macroscopic arteriosclerosis of the renal artery was somewhat associated with more primary non-function. However, there was no effect on delayed graft function, eGFR at 1 year, or long term graft survival. This study suggests that, if a 50+ deceased donor kidney shows immediate or delayed function, renal artery arteriosclerosis will not negatively affect long term transplant outcome. Given these data, we feel that kidney discard based on macroscopic assessment of arteriosclerosis should be discouraged.

Increased and safe utilization of high-risk donor livers for transplantation after ex situ resuscitation and assessment using sequential hypo- and normothermic machine perfusion

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Background: Despite persistent donor organ shortage, a high number of donor livers is currently not used for transplantation because of a supposed too high risk of early graft dysfunction/loss. We aimed to increase the number of transplantable livers by resuscitating and assessing hepatobiliary viability of initially declined high-risk livers, using a protocol of end-ischemic sequential *ex situ* hypothermic and normothermic machine perfusion.
Methods: In this prospective clinical trial, all nationwide declined livers were eligible for inclusion (Netherlands trial registry: NTR5972). The protocol consisted of one hour hypothermic oxygenated perfusion (10°C) for resuscitation, one hour of controlled oxygenated rewarming, and subsequent normothermic machine perfusion (NMP) for viability testing. A novel perfusion fluid containing a hemoglobin-based oxygen carrier was used for all temperature phases. During the first 150 min of NMP viability of the liver and biliary tree was assessed using the following criteria: perfusate lactate <1.7mmol/L, pH 7.35-7.45, cumulative bile production >10mL and biliary pH>7.45. Livers meeting these criteria were secondary accepted for transplantation. All recipients gave written informed consent. Primary endpoint was safety and feasibility, as reflected by a 3-months graft survival rate of at least 80%.
Results: Between August 2017 and October 2018, 16 livers underwent machine perfusion after an average of 288 (241-480) min of static cold preservation. All livers were derived from donation after circulatory death donors with a median age of 63 (range 42-82) years. During NMP, all livers cleared lactate and produced sufficient bile volume, but in 5 cases biliary pH remained below 7.45. The 11 (69%) livers that met all viability criteria were successfully transplanted, resulting in a 20% increase in the number of deceased donor liver transplants. Patient and graft survival at 3 months was 100%. Comparison of non-transplanted and transplanted livers revealed median donor hepatectomy time (70 [IQR 44-93] min vs. 44 [IQR 28-54] min; p=0.04) and median cold ischemia time (326 [IQR 286-480] min vs. 270 [IQR 241-294] min; p=0.02) as variables significantly associated with secondary graft acceptance during NMP.
Conclusions: Sequential hypo- and normothermic machine perfusion enabled resuscitation and selection of initially declined high-risk donor livers. This method offered a valuable tool to safely increase the number of transplantable livers by 20%.

First experience with ex-vivo lung perfusion for initially discarded donor lungs in the Netherlands, a single center study

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Background: Despite ongoing progress in lung transplantation (LTx) techniques, a shortage of donor lungs persists worldwide. Ex-vivo lung perfusion (EVLP) is a technique that evaluates, optimizes and enables transplantation of lungs that would otherwise have been discarded. Here we present our center's first EVLP experiences between July 2012 and June 2016, when we performed 149 LTx.
Methods: This study was a single center, retrospective analysis of a prospectively collected database. The EVLP group (n=9) consisted of recipients who received initially discarded donor lungs that were reconditioned using EVLP. The non-EVLP (N-EVLP) group (n=18) consisted of data-matched patients receiving conventional quality lungs in the conventional way. Cases were matched based on surgery dates, the recipients' underlying lung disease, and donor type (donation after brain death or controlled donation after circulatory death). Donor lungs that met any of the following indications were included in the EVLP procedure: 1) lungs with a PaO_2/fraction of inspired oxygen (FiO_2) < 40 kPa at a positive end expiratory pressure (PEEP) of 5 cmH_2O and 100% oxygen with clinically evident lung edema; 2) lungs that had a persistent low PaO_2/FiO_2 < 40 kPa after active lung recruitment without a clear reason. Both study groups were compared on primary graft dysfunction (PGD) grades 0-3, pulmonary function, chronic lung allograft dysfunction (CLAD) and survival.
Results: In the EVLP group, 33% (3/9) developed PGD1 at 72 hours post-LTx. In the N-EVLP group, 11% (2/18) developed PGD1, 6% (1/18) PGD2 and 11% (2/18) PGD3 at 72 hours post-LTx. At 3 and 24 months post-LTx, FEV1 as percentage of predicted was similar in the EVLP (78% and 92%) and N-EVLP group (69% and 89%). Forced vital capacity as a percentage of predicted was comparable in the EVLP (77% and 93%) and N-EVLP group (68% and 101%). CLAD was diagnosed in one N-EVLP patient at two years post-LTx. Three-year survival was 78% (7/9) (EVLP group) versus 83% (15/18) (N-EVLP group).
Conclusions: By accepting discarded lungs for EVLP, the addition of this single center EVLP procedure increased the number of LTx by 6.4% (9 EVLP/149 LTx). These results are in line with existing literature that suggests that transplantation of previously discarded donor lungs, recovered by EVLP, leads to equal outcomes compared to conventional LTx methods.

CD40 inhibition with CFZ533 - a fully human, non-depleting, Fc silent mAB - improves renal allograft function while demonstrating comparable efficacy vs. tacrolimus after kidney transplantation.

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Background: To assess the potential of CFZ533 (CFZ) as primary immunosuppressant in a calcineurin-inhibitor (CNI)-free regimen in de novo kidney transplant recipients
Methods: CFZ533 is a fully human, Fc-silenced, non-depleting, IgG1 mAb preventing CD40 pathway signaling and activation of CD40+ cell types. NCT02217410 is a 12-month multicenter randomized controlled Phase 2a clinical trial evaluating efficacy, safety, tolerability, and pharmacokinetics of CFZ in combination with mycophenolate mofetil (MMF) and corticosteroids (CS) compared with tacrolimus (TAC), MMF and CS in de novo kidney transplant recipients. All patients received induction with basiliximab and CS as per center practice.
Results: N=51 pts were transplanted and randomized (2:1) to either CFZ (N=33) or TAC (N=18). 25 of 51 pts (49%) received a living donor allograft. After CD40 target saturation, CFZ was dosed every 4 weeks. CFZ was well tolerated with no infusion related nor thromboembolic events. Month 6 interim results demonstrated comparable efficacy on the composite endpoint of treated biopsy proven acute rejection, graft loss, or death (21.2 vs. 22.2%) and better renal function (55.8 vs. 45.5 mL/min), less serious adverse events (SAE) (47.1 vs. 61.1%) and fewer infectious complications (50.0 vs. 77.8%) with no increase of opportunistic infections (viral overall: 26.5 vs. 50.0%; SAE CMV: 2.9 vs. 11.1%; BKV: 15.2 vs. 22.2%), and a lower rate of new-onset diabetes mellitus (14.7 vs. 38.9%) with CFZ vs. TAC. 12-month final study data will be available in the beginning of 2019.
Conclusions: CFZ533, a new anti-CD40 monoclonal antibody may have potential to become an effective CNI-free treatment for kidney transplant recipients improving transplant outcomes by preventing graft rejection without nephrotoxic (and other) CNI adverse effects.

Luminal preservation of the human small bowel graft reduces mucosal damage during cold storage

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Background: Graft survival rates in intestinal transplantation (ITx) are the lowest among solid organ transplantation[1]. Unique for ITx is the presence of a large volume of metabolically-active luminal content consisting of a complex mixture of microbes, dietary and waste products. Cold ischemia during storage (CS) decreases mucosal integrity during preservation and leads to bacterial translocation, predisposing for rejection of the graft. CS of the bowel is limited up to 10 hours, after which it is deemed unsuitable for transplantation[2]. Luminal preservation (LP) with polyethylene glycol (PEG) has shown promising effects in improving graft-viability in experimental models[3][4]. We started a project to analyse the effect of luminally-applied solutions on preservation injury of the human bowel. Here, we report our preliminary data.

Methods: So far, 8 bowels from brain-dead donors from our region were included. In all cases, standard vascular perfusion (VP) with ice-cold University of Wisconsin solution (UW) was performed. Five bowels served as a control group with no LP and standard CS in UW. Three bowels were filled with 1.5 litres of PEG prior to procurement and CS. Tissue samples were taken at procurement and after 7 and 14 hours of CS. Jejunal and ileal samples were analysed for Park/Chiu score. The project has been extended to a centre in Belgium to include Institut Georges Lopez-1 (IGL-1) for VP and first results still need to be analysed.

Results: Control samples show the natural decay of the graft's structure. Median Park/Chiu score for jejunum is 3 (maximum value=5), 4 (7) and 5 (5) in successive time points; for ileum 0 (2), 3 (4) & 4 (7) respectively. Median score with LP for jejunum is 1 (4), 3 (4) and 3.5 (4) in successive time points; for ileum 1 (2), 3 (3) & 3 (3), respectively. LP with PEG seems to maintain the epithelial lining, with increasing signs of oedema of the villi tips.

Conclusions: These promising preliminary data show that both jejunum and ileum with LP tend to maintain a low level of preservation injury. LP might thus improve graft viability and increase its preservation time-window. Further analyses will be performed to study bacterial location and protein and gene expression. Additional luminal solutions and their relationship with different VP solutions will also be studied.

Oxygenated hypothermic machine perfusion of kidneys donated after circulatory death: an international randomised controlled trial

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Background: An international, double-blinded, randomised, paired phase 3 trial designed to determine the effect on 1-year graft function of continuous oxygenated (HMPO) vs non-oxygenated hypothermic machine perfusion (HMP) in controlled DCD kidneys from donors aged 50 years or older.
Methods: At randomisation, one kidney from each donor was assigned to HMPO, the other to HMP. Kidneys were pumped immediately after retrieval until transplantation. The primary endpoint was estimated glomerular filtration rate (eGFR) at 1 year post-transplant (CKD-EPI) with 90% power at α=0.05 to detect a 8 ml/min/1.73m² difference. A pre-specified sensitivity analysis accounted for cases where no eGFR at 1 year was available due to graft loss (eGFR imputed by 10 mL/min/1.73m²) or patient death with functioning graft (last known eGFR carried forward). Secondary endpoints were delayed graft function, primary nonfunction, graft loss, and patient death. The primary analysis was performed according to intention to treat.
Results: The Netherlands, Belgium and part of the UK randomised 197 kidney pairs (median donor age 56 (range: 50-78) years), of which 106 were successfully machine perfused and transplanted (median recipient age 61 (21-79) years). Median total warm ischemia time was 28.5 (8-114) minutes and cold time was 11 (4.6-27.6) hours in HMPO and 10.3 (3.5-27.1) hours in HMP. Kidneys were pumped for 6.9 (1.7-24.3) vs 7.4 (1.3-23.8) hours. Of the 106 kidney pairs, delayed graft function of HMPO versus HMP was respectively 38 (35.8%) versus 38 (35.8%), primary nonfunction was 3 (2.8%) versus 5 (4.7%) (p=0.48), graft loss was respectively 3 (2.8%) and 11 (10.4%) (p=0.021) and patient death was 7 (6.6%) versus 8 (7.5%) (p=0.80).
For the primary analysis, 83 pairs were eligible for inclusion (23 pairs excluded due to all-cause graft failure of at least 1 kidney). No difference in eGFR at 1 year was observed between HMPO vs HMP (mean(SE): 50.5(2.1) vs 46.7(1.8) mL/min/1.73m², p=0.12). Sensitivity analysis, accounting for all-cause graft failure, showed a higher eGFR in HMPO (47.6(1.9) vs 42.6(2.0) mL/min/1.73m², p=0.035). Graft loss was lower after HMPO; other secondary outcomes including patient death were similar between the two groups.
Conclusions: This first randomised controlled trial comparing HMPO with HMP suggests that oxygenation improves 1 year kidney graft function when accounting for the beneficial effect on graft survival.

Prevalence of psychological distress and the correlation with medication non-adherence among lung transplant patients.

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Background: Psychological distress after lung transplantation (LTx) is a potential risk factor for morbidity and mortality. Knowledge about the association between depression, anxiety, post-traumatic stress, and medication non-adherence (MNA) in LTx patients is heterogeneous and limited. Therefore the aim of our study is to investigate the prevalence of anxiety, depression, and PTSD and their correlation with MNA before and after LTx.
Methods: We performed a single-center study with a cross-sectional design. Anxiety and depression were assessed with the Brief Symptom Inventory, symptoms of post-traumatic stress disorder (PTSD) with the Dutch version of the Impact of Event Scale, and medication adherence with the Basel Assessment of Adherence to Immunosuppressive Medications Scale.
Results: We assessed 35 waiting list patients (response rate 95%) and 113 patients after LTx (response rate 96%). In waiting list patients, 52% reported (sub)clinical symptoms of depression and in transplanted patients 23%. The BSI includes a question on suicidal thoughts and advises to interpret this question as a risk factor for depression. After LTx, 8 patients (7.1%) reported "few thoughts" and 2 patients (1.8%) reported "quite some thoughts" about ending their life. Prevalence of (sub)clinical symptoms of anxiety is 43% in waiting list patients and 33% in transplanted patients. After LTx, 12% reported clinical symptoms of LTx-related PTSD. Anxiety and medication adherence are significantly and positively correlated in transplanted patients (Pearson r = 0.20; p = .035). We found no relation between depression or PTSD and adherence. CF patients after LTx have an OR of 2.15 to be non-adherent to medication.
Conclusions: Symptoms of depression, anxiety, and PTSD after LTx are more prevalent compared to the Dutch general population but depression after LTx is less prevalent than in waiting list patients. Although physical wellbeing and quality of life after transplantation improves we observed a high prevalence of suicidal ideation in the transplanted patients. Higher levels of anxiety after LTx are related to better medication adherence. Anxious patients may try to avoid dyspnoea by taking medication conscientiously. CF patients after LTx are more at risk for MNA compared to patients with other native chronic lung diseases. These findings and the high disclosure of psychological distress before and after lung transplantation justifies systematic psychological screening in lung transplant care.

Hypothermic machine perfusion as a national standard preservation method for deceased donor kidneys

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Background: Dutch donation and transplantation professionals in collaboration with the Dutch Transplant Foundation have recently completed a two year project to implement non-oxygenated hypothermic machine perfusion (HMP) as standard preservation method for all post mortal donated kidneys. The scope of this study was to assess the effect of the implementation of machine perfusion in daily practice on early outcomes after kidney transplantation.
Methods: Of the kidneys donated and primed for preservation within the Netherlands from January 11th 2016 to December 31st 2017, all kidneys allocated to Dutch recipients were intended to be preserved by HMP. In this analysis also kidneys from DCD donors ≥50 years of age who were randomized in the COPE COMPARE study (oxygenated versus non-oxygenated HMP) were included. A recent historical cohort (2010-2014) with static cold storage (SCS) as standard preservation method was chosen as control group. Follow up data from these transplants were collected via the National Organ Transplant Registry (NOTR). The results of the evaluation included delayed graft function (DGF), graft function defined by eGFR, graft survival one year after transplantation and safety of HMP preservation.
Results: Of all 924 kidneys procured and preserved in the Netherlands during this project, 681 were transplanted in Dutch recipients. Of these kidneys, 82 percent was preserved by HMP. No kidneys were discarded because of the HMP preservation procedure. Within the historical cohort 1812 kidneys from a Dutch donor were transplanted within the Netherlands, all preserved by SCS. DGF occurred in 38 percent of the project cohort versus 46 percent of the historical cohort (p=0,001). A multivariate regression analysis showed an odds ratio of 0,64 for the risk of DGF when using HMP as standard preservation method instead of SCS (p=<0,001). At one year after transplantation the mean eGFR for the project and the historic cohort was 44 (SD 22,3) and 46 (SD 21,4) ml/min/1.73m2 (P=NS), respectively. One year graft survival did not show a significant difference with 94,4 percent in the project cohort, compared to 93 percent in the historical cohort.
Conclusions: The use of hypothermic machine perfusion as standard preservation method for all deceased donor kidneys in the Netherlands was associated with a significant reduction of DGF. To assess long term follow-up results, a longer follow-up period and data is required.

Tacrolimus monotherapy in immunologically low-risk kidney transplant recipients: a randomized controlled trial.

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Background: Attempts to wean immunosuppressive drugs in order to diminish infection and malignancy must be balanced to prevent rejection. Tacrolimus combined with mycophenolate mofetil is the cornerstone of current immunosuppressive regimens. We have performed a randomized controlled trial to investigate the safety of discontinuing mycophenolate mofetil.
Methods: Patients without an immunological renal disease with ≤3 mismatches with their donor and peak panel-reactive antibodies (PRA) of ≤4% were asked for their consent at admission. Steroids were tapered and discontinued at month 5. After a run-in period of 6 months, patients with eGFR >30 ml/min, proteinuria <50 g/mol, excluding those who received T cell depleting therapy and/or rejection after month 3, were randomized. Standard tacrolimus with mycophenolate mofetil (TAC/MMF) was compared with the intervention: reducing by 50% and discontinuation of MMF at month 9 after transplantation (TACmono). Once-daily tacrolimus was targeted at 5-8 ug/L trough levels in both groups.
Results: 718 patients received a kidney transplant (living and deceased donor) between August 2014 and April 2018. 24% of them met inclusion criteria. At admission, 121 patients were included. After the 6 month run-in period 79 recipients were randomized to TACmono (n=38) or TAC/MMF (n=41). Baseline characteristics were similar for TACmono versus TAC/MMF with a mean recipient age of 59.6 vs 59.0 years, mean donor age of 48.5 and 48.8 years, percentage male 76% vs 71% and pre-emptive transplantation in 37% vs 34% of recipients. TAC trough levels were 7.5 and 7.2 ug/L at randomization. 3 TACmono and 2 TAC/MMF recipients experienced biopsy-proven acute rejection. Rejection episodes were reversible with methylprednisolone an reinitiating MMF. Renal function was significantly better after 12 months in TACmono recipients (61.7 vs 52.1 umol/L, p=0.04 per protocol analysis and 59.7 vs 52.1 umol/L, p=0.09 intentention to treat). TAC trough levels were similar 6.4 vs 6.1 (p=0.4). No allograft losses or patient deaths have occurred in 15 months follow-up.
We are currently analyzing vaccination responses and infectious episodes.
Conclusions: Tacrolimus monotherapy in immunologically low-risk recipients 9 months after kidney transplantation is safe.

Pneumococcal and tetanus vaccination in tacrolimus treated kidney transplant recipients with and without mycophenolate mofetil: a randomized controlled trial.

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Background: The Gezondheidsraad (Dutch medical council) advices to adopt the anti-pneumococcal vaccine PPV23 for all people of 60 years and older in the Rijksvaccinatieprogramma. Tacrolimus/ mycophenolate mofetil (TAC/MMF) is the current standard for immunosuppression after (kidney) transplantation. The impact of these drugs on pneumococcal vaccination is unknown. We have performed a randomized controlled trial in immunologically low-risk kidney transplant recipients comparing TAC/MMF with TAC monotherapy. This study provides a model to study differential effects of these drugs on vaccination responses.
Methods: Kidney transplant recipients (eGFR >30 ml/min; proteinuria <50 g/mol; free of depleting therapy; free of steroids) were randomized 6 months after transplantation to standard TAC/MMF or intervention TACmono. 63 per cent of recipients were ≥60 years. Twelve months after transplantation patients were vaccinated with pneumovax23 (PPV 23) and tetanus toxoid 40 IU. Serology was sampled directly before and 3 weeks after vaccination. The multiplex immunoassay measured antibody levels against 16 different common pneumococcal serotypes. If 9 or more titers were >1 ug/mL the vaccination response was defined as protective. None of the recipients had received prior anti-pneumococcal vaccination.
Results: Only 3 out 57 patients had protective anti-pneumococcal antibodies before vaccination. 42% of combined TAC/MMF treated patient had protective antibodies after vaccination, versus 77% of patients treated with TAC only (p 0.01). Age and renal function had no impact on antibody responses: in multivariate analysis, only the type of the immunosuppressive regimen correlated with protective antibody levels (Expb 1.18; p 0.012). All but two patients had protective baseline antibody titers against tetanus, although none of the patients reported vaccination in 5 years prior. The anti-tetanus titer increased 2.1 times in TAC/MMF versus 10.7 in TACmono treated recipients after vaccination (p <0.0001).
Conclusions: Treatment with TAC/MMF abates antibody responses after pneumococcal and tetanus vaccination. As for the recommended PPV23 vaccination, especially the addition of MMF seriously hampers protective responses. We are currently enrolling an extension study in which patients receive a PPV23 booster vaccine after 5 years.

A decade of ABO-incompatible kidney transplantation in the Netherlands.

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Background: In 2006, ABO-incompatible (ABOi) kidney transplantation was introduced in the Netherlands. It has become a standard procedure in many centers. We compared graft and patient survival between ABOi and ABO-compatible (ABOc) transplant recipients.
Methods: Data on all kidney transplantations performed since the first ABOi transplantation were obtained from the Dutch Organ Transplant Registry. Outcomes for ABOi, ABOc living and ABOc deceased donor transplantations were recorded. Using propensity scores, ABOi recipients were matched to deceased donor recipients in a 1:4 ratio. Likewise the ABOi recipients were matched to ABOc living donor recipients. The propensity score model included transplant center, recipient age, number of transplantations, peak panel-reactive antibodies (PRA) and dialysis duration.
Results: 10.689 Kidney transplantations were performed between March 2006 and January 2018, of which 277 ABOi procedures. If patients received a second ABOc kidney allograft in this period, only the first ABOc transplantation was included. 9.718 individual ABOc recipients were identified. After matching, baseline characteristics for the ABOi compared to the ABOc-living donor group were: recipient mean age 54 vs 53 years, donor mean age 55 vs 54 years, mean total HLA mismatches 3.2 vs 3.5, PRA 4% in both groups, retransplant 16% vs 8% and median dialysis duration 244 vs 195 days. 66% of ABOi recipients were blood group O. Induction therapies in ABOi recipients consisted of rituximab alone (57%), rituximab with basiliximab (13%) or alemtuzumab (30%). ABOi recipients had a higher risk of death-censored graft failure compared to ABOc living donor recipients (HR=2.22, 95%CI 1.36-3.64) and higher risk of death (HR=1.17, 95%CI 0.73-1.89), mostly in the first year of follow-up. Conversely, outcome risks were lower in the ABOi group compared to the deceased donor cohort (death-censored graft survival HR=0.66, 95%CI 0.43-1.01; and patient death HR=0.58, 95%CI 0.36-0.92).
Conclusions: ABO-incompatible kidney transplantation is favorable compared to deceased donor transplantation, but outcomes are inferior to matched ABOc living donor recipients. We are currently analyzing modifiable risk factors in order to improve outcomes after ABOi kidney transplantation.

Predictors for graft survival after pregnancy in kidney transplant recipients

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Background: Pregnancy after kidney transplantation (KT) is increasing during the last decades. Generally, pregnancy outcomes after KT are good. However, there is a high risk of gestational hypertension, preeclampsia and dysmaturity. Less is known about the effect of pregnancy on the kidney transplant. For counselling prior to pregnancy it is important to know risk factors for graft loss, and consequently recurrence to dialysis or re-transplantation, after pregnancy.
Methods: We conducted a nationwide retrospective multi-center cohort study in women with a pregnancy (>20 weeks) after KT in the Netherlands from 1960 to 2017. Data on transplantation, pregnancy and pregnancy outcomes were collected from health records. To explore predictors associated with graft survival after pregnancy we performed a Cox Regression Analysis.
Results: We could include 167 KT women with 244 pregnancies of which 96% ended in a live birth. 181 (74%) pregnancies were with the first kidney, 53 (22%) pregnancies were with a pre-emptive transplantation. Graft loss was present after 62 (25%) pregnancies at a median time after delivery of 6 yrs (range 0-30 yrs). In 20 (8%) pregnancies graft loss occurred within 3 years after delivery. In 34 (50%) women the cause of graft loss was rejection. In regression analysis preconceptional creatinine (p 0.00), gestational age of the pregnancy (p 0.02), postmortal donor transplantation (p 0.00) and pregnancy after first KT (p 0.02) were associated with better graft survival censored for death. Time between KT and delivery, preeclampsia and more pregnancies after KT were not associated with worse graft survival.
Conclusions: A worse pre-conceptional renal function, first kidney and a shorter gestational age are associated with a higher risk of graftloss in women with a KT. In contrast with the graftsurvival results in the general KT population, KT with a postmortal donor was associated with better graft survival after pregnancy. This may be the result of selection in the early days of transplantation, where pregnancy was only advised to women with relatively good kidney function. Further analysis of the individual slopes of eGFR pre- and post-pregnancy will be necessary to identify predictors for worse graft outcome after pregnancy in KT recipients. Although, in general pregnancy outcomes after KT are good, we have to realise that a significant proportion of women will have to be on dialysis or re-transplanted again while their children are still young.

Identification of new drug targets to prevent ischemia-induced bile toxicity using a human biliary organoid model.

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Background: Ischemic cholangiopathy (IC) is the most severe complication after liver transplantation (LT). Hypoxia during transplantation might accelerate bile toxicity in cholangiocytes, due to insufficient protection by CFTR-related bicarbonate (NH_3) secretion and thereby contribute to IC development. Liver-derived organoids (LDOs) resemble cholangiocyte-like cells which could be suitable models for testing this hypothesis. We investigated if LDOs have functional cholangiocyte transport-channels and could serve as a model for hypoxia-related biliary injury as well as be used for IC related drug-discovery purposes.
Methods: LDOs, cultured from donor livers reserved for LT, were analyzed on gene- and protein level for cholangiocyte-specific transporters (CFTR and AE2). Channel functionality was tested using an Ussing-chamber assay in 2D-grown organoids (n=42). Forskolin (cAMP-activator) added to the apical side of the cells, initiated CFTR activation which was specifically inhibited by GlyH. Hypoxic conditions were achieved by nitrogen gas (95%N_2/5%CO_2) exposure. To study bile-related toxicity, undiluted bile was added under oxygen and hypoxic conditions and cell death was analyzed. Finally, compounds were tested for the ability to abrogate the hypoxic-induced inhibition of CFTR.
Results: CFTR was expressed in all LDOs on both gene (qPCR) and protein (Western blot) level. Moreover CFTR could be activated by Forskolin in the Ussing chamber set-up. CFTR activity was lower when measured under hypoxic conditions compared to oxygen (1.66± 0.45 vs. 4.18 ± 0.48, p=0.005). Furthermore, a significant decrease in activity was observed when the same 2D-organoids were switched from oxygenated to hypoxic conditions (8.00 ±1.19 vs. 5.89±1.26, p=0.02). Further experiments showed that NH_3 is the driving factor when CFTR is activated in LDOs, suggesting that during hypoxia less NH_3 is excreted into the bile. When 2D-grown LDOs were exposed to bile, it resulted in more cell death in hypoxic versus oxygen conditions (31.2%±4.32 vs. 19.18±4.81, p=0.04). Most importantly, addition of compound C (cAMP-inhibitor) was able to rescue CFTR activity under hypoxic conditions.
Conclusions: LDOs provide an excellent model to study cholangiocyte-transporters. We demonstrate that hypoxia inhibits CFTR-related bicarbonate secretion and cAMP-inhibitor compound C can restore this. This encourages further clinical studies to test whether cAMP-inhibitors can prevent hypoxia-related biliary injury during graft preservation and after LT.

Immunologically tolerant liver transplant recipients are characterized by donor-specific hypo responsiveness of circulating T-cells

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Background: Lifelong treatment with immunosuppressive drugs (IS) to prevent graft rejection in transplant recipients is accompanied by side effects. Some recipients are considered to be immunologically tolerant towards their graft, as they have been safely withdrawn from IS late after liver transplantation (LTx). If tolerant (TOL) LTx recipients can be recognized and withdrawn earlier after LTx, related side effects may be reversed or avoided. Several studies have examined peripheral blood markers to identify TOL LTx recipients, but an accurate tolerance profile has not been determined yet. In this study, we evaluated CD137-expressing donor-specific T-cells upon a short-term stimulation as a potential identifier of tolerance.
Methods: TOL LTx recipients (n=10) withdrawn from IS for on average 4.2 years, and a control group on regular IS regimen (CTRL; n=12) matched for time after LTx (on average 15.2 years), primary disease, age, gender and CMV serostatus were included. Recipient peripheral blood mononuclear cells (PBMCs) were stimulated overnight in vitro with donor(-like) or third party splenocytes with the same number but different HLA mismatches as with donor. With flow cytometry, responses towards splenocytes were analyzed by quantifying expression of CD137, an activation-induced marker for antigen-specific T-cells. Naïve and memory T-cells were characterized by CCR7 and CD45RA and regulatory T-cells (Tregs) were characterized by FoxP3 and CD45RA expression.
Results: Phenotypically, total CD4 and CD8 T-cells, resting Tregs and activated Tregs did not differ between TOL and CTRL. Donor-specific CD4 and CD8 T-cell responses (ratio CD137+ T-cells: donor/unstimulated) were significantly lower in TOL compared to CTRL (mean CD4 TOL 1.4 vs CTRL 3.1 p=0.036; mean CD8 TOL 1.1 vs CTRL 2.4 p=0.049), whereas this was not observed for third party stimulation. In addition, less donor-reactive effector memory (EM) cells were observed within CD4 and CD8 T-cells in TOL compared to CTRL.
Conclusions: In TOL LTx recipients circulating donor-reactive CD4 and CD8 T-cells, in particular the EM T-cell compartment that are capable of migrating to the graft, are less frequent. This selective loss of EM T-cells may underlie hypo responsiveness to the graft in TOL. Overall, these results indicate that quantification of donor-specific T-cell reactivity by measuring activation induced CD137 hypo responsiveness may enable identification of TOL LTx recipients.

The Potential of Donation after Circulatory Death Heart Transplantations in the Netherlands

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Background: The number of patients on the waiting list for a heart transplant is still rising while the number of transplantations is decreasing. Currently, only donation after brain death (DBD) is performed in heart transplantation. However, in England and Australia the first centers have started accepting hearts from donation after circulatory death (DCD) with excellent results. This represents a new pool of donors. Cardiac screening in DCD procedures is not performed in the Netherlands. In this study, the potential of DCD heart donors in the Netherlands was investigated with the data supplied by the "Nederlandse Transplantatie Stichting".
Methods: We retrospectively reviewed all DCD procedures in the Netherlands from January 2013 until December 2017 and applied the in- and exclusion criteria from England and Australia; age, DCD class III, medical history (excluding cardiac disease, hepatitis B/C, etc.) and level of inotropic/vasopressor drugs.
Results: In these 5 years, 1006 DCD donors used for transplantation were identified. Of these, 319 donors were ≤50 years. After applying DCD exclusion criteria, 112 potential DCD heart donors remained. When the age limit was extended to ≤57 years, the number of potential DCD heart donors increased to 201. In comparison, in the same period 215 patients underwent a DBD heart transplant in the Netherlands.
Conclusions: DCD heart transplantation has a great potential in the Netherlands to decrease the time on the waiting list and reduce waiting list mortality. Cardiac screening in DCD procedures should become standard care to facilitate the potential of DCD heart transplantation.

Bile as a non-invasive source of cholangiocyte organoids for develping patient-specific disease modelling and personalized regenerative medicine.

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Background: Bile duct related diseases are the leading cause for pediatric liver transplantation and adult re-transplantation of a liver graft. Studying biliary diseases has long-term been hampered by the inability to culture bile duct lining cholangiocytes long-term. Recently was shown that Extra-hepatic Cholangiocyte Organoids (ECOs) that are derived from extra-hepatic bile duct (EHBD) tissue can be long-term expanded in culture. However, disease modeling or personalized regenerative medicine applications are limited since highly invasive bile duct biopsies are required to obtain these ECOs from individual patients. Therefore the aim of the current study is to investigate whether ECOs can be cultured from less invasively acquired bile fluid.

Methods: Bile-derived cholangiocyte organoids (BCOs) were cultured, according to the previous published protocol and collected from gallbladder bile obtained from donor livers for transplantation and from bile obtained by endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography drain (PTCD) in patients. In addition, ECOs were initiated from three different patients and compared to BCOs on the genetic level (qrt-PCR), protein level (either immunohistochemistry, immunofluorescence or Western blotting) and functional level by testing the cholangiocyte specific transporter channels (ussing chamber and transport assay).

Results: Cultures were initiated from 1 ml of bile obtained from all different sources. Bile-derived cholangiocyte organoids could be effectively (8/9 attempts) expanded from all sources of bile from patients with a variety of diseases (primary sclerosing cholangitis, cholangiocarcinoma, bile stones and biliary stenosis after liver transplantation). BCOs expressed similar cholangiocyte markers on gene and protein level as tissue-derived ECOs and both lacked either stem cell- or hepatocyte markers. Furthermore, these cells expressed and responded similarly to stimulation and inhibition of different cholangiocyte ion-channels. Interestingly, cholangiocyte-organoids from a patient with cystic fibrosis (CF) clearly lacked CFTR channel activity, showing that cholangiocyte-organoids can be used as a disease model to study biliary diseases.

Conclusions: Our study showed that bile provides a novel minimally-invasive source of patient-specific cholangiocyte organoids. This creates new opportunities to study autologous bile duct regeneration and develop patient-specific disease models.

10 years of islet transplantation in The Netherlands

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Pancreatic islet transplantation is performed at the Leiden University Medical Center since 2007. Starting as an experimental procedure, it is now increasingly commonplace. Here we describe the indications, procedure, and outcomes of pancreatic islet transplantation in The Netherlands.
Methods: Indications for allogeneic islet transplantation included patients with severe beta cell failure, such as type 1 or cystic fibrosis-related diabetes, in combination with severe hypoglycemia-related problems and/or progressive complications. Islet autotransplantation was performed in patients who required pancreatectomy for non-malignant pancreatic disease (i.e. chronic pancreatitis). Islet isolation was performed through combined enzymatic and mechanical digestion of the pancreas, followed by gradient density separation. The final product was tested for function and safety, after which the islets were infused through the portal vein under local anesthesia. Immunosuppression, when indicated, included T-cell depletion, prednisolone, mycophenolate and tacrolimus.
Results: 35 patients (21M/14F, age 51±10.3 years) underwent 55 allogeneic and two autologous islet transplantations. Islet graft function occurred in 34/35 of recipients with 46% of patients becoming insulin independent. Over time islet function declined, with insulin independence in 14% and partial islet function in 89% of patients after 47.9±30.0 months (range 4-123). HbA1c was reduced from 66.8±16.8 to 52.8±16.2 mmol/mol ($p<0.001$). In addition, patients with severe hypoglycemic events decreased from 39% to 6%.
Conclusion: Pancreatic islet transplantation restores endogenous insulin production in patients with diabetes due to severe beta cell failure or after pancreatectomy, leading to marked improvement in glycemic regulation and hypoglycemic events. Long term insulin independence is achieved only in a minority.

Cognitive Improvement in Kidney Transplant Recipients Exceeds Improvement in Kidney Donors and is Associated with Structural and Functional Changes on MRI

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Background: Several studies have reported improved cognitive outcomes after kidney transplantation, but these studies either did not include controls, or lacked extensive neuroimaging. In addition, there is uncertainty whether kidney donation is a safe procedure in terms of cognitive outcomes.
Methods: We designed a prospective study in kidney transplant recipients, using kidney donors as controls. The primary outcome was change in neurocognitive function after one year in recipients compared to donors, which was evaluated using the Amsterdam Neuropsychological Task battery and verbal fluency tests. Secondary outcomes included changes in depression and anxiety (measured by the Hospital Anxiety and Depression scale), and changes in fatigue (measured by the Checklist for Individual Strength). In addition, kidney transplant recipients were evaluated with MRI-scans at baseline and at year 1. The MRI protocol included conventional MRI (3D-T1, T2, FLAIR, 3D-FLASH), automated volumetric measurement, diffusion tensor imaging, magnetic resonance spectroscopy, arterial spin labelling, and a resting state functional MRI.
Results: 27 recipients and 22 donors were included. For both recipients and donors, neuropsychological testing scores improved one year after transplantation (donation). Recipient improvement exceeded donor improvement on tasks measuring attention and working memory. This was significantly correlated with an increase in white matter volume and N-acetylaspartate/creatine in kidney transplant recipients.
Conclusions: Kidney transplant recipients improve significantly more in attention and working memory after transplantation than kidney donors. This is possibly related to an improvement in white matter integrity after transplantation. Kidney donation is a safe procedure in terms of cognitive outcomes.

Disrupted regulation of serpinB9 in circulating T cells is associated with an increased risk for post-transplant skin cancer

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Background: Non-melanoma skin cancer such as cutaneous squamous cell carcinoma (cSCC) is a serious complication after organ transplantation and patients would benefit from an early risk assessment. We hypothesized that functional differences in circulating T cells may represent risk factors for post-transplant cSCC development.
Methods: In a first cohort of 19 kidney transplant recipients with a future cSCC and 19 matched kidney transplant recipients without cSCC, genome-wide DNA methylation was measured by Illumina's 450k arrays. Differentially methylated regions (DMRs) were identified and the most significant region was validated with pyrosequencing in a second cohort of 45 kidney transplant recipients during recurrent cSCC. Downstream effect on RNA and protein expression was measured with RT-qPCR and flow cytometry.
Results: Before the clinical onset of cSCC, the most significant DMR identified was located in the *SERPINB9* gene. *SERPINB9*, an intracellular inhibitor of granzyme B (an inducer of apoptosis), was significantly higher methylated in cSCC patients compared to non-cSCC patients ($p=1.1 \cdot 10^{-13}$). Also in the second cohort during recurrent cSCC, median DNA methylation of *SERPINB9* was higher in the cSCC patients compared to the non-cSCC patients (58.7% (32.5%-81.3%) and 50.2% (21.8%-77.5%); p=0.004). RNA expression was significantly correlated to DNA methylation only in the non-cSCC patients (r=-0.64, p=0.0003), indicating a disrupted transcription of *SERPINB9* in the cSCC patients. After poly-clonal stimulation, serpinB9 expression increased both in cSCC and non-cSCC patients but expression levels were significantly lower in cSCC patients compared to the non-cSCC patients (98.2% (93.0%-99.0%) vs 99.1% (97.2%-99.7%); p=0.006).
Conclusions: DNA methylation, transcriptional regulation and protein expression of serpinB9 in circulating T cells differs between cSCC and non-cSCC patients. This disturbed regulation of serpinB9 represents a novel risk factor for the development of cSCC after kidney transplantation.

Inhibitory monoclonal antibody to factor B attenuates brain death-induced renal injury and inflammation.

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Background: The majority of organs used for transplantation are retrieved from brain-dead organ donors. Brain death is characterized by irreversible loss of all brain function resulting in hemodynamic instability, hormonal changes, and immunological activation. Recently, brain death has been shown to cause activation of the complement system. Furthermore, complement activation in brain-dead donors is adversely associated with renal allograft outcome. Modulation of the complement system in the brain-dead donor might therefore form a promising strategy to improve organ quality prior to transplantation. This study investigated the effect of an inhibiting antibody against factor B on brain death-induced renal inflammation and injury.

Methods: Brain death was induced in male Fisher rats by inflating a subdural placed balloon catheter. Anti-factor B (anti-FB) or saline was administered intravenously thirty minutes prior to the induction of brain death (n=8/group). Sham-operated rats served as controls (n=4). After 4 hours of brain death, renal function, injury, inflammation and complement activation was assessed.

Results: Pretreatment with anti-FB resulted in significantly less local and systemic complement activation in brain-dead rats. Moreover, anti-FB treatment improved renal function, reflected by significantly reduced serum creatinine levels in anti-FB treated rats (saline: 60μM, anti-FB: 45μM, sham: 30μM). Furthermore, anti-FB significantly attenuated histological injury as seen by the reduced tubular injury score and lower renal gene expression of kidney injury marker-1 (KIM-1). More specifically, KIM-1 mRNA expression was reduced by more than 75% in anti-FB treated brain-dead rats. In addition, anti-FB treated rats had significantly less influx of neutrophils compared to controls, while no effect was seen on macrophage influx. In accordance, renal gene expression of IL-6, MCP-1 and VCAM-1 were also significantly reduced after anti-FB treatment, while a trend was seen for lower expression of IL-1β and P-selectin.

Conclusions: Altogether, this study shows that donor treatment with anti-FB significantly improved renal function, reduced renal damage and inflammation prior to transplantation. Therefore, inhibition of the alternative pathway, more specifically anti-FB, might be a promising strategy to reduce brain death-induced renal injury in organ donors.

The renin-angiotensin system is present and functional in ipsc-derived kidney organoids

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Background: The intrarenal renin-angiotensin system (RAS) arises early during kidney development and is important for proper nephrogenesis. The lack of a suitable human model to study the intrarenal RAS hampers deeper investigation into the relevance of this system. Recently protocols for the *in vitro* generation of kidney organoids from induced pluripotent stem cells (iPSC) have been developed.
Methods: Therefore, in this study we investigated the presence and functionality of the RAS in iPSC-derived kidney organoids. Four human iPSC lines were grown on Geltrex and treated with CHIR99201 (a Wnt agonist) and fibroblast growth factor 9, after which the cells were pelleted and transferred to a transwell membrane. The resulting organoids showed a 10- to 40-fold increase in mRNA for kidney-specific markers after 25 days of culture, including a marker for renin-producing stromal cells, FOXD1. Essential renal structures were observed using immunohistochemistry. Moreover, there was a 10-fold increase in the expression of the organic anion transporters OAT1 and OAT3, suggesting tubular function.
Results: Interestingly, the mRNA level of angiotensinogen (AGT) increased more than 100-fold as early as day 7 of the culture in comparison to iPSC and remained stable until day 25. Also, angiotensin receptor type 1 and type 2 mRNA expression increased and remained highly expressed throughout the culture, while high levels of ACE were also maintained in kidney organoids. Finally, a 10- to 100-fold increase in the mRNA expression of renin was observed at day 25. The use of an indirect enzyme-kinetic assay revealed the functionality of renin in the kidney organoids at day 25, as measured by the conversion of exogenously administered AGT to angiotensin I. Moreover, analysis of the medium harvested from kidney organoid cultures at day 25 exhibited varying amounts of renin activity, ranging from 12 to 200 ng angiotensin I/ml per hour. The addition of the cyclic AMP-elevating agents forskolin and dibutyryl cyclic AMP to the culture for 24 hours increased the mRNA expression of renin drastically (up to 1000-fold), indicating that the production of renin in the kidney organoids may be a regulated and inducible process.
Conclusions: In summary, we demonstrate the presence and functionality of components of the RAS in human iPSC-derived kidney organoids. This provides the opportunity to study the intrarenal RAS and its regulation in an *in vitro* human model.

Targeted proteomic analysis detects acute T cell-mediated kidney allograft rejection in belatacept-treated patients

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Background: There is an unmet need for reliable minimally-invasive diagnostic biomarkers for immunological allograft monitoring and detection of acute kidney transplant rejection. Here, targeted proteomic analysis was applied to compare 92 proteins in sera of belatacept-treated patients who had a biopsy-proven, acute T cell-mediated rejection (aTCMR) with patients without an aTCMR.
Methods: Serum samples were collected from kidney transplant recipients who participated in a prospective, randomized-controlled trial between 2013 and 2015. Proximity extension immunoassay (PEA) was used to measure 92 inflammation-related protein concentrations in pre-rejection (day 30 after transplantation) and rejection sera of 11 patients with an aTCMR and 9 patients without an aTCMR. PEA uses two matched oligonucleotide-labelled antibody probes for each protein and PCR to measure normalized protein expression values.
Results: Five proteins (CD5, CD8A, NCR1, TNFRSF4 and TNFRSF9) were expressed significantly higher in samples of patients with an aTCMR compared with samples of patients without an aTCMR (adjusted p-value<1.14E-02) and had a good predictive capacity for an aTCMR (area under the curve of a receiver operator curve ranged from 0.83 to 0.91 [p<0.014]). The pathways most enriched among these 5 proteins are related to T cell activation, T cell proliferation, and NK cell-mediated immune responses. Non-hierarchical clustering analysis showed distinct clustering of samples of patient with an aTCMR and of samples of patients without aTCMR. This clustering was not seen in pre-rejection samples. In pre-rejection samples, IFN-γ was expressed at a significantly lower level (NPX value median -0.15, IQR -0.27 - 0.04) than in samples of patients without rejection (median 0.13, IQR -0.07 - 0.15, adjusted p-value=3.67E-03).
Conclusions: Targeted proteomic analysis with PEA was used for the first time in kidney transplant patients and detected aTCMR in sera of belatacept-treated patients. PEA appears to be a promising minimally-invasive technique to diagnose an aTCMR.

Donor-specific memory T cell responsiveness decreases after kidney transplantation

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Background: High numbers of donor-reactive IFN-γ and IL-21 producing peripheral blood mononuclear cells (PBMCs) pre transplantation have been shown to be associated with early acute rejection. However, knowledge about the presence of these cytokine producing cells in patients more than 1 year after transplantation is lacking. In the present study, we investigated the frequency of donor-specific IL-21 and IFN-γ producing cells in renal transplant patients prior to transplantation until 5-7 years after transplantation.
Methods: PBMC samples from 44 kidney transplant patients were obtained pre transplantation, at 1 year and at 5-7 years after transplantation. The frequency of IL-21 and IFN-γ producing PBMCs was analyzed by enzyme-linked immunospot assay (Elispot). Patient PBMC were stimulated with irradiated donor or third-party cells, which were completely HLA-mismatched with donor and recipient. Unstimulated patient PBMC served as negative control. Stimulation with a cocktail of peptides to influenza, CMV and EBV (ICE) and staphylococcal enterotoxin B (SEB) served as positive control for the HLA class I and class II response, respectively.
Results: The number of donor-reactive IL-21 and IFN-γ producing PBMCs was lower at 1 year compared to pre transplantation [median and interquartile range: $22/3x10^5$ PBMC (10-57) vs. $6/3x10^5$ PBMC (4-16), $p<0.0001$] and $26/1x10^5$ PBMC (12-51) vs. $7/1x10^5$ PBMC (5-17), $p=0.002$, respectively]. This difference with pre-transplantation samples was also significant in samples obtained 5-7 years post transplantation [$22/3x10^5$ PBMC (10-57) vs. $11/3x10^5$ PBMC (5-25), $p<0.0001$] and $26/1x10^5$ PBMC (12-51) vs. $11/1x10^5$ PBMC (5-26), $p=0.009$, respectively]. In contrast, the response against 3rd-party cells, ICE and SEB remained stable over time.
Conclusions: Our data suggest that donor-specific hypo-responsiveness is present at 1 year after kidney transplantation and can still be demonstrated 5-7 years later. At the same time, anti 3rd-party immunity and responses to antigens presented by HLA class I and class II are maintained. This could imply that allograft tolerance might occur from one year after transplantation onwards. A better understanding of the mechanisms underlying allograft tolerance could help overcome chronic rejections and immunosuppressive side effects.

A single nucleotide donor C3 polymorphism associates with clinical outcome after lung transplantation

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Background: Development of rejection is still a severe problem and causes high mortality rates after lung transplantation (LTx). Complement activation is important in the development of acute rejection (AR) and bronchiolitis obliterans syndrome (BOS), with C3 as a key complement factor.
Methods: Since a single nucleotide polymorphism (SNP) in the C3 gene (rs2230199) is associated with long-term outcome after solid organ transplantation, we investigated this SNP in relation to LTx. In addition, we looked at local production of C3 by analyzing bronchoalveolar lavage fluid (BALF) of LTx patients using isoelectric focusing (IEF).
Results: We demonstrated the presence of C3 in BALF and showed that this is produced by the donor lung based on the genotype of SNP rs2230199. We also analyzed donor and patient SNP configurations and observed a significant association between the SNP configuration in patients and episodes of AR during 4-years follow-up. Survival analysis showed a lower AR-free survival in homozygous C3 slow patients (p=0.005). Furthermore, we found a significant association between the SNP configuration in donors and BOS development. Patients receiving a graft from a donor with at least one C3 fast variant for rs2230199 had an inferior BOS-free survival (p=0.044).
Conclusions: In conclusion, our data indicate local C3 production by donor lung cells. In addition, a single C3 SNP present in recipients affects short-term outcome after LTx, while this SNP in donors has an opposite effect on long-term outcome after LTx. Further research is needed to validate these results in a larger cohort.

Organ resilience contributes to different impact of delayed graft function on graft survival in kidneys donated by brain death and circulatory death donors.

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Background: Despite a three times higher incidence of delayed graft function (DGF) in kidney grafts Donated after Circulatory Death (DCD) donors compared to those Donated after Brain Death (DBD), large studies show equivalent long-term graft survival with DBD and DCD grafts. This implies differential impacts of DGF on DCD and DBD graft survival. Maybe DGF is more severe in DBD grafts, and/or DCD grafts are more resilient. The aim of this study was to assess the biological basis of differential impacts of DGF on long-term outcome of DBD and DCD grafts.
Methods: The impact of DGF on long-term graft survival was analysed for 3744 DBD and 2891 DCD kidney transplants performed in The Netherlands between 2000 and 2018. The severity of DGF was estimated for 640 DBD and DCD kidneys transplanted at the LUMC by evaluating the number of posttransplant dialyses and postoperative functional recovery (eGFR).
In parallel to findings in tumour biology, where p53, phospho-EGFR, IGF-1R, phospho-mTOR, phospho-MAPK14, PCNA, BCL2 and PPARγ are associated with tumour resilience, we determined expression of these factors by immunohistochemistry in pre-reperfusion kidney biopsies (DBD n=40; DCD n=40). Gene expression profiles (array analysis) followed by Ingenuity Pathway Analysis was performed to identify pathways differentially activated in 8 DBD and 7 DCD grafts.
Results: Our data confirmed a higher incidence of DGF in DCD grafts (DCD 42% vs. DBD 18%). This higher incidence of DGF did not impact long-term graft survival. Multivariate analysis showed that this was mainly due to differential impact of DGF on long-term outcomes, with a major impact in DBD grafts (RR: 1.62, 95%CI: 1.24-2.11) but no significant impact in DCD grafts (RR: 1.29, 95%CI: 0.96-1.73). This was not caused by a more severe form of DGF in DBD grafts, a conclusion based on equal numbers of DGF-associated dialyses and superior posttransplant eGFRs in DBD grafts.
Immunohistochemistry showed expression of all components of the resilience network in biopsies. Pathway analysis identified 24 differentially expressed pathways with the resilience associated pathways EGF-signalling (p:0.003), BRCA1 (p:0.005) and p38-MAPK-signalling (p:0.009) in the top-6.
Conclusions: The absent impact of DGF on long-term graft survival in DCD kidneys is paralleled by activation of dedicated resilience pathways. Targeting of these pathways may provide a major opportunity to modulate organ resilience in kidney transplantation.

Expanding the donor pool by extended DCD lung donation

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Introduction: Almost half of the lung transplantations in the Netherlands are performed with donation after circulatory death (DCD) donors. However, over 25% of the DCD donations are cancelled because the agonal phase exceeds the current maximum length for donation: 120 minutes. Pig models testing lungs ex-vivo (EVLP) have shown that a prolonged agonal phase doesn't compromise the quality of the lungs. Given the possibility to test lungs on the EVLP before transplantation the length of the agonal phase might be less important in DCD lung donation. In 2017 four suitable DCD lung donations out of 20 DCD procedures in our center were cancelled due to a prolonged agonal phase. In 2018 three out of 18 DCDs were cancelled so far. We therefore here present a protocol to accept DCD lung donation irrespective of length of the agonal phase.
Methods: Informed consent will be obtained from patients on the lung transplant waiting list from our center to receive extended DCD (eDCD) lungs. All suitable DCD lung donors from our center will be included. When a donor exceeds the 2 hour agonal phase limit for regular organ donation, the donor becomes an eDCD donor and donation then is limited to the lungs. When a donor passes, after five minutes 'no touch', the donor will be transported to the OR for intubation. Lungs will be inflated by CPAP until the thoracic surgeons are available for procurement. After opening of the chest the lungs will be ventilated according to Dutch DCD guidelines. All eDCD lungs will be evaluated during EVLP after procurement. When the lungs are suitable for transplantation after evaluation on the EVLP they will be transplanted in a recipient who gave consent to receive eDCD lungs.
Discussion: Currently, many potentially suitable lungs are not procured due to the prolonged agonal phase. It is going to be a logistic challenge to procure these lungs after a prolonged agonal phase. However, with the use of EVLP, lungs can be evaluated before transplantation and logistics can be managed. Therefore, we expect to increase the number of lung donations in our center with 3-5 per year by eDCD .

Anti-hypertensive drug adherence in lung transplant recipients

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Background: Lung transplant recipients are on life-long use of immunosuppressants. These immunosuppressive drugs cause side effects, and will increase the chance to develop hypertension and renal impairment. Despite the importance of adherence for taking antihypertensive drugs, no studies have been performed in patients after lung transplantation. The nurse practitioner can play an important role in diagnosing, treating and informing lung transplant recipients about antihypertensive medication when necessary during follow up.
To evaluate the role of the Nurse Practitioner (NP) and to stimulate drug adherence and provide good information to patients it was necessary to identify factors which are involved in adherence. This study was initiated to evaluate the extent of anti-hypertensive drug adherence in lung transplant recipients with hypertension and/or renal impairment. It was also meant to gain more insight in what motives could contribute to adherence. The next goal was to contribute to better information and support to lung transplant patients by an NP.
Methods: A total of 21 lung transplant recipients with Cystic Fibrosis (CF) filled in a questionnaire in which the adherence to antihypertensive agents was measured. In addition, the attitude towards drug use was measured. The questionnaire contained the MMAS-questionnaire and nine different theses. Thereafter, eight of the 21 patients were interviewed by semi-structured interviews. Different motives to adherence were assessed in those interviews. A list of topics was used.
Results: Incidence rates of high adherence was 76.2% and 23.8% scored a medium adherence. Overall, the attitude towards drug use was positive. Most of the lung transplant recipients (88.9%) agreed with the treatment with medication and no one experienced difficulty in taking medication.
The patients found it hard to differentiate between the side effects of antihypertensive drugs and the side effects of other medication. More than half (55.6%) who completed the questionnaire indicated that the information at the start with antihypertensive drugs was insufficient.
Conclusions: A high degree of adherence was scored. Motives that could reduce adherence were absence of complaints due to hypertension and/or renal impairment, side effects of antihypertensive agents, high number of medication, reduced importance of antihypertensive agents compared to immunosuppressants, absence of daily routine and limited information. The patients had limited knowledge about the role of a NP.

Leverdonatie bij leven ten behoeve van een kind, een update van ons programma en de rol van de verpleegkundig specialist leverdonatie.

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Background: Levende donor levertransplantatie is ontstaan vanwege een tekort aan postmortale donorlevers en de toenemende urgentie voor een levertransplantatie bij een jong kind met eindstadium leverfalen. De achteruitgang van de conditie van het kind doet de kans op postoperatieve complicaties (en op overlijden) toenemen. Vaak betreft het een kind met biliaire atresie bij wie de Kasai-operatie niet aanslaat en waarbij levertransplantatie de enige behandeloptie is. Levende donor levertransplantatie(LDLT) wordt sinds 2004 in toenemende mate uitgevoerd. De resultaten bij kinderen na levertransplantatie met een gedeelte van de lever van een levende donor(vaak segment 2,3) zijn succesvol , met een 5-jaarsoverleving van 95%. Mede dankzij een uitgebreid gescreende, gezonde donor (meestal een ouder) en optimale timing van de operatie. Nieuw in het LDLT programma is een toename van het aantal altruïstische leverdonoren, die reeds een donornefrectomie ondergingen. De keerzijde van LDLT is de potentiële morbiditeit (15-25%) en mortaliteit (0,15-0,50%).
Results: Vanaf 2004 zijn er in totaal 60 LDLT in ons centrum verricht, waarvan in 2018 12 LDLT. In 2018 werden in totaal 30 donoren (gedeeltelijk) gescreend.
LDLT is teamwork en vraagt om een multidisciplinaire benadering. De verpleegkundig specialist leverdonatie speelt hierin een belangrijke rol. Zij werkt samen met de internist-hepatoloog in het kader van de medische screening van de donor. Zij werkt o.a. samen met de kinderafdeling, afdeling chirurgie, anesthesie en paramedici. Zij coördineert, zorgt voor continuïteit en is een belangrijk aanspreekpunt voor de donor. Zij geeft voorlichting en begeleidt de donoren en naasten gedurende de gehele procedure.
Conclusions: Separate aandacht voor de donor is belangrijk, zeker wanneer de meeste aandacht uit gaat naar het zieke en getransplanteerde kind. In ons centrum vervult de verpleegkundig specialist hierin een specifieke rol.

Moet ambulante bloeddrukmeting onderdeel zijn van screening nierdonatie bij leven?

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Background: Hoge bloeddruk is, samen met overgewicht, oudere leeftijd en nierziekten, een bekende risicofactor voor het krijgen van nierschade en nierfunctieverlies. In Nederland komt hypertensie voor bij 25% van de volwassenen in de leeftijd van 20 tot 70 jaar.
Tot 2002 was hypertensie een absolute contra-indicatie voor het doneren van een nier bij leven. Omdat milde hypertensie in de bevolking vaak voorkomt mogen sinds 2002 hypertensieve donoren een nier doneren, op voorwaarde dat de bloeddruk met maximaal twee bloeddruk verlagende middelen onder controle is.
Het is onbekend hoeveel nierdonoren in ons centrum hypertensie hebben of behandeld worden voor hypertensie voor nierdonatie.
Methods: Retrospectief dossieronderzoek bij nierdonoren die tussen mei 2017 en mei 2018 voor screening kwamen en een ABPM kregen. Daarnaast werden gegevens verzameld over bloeddruk in de spreekkamer, herhaalde APBM indien hypertensie, leeftijd en geslacht, nierfunctie, albuminurie, medicatiegebruik en medicatie start.
Results: Van 66 nierdonoren, 22 man en 44 vrouw, hadden 38 donoren (58%) hypertensie (>140/90mmHg) in de spreekkamer. De gemiddelde bloeddruk bij ABPM was 128/74mmHg. Na ABPM hadden 12 donoren hypertensie en maar liefst 43 van de 53 normotensieve donoren hadden een witte jas-effect. Bij 5 van de 12 donoren met hypertensie (>130/80 of dag >135/85 of nacht >120/70mmHg) werd geen medicatie gestart, 2 gebruikten thuis al medicatie, waarvan 1 donor medicatie erbij kreeg en 5 donoren startten met medicatie. Bij 4 donoren werd een tweede ABPM ter controle uitgevoerd, die een goede bloeddruk liet zien. Bij de 2de spreekkamer bloeddrukmeting (N=41) tijdens de screening, werd bij 15 donoren nog steeds een verhoogde spreekkamer bloeddruk gemeten.
De eGFR was bij 62% van de donoren >90ml/min en bij de overige donoren tussen de 60-89ml/min. Albuminurie tussen 3-30mg/mmol kwam voor bij 10 donoren. De overige donoren hadden geen albuminurie.
Conclusions: Ambulante bloeddrukmeting geeft waardevolle informatie over het wel of niet aanwezig zijn van hypertensie bij nierdonoren bij aanvang van de screening en of er sprake is van een witte jas-effect.
Deze gegevens helpen bij het maken van een besluit over wel/niet starten van medicatie en of donoren voor de toekomst beter thuis bloeddruk kunnen meten in plaats van bij een zorgverlener. Donoren met bewezen hypertensie tijdens de screening zouden behandeld moeten worden vóór nierdonatie.

AB0 incompatibele niertransplantatie anno 2018 in het UMCG, 10 jaar ervaring

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Background: Sinds 2008 worden er AB0 incompatibele transplantaties uitgevoerd in het UMCG. Tot 2015 waren dat er 20. In 2015 is het protocol aangepast en hebben we met het nieuwe protocol nu 30 patiënten getransplanteerd.
Methods: retrospectief onderzoek naar de resultaten
Results: De resultaten van de laatste 30 transplantaties zijn vergelijkbaar met de resultaten van compatibele living niertransplantaties . We kijken dan naar complicaties en rejectie.
Conclusions: Voor patienten die geen bloedgroep compatibele levende donor hebben en in de cross-over geen match hebben is dit programma een uitstekend alternatief

High intra-patient variability in tacrolimus exposure is not associated with immune-mediated graft injury after liver transplantation

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Background: A high intrapatient variability in tacrolimus exposure is associated with impaired long-term clinical outcome after kidney transplantation. It remains to be determined if a high tacrolimus intrapatient variability is equally detrimental for liver transplant recipients. The objective of this study was to investigate the association between intrapatient variability in tacrolimus exposure and immune-mediated graft injury after liver transplantation.
Methods: For 326 liver transplant recipients, transplanted between 2000 and 2015, tacrolimus intrapatient variability was calculated from at least 5 tacrolimus trough samples obtained between month 6 and 18 after liver transplantation and was expressed as the coefficient of variation. The primary composite endpoint consisted of immune-mediated graft injury (chronic rejection, biopsy proven late-acute rejection and suspected late-acute rejection) after month 6 post-liver transplantation. Secondary outcomes were the association between tacrolimus intrapatient variability on (1) loss of renal function per year of follow-up and (2) cytomegalovirus viremia after month 6 post-liver transplantation.
Results: Of the 326 included liver transplant recipients, 70 patients (21.5%) reached the primary endpoint. Median tacrolimus coefficient of variation was 28%. There was no significant difference in reaching the primary composite endpoint between the low and high tacrolimus variability group (p=0.068). Tacrolimus intrapatient variability modeled as a continuous variable remained non-significantly associated with the risk of reaching the primary endpoint in a multivariable analysis. MELD-score pre-transplantation and the number of acute rejections were identified as independent predictors for immune-mediated graft injury (p=0.049, p=0.016). For the secondary endpoints, a higher tacrolimus variability in combination with a low kidney function at baseline (eGFR < 40 ml/min) was associated with greater loss of renal function per year of follow-up (p=0.007). Tacrolimus variability was not associated with late cytomegalovirus viremia.
Conclusions: High intrapatient variability in tacrolimus exposure beyond month 6 post-liver transplantation was not found to be associated with immune-mediated graft injury.

Personalized screening schedules to monitor the development of chronic renal allograft failure

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Background: In the current study, we aimed to optimize the monitoring of kidney transplanted patients based on personalized risk estimates and compare such personalized screening with the one-size-fits-all protocol that is currently being used in our hospital. Such a personalized screening approach could potentially lead to a lower medical and financial burden in renal transplant patients with stable transplant function without losing important information on patients at risk for irreversible graft failure that would require timely intervention.
Methods: We included adult patients transplanted between 1996 and 2009 who had >1 additional SCr (umol/L) and spot or 24-hour urine collection to calculate the urine PCR (g/mol). A Joint Model was constructed to model the association between longitudinal markers of renal function and death-censored graft failure. As a proof of concept, we applied personalized screening intervals and compared this to the fixed screening approach in the number of screening intervals and graft failure offset, defined as the time difference between estimated intervention time and observed graft failure time.
Results: We included 238 renal transplanted patients with 13062 SCr measurements and 9616 PCR measurements. Majority were recipients of deceased donors (74.1%). Mean recipient age was 50.7 (SD 12.7) years, and majority firstly transplanted (84.5%). Death-censored graft survival was 83.9% (95%CI 78.2-89.6) at 5 years. A joint model that included both the SCr and the PCR trajectories did not reveal an increased time-dependent (t)AUC compared to a model that only included SCr trajectories ([t]AUC > 0.8 up till 2.5 years). The personalized screening approach resulted in obtaining less SCr measurements with a median (IQR) of 14 (6.0) versus 29 (8.5) visits. The time to intervene and overcome the risk for graft failure was comparable with the fixed schedule (14% versus 12% missed cases with graft failure).
Conclusions: A personalized screening could be applied for monitoring renal transplant patients. Patients who remain relatively stable may not require frequent measurement of SCr, and patients for whom the graft function deteriorates faster, a frequent schedule of SCr may be required to determine the best moment for intervention. Our findings have to be externally validated in other observational cohorts.

Reducing hepatectomy times in all Dutch organ procurement teams

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Recent literature shows that a hepatectomy time >60 minutes negatively influences DCD liver transplant results. An internal audit showed that approximately half of the DCD donor hepatectomies performed in the Netherlands took more than one hour. This led to a joint challenge by the Independent Procurement Teams (IPTs) to decrease DCD donor hepatectomy time without impairing procurement quality.
Between March and June 2018, we intervened by creating awareness, identifying local habits of IPT's, stimulating cooperation and knowledge exchange between teams and refreshing theory and techniques on organ procurement. We analyzed DCD and DBD hepatectomy times in general and in the five IPTs before and after the intervention period, stratified by donor type. We adjusted for BMI, age and the combination with thoracic procurement in a multivariate linear regression model.
We analyzed 237 donor livers procurements between August 2017 and November 2018. This cohort included three different periods: a historical (n=103, 7 months), intervention (n=53, 3 months) and post intervention (n=81, 5 months*) period. The mean DCD hepatectomy time in the historical group was 76 ± 35 minutes. This significantly decreased during and after intervention to 49 ± 20 minutes and 42 ± 12 minutes respectively (ANOVA, $p<0.001$). 97% of all DCD hepatectomies were retrieved within one hour compared to 42% in the historical group. A beneficial significant effect on procurement times was also seen in DBD livers, from 51 to 46 and 40 minutes in respectively the historical, intervention and post intervention period(ANOVA, p0.011). Before the intervention there were substantial differences in liver extraction time between IPTs. After the intervention, all IPTs had decreased their DBD and DCD hepatectomy times and mutual differences decreased. Multivariate analysis showed that the decrease of hepatectomy times was not due to confounders. Faster procurement had no negative effect on reported surgical liver injuries, liver acceptance and transplantation.
Our results show significant and clinically relevant reduction in hepatectomy times during DCD and DBD organ procurement procedures in the Netherlands through a national collaboration and joint effort to raise awareness and exchange knowledge and skills.

*this evaluation will be extended with data until December 2018.

Using a Massive Open Online Course on Clinical Kidney, Prancreas and Islet Transplantion in different settings of transplant education

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Background: In 2016 our center launched a Massive Open Online Course (MOOC) on Kidney, Pancreas and Islet Transplantation. As opposed to on-campus education, this course delivers learning objectives online through a series of short videos, interactive patient cases, animations, discussions and interviews. The MOOC targets (bio)medical students and healthcare professionals. Integration of different settings of our MOOC both globally and in campus were evaluated.
Methods: The MOOC was offered monthly to learners worldwide and demographic data were obtained. Integration of the MOOC into the 2nd year of the local medical curriculum took place in two regular courses. For the first course, parts from the MOOC were used to replace traditional teaching; in the second course several movies, the discussion forum and a clinical patient case assignment were offered. Students were asked to fill out a questionnaire using a 5-point Likert scale. In addition, the complete MOOC was offered to students from the University extracurricular Honours track (HT) and the yearly Transplantation Summerschool (LOTS) for bachelor students.
Results: Over 10.000 learners from over 90 countries signed up for the MOOC. 76% learners had a higher education. 325 students signed up for the MOOC to use materials during the on-campus courses. 56 students (17%) responded to the online questionnaire. Respondents indicated that the MOOC elements were an interesting addition to the face to face curriculum (3.3 ±0.9) and that the online lectures and discussion forums were inspiring (3.1 ±1). Of the students 62% explored to some extent other parts of the MOOC outside the provided assignments. For the HT and LOTS, 20 students signed up for the MOOC. Their engagement with the online materials and participation in discussion forums seems to be much higher compared to the medical school students as almost all students explored optional parts of the MOOC.
Conclusion: Individual online resources in a medical MOOC or an entire MOOC can be used successfully in different settings of transplant education, including worldwide teaching and in on-campus teaching. The high quality materials, interactivity and online discussions offer added value to traditional classroom teaching. Students in the regular medical curriculum slightly explore other parts of the MOOC, while HT and LOTS students do that in great extent. Further research is needed to see how students can be more encouraged to gain as much as possible from the content rich resources in the MOOC.

New ways of reporting on Dutch lung transplant waiting list and outcomes

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Through standardized information the Dutch Transplant Foundation (NTS) and the national thoracic transplantation advisory committee (LOTTO) want to provide patients insight in factors that influence lung waiting list and transplant outcomes. The first issue of the yearly patient report includes the waiting list of 1/1/2018, overviews on lung waiting list dynamics, mortality and transplantation, and transplant outcome. The data are stratified for ranges of Lung Allocations Scores (LAS) and 5 groups of primary diagnoses for transplantation (obstructive lung disease, pulmonary vascular disease, cystic fibrosis or immunodeficiency, restrictive lung disease, and other lung diseases).
The report shows a stable waiting list with 181 and 182 patients on 1/1/2015 and 1/1/2018 respectively, with 2 or 3 patients on high or exceptional LAS. However, the proportion of patients with obstructive lung disease increased 15% while for cystic fibrosis it declined with 45%. Mean LAS scores were lowest for obstructive lung diseases on both times (32.6 and 32.1 respectively). The patients in this group therefore have the longest average transplant waiting time (1.9 year, versus 0.6-1.5 year in other groups). Patients with restrictive lung disease died more rapidly on the waiting list, 68% of the patients that died on the waiting list died within 6 months, versus less than 30% in the patients with obstructive lung disease, pulmonary vascular disease and cystic fibrosis. However, this group of patients has a relatively short waiting time for transplantation (0.8 year). In the restrictive lung disease group more patients (27%) received a single lung transplant (others range: 3-10%). Overall 5-year survival (in the 2009-2013 cohort) and 1-year survival (in the 2015-2017 cohort) were 69% and 83% respectively.
The first annual lung transplant waiting list and outcome report provides insights in the current Dutch lung transplant waiting list and differences per patient group which can be useful for informing patients.

Long term graft function and graft loss following pregnancy in kidney transplant recipients: a systematic review and meta-analysis.

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Background: The incidence of pregnancy in kidney transplant recipients is increasing. Although short-term graft outcomes are positive, less is known on long term effects of pregnancy on graft loss and serum creatinine. The aim of this study is to investigate the effect of pregnancy on graft function.
Methods: We conducted a systematic review scoping graft loss and serum creatinine change after pregnancy in kidney transplant recipients. Data that was extracted includes pre-pregnancy and post-pregnancy serum creatinine, whether graft loss occurred post-pregnancy and predictors of adverse outcome.
Results: Our search yielded 36 studies on graft loss after pregnancy and 19 articles on pre- and post-pregnancy serum creatinine. Pooled incidence of graft loss and mean change of serum creatinine pre- versus post pregnancy (delta serum creatinine (ΔSCr) in different periods of time. Patient data was pooled by subcategories for graft loss and ΔSCr. Graft loss within two years post-pregnancy occurred in 7.0% of the cases, graft loss two to five years post-pregnancy in 9.2%, five to ten years 21.5% and graft loss more ten years post-pregnancy occurred in 33.6% of the patients. ΔSCr was significantly deteriorated in patients with short term follow up, less than two year post-pregnancy. Deterioration of SCr post-pregnancy compared to pre-pregnancy SCr within two year post-pregnancy is 0.10 mg/dL [0.02;0.28], p=0.01. In the other subcategories, follow up two to five year, and five to ten year post-pregnancy, no significant difference in ΔSCr was present. Compared to control groups no difference was found in graft loss and ΔSCr. Only a marginal increase of serum creatinine shortly after pregnancy was found in kidney transplant recipients. Reported predictors of adverse outcomes on graft function and risk of graft loss are hypertension prior to pregnancy, presence of proteinuria prior to pregnancy, preeclampsia, transplant to conception interval and higher level of serum creatinine prior to pregnancy.
Conclusions: The outcomes of graft loss and serum creatinine after pregnancy in kidney transplant recipients are reassuring. The findings of this meta-analysis are encouraging when we compare graft loss after pregnancy to graft loss in kidney transplantation recipients without pregnancy. It does not seem that pregnancy after kidney transplantation shortens graft survival.

Pancreas donation after euthanasia - a suitable islet source for transplantation?

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Background: In the Netherlands organ donation after euthanasia (medically assisted cardiocirculatory death category 5 (DCD5)) is possible. The percentage of DCD5 out of the total number of organ donations is steadily increasing (0.3% in 2012 to 5% in 2017). DCD5 donor pancreata for islet transplantation would be useful in the context of organ shortage. Nonetheless, it is still unclear whether a DCD5 procedure, that entails neuromuscular blockade with nicotinic receptor antagonists, affects the number and function of isolated islets. The aim of this study was to evaluate the suitability of DCD5 organs for islet transplantation and to compare islet yield and function with organs procured during DCD awaiting cardiac arrest (DCD3), the most common controlled DCD procedure.
Methods: DCD5 organs (n=16) and DCD3 organs (n=48) were accepted for islet isolation. Donor and organ characteristics, islet isolation outcome and islet survival were analyzed. Additionally, islet function was determined using a dynamic glucose stimulation assay. Data are represented as mean ± SEM.
Results: DCD5 and DCD3 donors had a comparable age (52 ± 2.6 and 46 ± 1.6 resp (p=0.054), BMI (25 ± 1.3 and 26 ± 0.6, p=0.21) and pancreas weight (96 ± 4.5 and 112 ± 4.5 (p=0.062). There was no significant difference in islet yield (total IEQ DCD5: 368,000 ± 42,000, DCD3: 530,000 ± 82,000 (p=0.052)), IEQ/gram digested tissue (DCD5: 4626 ± 530, DCD3: 5500 ± 462 (p=0.313)) or islet survival (DCD5: 81 ± 6%, DCD3: 86 ± 4% (p=0.502)). Upon a glucose challenge DCD5 islets showed a significant lower insulin secretory response with reduced area-under-the curve for insulin (DCD5: 12 ± 2.2 and DCD3: 32 ± 3.7 (p=0.003)).
Conclusions: Islet yield and survival is comparable after isolation from DCD5 and DCD3 organs. Despite the lower insulin secretory response DCD5 organs are likely to be a suitable islet source for islet transplantation but clinical studies are needed.

A comparison of the BAR, DRM, DRI, sRRI, ET-DRI, D-MELD and SOFT score to predict outcome after liver transplantation in the SRTR database

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Background: Several risk models have been developed to predict outcome after liver transplantation (LT) in the last decade. This study analyzes the ability of most well-known risk models to predict patient, overall graft and death-censored graft survival at short- and long-term follow-up after transplantation.
Methods: Data included information from the SRTR database on LTs from deceased donors performed in adults (≥18 years old) from January 1st, 2005 until December 31st, 2015. For all LTs the BAR-score, DRI, ET-DRI, DRM, sRRI, SOFT and D-MELD scores were calculated. Model performance was evaluated by the discriminative capacity and area under the ROC-curve (c-statistic) for patient survival, overall graft survival and death-censored graft survival. High-risk transplantations were defined as scores above 80th percentile according to the respective risk models.
Results: In the study period, 62,294 LTs were included. Patient survival at 3 months was best predicted by the SOFT (c-statistic: 0.68) and BAR score (c-statistic: 0.64) while the DRM and SOFT score had the highest predictive capacity at 5 years (c-statistic: 0.59). Overall graft survival was best predicted by the SOFT-score at 3-months (c-statistic: 0.65), and by the SOFT and DRM score at 5-year follow-up (c-statistic: 0.58). Death-censored graft survival at 5-year follow-up is best predicted by the DRI (c-statistic: 0.59) and ET-DRI (c-statistic: 0.58). For patient- and overall graft survival, high-risk transplantations were best defined by the DRM at 5-year follow-up. High-risk transplantations for death-censored graft survival were best defined by the DRI.
Conclusions: This study shows that outcome after liver transplantation is best predicted at short-term follow-up. Models dominated by recipient variables, like the BAR and SOFT score, have best performance for predicting short-term patient survival. Models that also include sufficient donor variables like the SOFT-score and DRM, have better performance for long-term graft survival. The DRI and ET-DRI include solely donor variables and best predict death-censored graft survival.

Donor hematocrit is an independent predictor for the development of non-anastomotic biliary strictures after donation after circulatory death liver transplantation

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Background: Donation after circulatory death (DCD) livers are increasingly used for transplantation to overcome donor organ shortage. These livers, however, develop non-anastomotic biliary strictures (NAS) in up to 30%, frequently resulting in graft loss or even death. The high incidence of NAS cannot be completely explained by the currently known risk factors. Blood hematocrit is a determinant of blood viscosity and might therefore affect graft flush out during procurement. We aimed to investigate the impact of donor hematocrit (among other known risk factors) on the development of NAS after DCD liver transplantation.
Methods: DCD liver transplantations performed between 2003-2017 in the two participating centers were included. Exclusion criteria were retransplantation, use of machine perfusion and unknown donor hematocrit. NAS was defined as bile duct strictures at any location but the anastomosis. Continuous data are expressed as median (interquartile range). Uni- and multivariate logistic regression analysis were used to identify risk factors for the development of NAS. Variables with a p-value below 0.2 in the univariate analysis were included in the multivariate analysis.
Results: A total of 235 DCD liver transplantations were included. Median donor hematocrit was 34 (30-39) %, donor age 47 (36-54) years, time between withdrawal of life support and cold perfusion 31 (26-38) min, and cold ischemia time (CIT) 408 (356-460) min. Univariate analysis identified donor age (p=0.005), CIT (p=0.102), time between withdrawal of life support and cold flush (p=0.107) and donor hematocrit (p=0.045) as (near) significant risk factors for NAS. After multivariate analysis, only donor hematocrit (OR 1.054, 95% CI: 1.003-1.108, p=0.039) remained as an independent risk factor for NAS. Livers from DCD donors with a hematocrit >36% had a more than 2-fold higher risk to develop NAS.
Conclusions: Donor hematocrit is a strong risk factor for the development of NAS after DCD liver transplantation.

Post-operative Duplex ultrasound predicts early complications and renal function after kidney transplantation.

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Background: Assessing early complications after kidney transplantation (KTX) remains difficult. The renal resistive index (RI) is used to differentiate between normal and abnormal functioning allografts after KTX. However, the clinical applicability in the post-operative setting is insufficiently determined and conflicting data concerning the short-term allograft outcomes are reported. In the current study, the clinical value of the RI with emphasis on surgical complications, one-year kidney function (measured(m)GFR) and one-year patient survival is assessed.

Methods: We performed a single-center, retrospective case-control study. All patients (N=344) who underwent KTX between November 2015 and July 2017 were included. Duplex ultrasound was performed within 24 hours after KTX on the post-anaesthesia care unit. The RI was calculated as: (peak systolic velocity–end diastolic velocity)/peak systolic velocity and is defined as the mean of a measurement in the artery of the upper pole, between the poles and the lower pole. Surgical complications were classified using the Comprehensive Complication Index (CCI).

Results: The mean intrarenal RI was 0.64 ± 0.08. The RI was significantly higher in donation after brain death (DBD) and cardiac death (DC) kidney grafts compared to living donor kidneys (respectively 0.66 and 0.67 vs. 0.62, $p<0.001$). One-year patient survival was lower in patients with a RI>0.70 than in patients with a RI≤0.70 ($p=0.029$). The median CCI in kidney transplant recipients was 8.7 [IQR 0-21]. The median CCI was higher in patients with a RI>0.70 compared to patients with a RI≤0.70 (respectively 8.7 vs 12.2, $p=0.012$). The RI was negatively correlated with one-year mGFR ($r=-0.14$, $p=0.030$). In a stepwise linear regression model, recipient age ($\beta=0.21$, $p<0.001$), cold ischemia time ($\beta=0.21$, $p<0.001$) and diastolic blood pressure ($\beta=-0.18$, $p<0.001$) were factors associated with the RI, independent of important confounders (recipient and donor gender and BMI, donor age, recipient smoking status, systolic blood pressure, antihypertensive use, type of donation, the presence of acute tubular necrosis and delayed graft function).

Conclusions: This study showed that a RI>0.70 is associated with a higher CCI, a lower mGFR and a worse one-year patient survival. Also different measurements were determined between deceased and living kidney grafts. The association is most likely determined by worse cardiovascular system of the patients. We suggest taking these factors into consideration when interpreting post-operative duplex ultrasound.

Aorto-iliac calcification is a risk factor for inferior patient and graft survival in kidney transplant recipients; a systematic review and meta-analysis

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Background: While the incidence of transplanting a kidney onto atherosclerotic iliac arteries is becoming more common, little is known about the clinical outcome. We performed a systematic review and meta-analysis to investigate patient and graft survival of kidney transplant recipients with aorto-iliac calcification (AIC) compared to recipients without aorto-iliac calcifications (nAIC).
Methods: We performed a literature search in 5 databases including Embase, Medline, Cochrane, Web of Science and Google Scholar. Articles from January 1st, 2000 until September 11th, 2018 were included. The methodology was in accordance with the PRISMA statement. Relevant outcomes for meta-analysis were patient survival, (death-censored) graft survival and delayed graft function. The survival data for meta-analysis was deduced from Kaplan-Meier curves and presented as a pooled risk ratio using a random effect model. The quality of the evidence was assessed using the GRADE criteria.
Results: Twenty observational studies were identified from which 8 were eligible for meta-analysis. Short term and long term patient survival were significantly decreased in recipients with AIC (1-year patient survival: RR 2.19, 95% CI 1.39-3.44, p<0.001, 5-year patient survival: RR 2.47, 95% CI 1.75-3.48, p<0.001). One-year uncensored graft survival was inferior in recipients with AIC (risk ratio (RR) 3.15, 95% confidence interval (CI) 1.30-7.64, p=0.01). However, the 1-year and 3-year death-censored graft survival was similar in recipients with and without AIC (1-year: RR 2.26, 95% CI 0.58-8.82, p=0.24, 3-year: RR 2.19, 95% CI 0.49-9.82, p=0.31). The risk of delayed graft function was not increased in recipients with AIC (RR 1.124, 95% CI 0.98-1.58). Mean 1-year patient survival, uncensored graft survival and death-censored graft survival in recipients who received a kidney transplant on a prosthetic graft was 93.5%, 93.5% and 89.1% respectively. The quality of the evidence was graded as low or very low.
Conclusions: Patient and uncensored graft survival is significantly inferior in kidney transplant recipients with AIC. Death-censored graft survival is unaffected. The short term results of kidney transplantation on a prosthetic graft seems favorable.

Parainfluenza infections in lung transplant recipients; from bedside to bench and back

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Background: Parainfluenza virus (PIV) infections have been recognized as a significant cause of morbidity in the form of Bronchiolitis Obliterans Syndrome (BOS) in lung transplant recipients (LTR).
Methods: We report a bedside to bench and back strategy by using an in vitro model of human airway epithelium cells of bronchial origin (HuAEC) in an air-liquid interface to study the efficacy of experimental PIV-3 inhibitors with subsequent retrospective assessment of the effectiveness of ribavirin treatment in these patients.
Results: 12 LTR were identified with a PIV infection and FEV1 decline of 8.3% (IQR 21%); 9 had BOS grade < 3 of whom 6 developed new or progressive BOS. We then studied the replication of PIV-3 on HuAEC and the antiviral effect of nucleoside analogues. Apical infection of these cultures with a clinical isolate of PIV-3 showed significant viral replication. To explore the effect of antiviral treatment cells were exposed, at the basal site, to nucleosides (100 µM Ribavirin or 100 µM of Favipiravir) from day -2 until day 4 post-infection A clear inhibition (>4 log PIV-RNA reduction) of PIV-3 replication in the presence of Ribavirin could be observed while there was no effect of Favipiravir. When Ribavirin treatment was stopped, PIV-3 replication increased in 48 h to the level of untreated cultures. We then compared outcomes of 21 ribavirin treated *vs.* the 12 untreated PIV infected LTRs. Overall incidence of new or progressive BOS at 6 mo. post infection was 10/28 (< BOS 3; 36%), with a median FEV1 decline of 4.9% compared to pre-infection ($p<0.01$). Hospitalization rate was 61% (median 5 d. range 2-49 d.); there were no deaths. At baseline no differences in BOS grade pre-infection, FEV1 decline at presentation, underlying disease, time since transplantation, coinfections, PIV subtype or total delay between the groups were seen. The ribavirin treated group had a significantly lower median FEV1 decline 6 mo. post-infection *vs.* pre-infection compared to ribavirin untreated LTR (2.9% [IQR 4.7%] *vs.* 8.3% [IQR 21%] $p=0.04$). Incidence of new or progressive BOS was also significantly lower in the ribavirin group compared to ribavirin untreated (4/19 [21%] *vs.* 6/9 [67%] $p=0.04$).
Conclusions: In conclusion, *in vitro* results of ribavirin are confirmed by observational data of ribavirin on PIV infections in LTR. Preservation of long-term FEV1 in LTR seems a potential benefit of ribavirin but needs to be studied in a larger cohort.

Graft failure by rejection in adolescent kidney transplant recipients

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Background: Several registries report a high risk of graft loss in kidney transplantation during adolescence. We hypothesize that this high risk is associated with an active immune system during puberty. In the current study we evaluate episodes of acute rejection and causes of graft loss in patients of different age groups. The aim is to study if adolescents have a higher risk of acute rejection and (early) graft loss due to acute or chronic rejection.
Methods: We performed a retrospective single center study in kidney transplant recipients, receiving their first graft between 1990 and 2018, at age 6-25. Exclusion: ABOI and living unrelated donation including cross-over and altruist donation. Electronic patient files were searched for all for-cause graft biopsy reports, and for date and cause of graft failure and/or death. A graft biopsy reporting positive signs of active rejection is defined an acute rejection episode (ARE). Definition of graft failure by active and/or chronic rejection as indicated in the Eurotransplant registry.
Results: We included 250 kidney transplant recipients, 120 pediatric (46% living donor) and 130 adult patients (83% living donor). In 54% of the pediatric and 65% of adult patients at least one for-cause graft biopsy was obtained. Sixty seven patients had signs of ARE in at least 1 biopsy, with the highest incidence in the age 20-25 years group (27%, n=20) and the lowest in the age 6-10 years group (16%, n=5). ARE-free survival was best in the youngest group (6-10 years, n=32), at 2 years post-transplant 90% and at 8 years 86%; followed by the 10-15 years old (n=49) 86% and 81%. The older recipients showed a higher incidence of AREs, with a ARE-free survival in 15-20 years old (n=94) of 86% and 68% at 2 and 8 years post-transplant, and in 20-25 years old (n=75) of 84% and 65% respectively (log rank p=0.063). Subsequently graft losses due to active and/or chronic rejection were studied. Graft survival was best in the 6-10 years old: at 2 years post-transplant 97% and 8 years post-transplant 89%; followed by the 20-25 years old: 97% and 85%. Worst graft survival was seen in the middle groups: in 10-15 years old 96% and 67%; and in 15-20 years old 93% and 67% respectively (log rank p=0.073).
Conclusions: The oldest kidney transplant recipients showed the highest incidence of ARE. The worst graft survival due to active and/or chronic rejection was seen in the adolescent groups, as we expected. The differences between the age groups only showed a trend in significance.

Clinical outcomes of DCD type V liver transplantation: donation after euthanasia

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Background: Due to the growing shortage of donor organs, physicians and surgeons are forced to accept livers from donation after circulatory death (DCD) donors. One special group of DCD organs are those obtained after euthanasia (DCD type V according to the modified Maastricht classification). To create more awareness on the possibility of organ donation after euthanasia, it is of great importance to evaluate the results of transplantation with this type of graft. The aim of this study was to evaluate the outcome of DCD type V liver transplantation (LT) in the Netherlands.
Methods: All DCD type V LT performed in the Netherlands until 2018 were included in this retrospective study except for the cases in which the graft has been preserved with machine perfusion. Continuous data are expressed as median (inter quartile range), categorical data as number (percentage).
Results: Until 2018, 22 DCD type V LT have been performed in the Netherlands. Five cases in which the liver was preserved by machine perfusion were excluded. Median age of donor and recipient was 53 years (45-57) and 53 years (45-63), respectively. A neurodegenerative disease was the most common underlying disease in donors requesting euthanasia, followed by multiple sclerosis. Median time between administration of the euthanaticum and cold perfusion in the donor was 24 minutes (21-30). Peak AST and ALT levels in the recipients were 867 U/L (730-2701) and 757 U/L (608-2739) respectively. After a median follow up of 2.5 years all recipients are still alive. Three patients (17.6%) required a retransplantation, due to PNF (n=1) or post-transplant cholangiopathy (n=2), all within the first year after the prior LT.
Conclusions: Liver transplantations with grafts from donors who underwent euthanasia yield satisfying results during the relatively short follow up period that is currently available. Comparison of these results with DCD type III LT and donation after brain death (DBD) LT is currently ongoing.

Liver donors with metabolic disturbances can extend the donor pool

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Background: Metabolic complications after liver transplantation (LT) are common and affect graft and patient survival. To increase the donor pool sufficiently, more grafts from donors with metabolic disturbances are used for transplantation. Furthermore, due to our Western lifestyle, metabolic comorbidities will become more common among potential organ donors. Thus, it's important to determine whether livers from these donors can be used safely and do not derogate long term graft and patient survival after LT.
Methods: Data from liver donors and recipients who underwent full-size LT between 2007 and 2011 were collected. The effect of donor age, Body Mass Index (BMI), hypertension, dyslipidemia, steatosis, smoking, alcohol use, in combination with known non-metabolic risk factors, such as warm ischemia time (WIT) and cold ischemia time (CIT) on graft and patient survival was analyzed. Recipient age, BMI and non-alcoholic steatohepatitis, as an indication for LT, was also included in the models.
Results: A total of 211 LT were performed (DBD n = 166, DCD n = 45). The 1-, 5- and 10-year overall graft survival was 79%, 58%, and 45%. Patient survival was 85% at year 1, 68% at year 5 and 51% at year 10 post-transplantation. In multivariable analysis, donor hypertension (p=0.369), dyslipidemia (p=0.165), steatosis grade (10-20% p=0.519, 20-33% p=0.337, >33% p=0.601), smoking (p=0.986) or alcohol abuse (p=0.638) had no significant effect on patient survival. Similar results were seen for graft survival. In all models, independent risk factors for graft survival were donor obesity and WIT.
Conclusions: These data suggest that graft and patient survival after LT is not influenced by donor hypertension, dyslipidemia, steatosis, smoking, or alcohol abuse. Our results imply that the donor pool can be safely expanded using donors with metabolic disturbances.

Broadly profiling the activation status of circulating immune cells in c-aABMR reveals increased CD38 and CD16 expression on monocytes and NK cells

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Background: Chronic-active antibody mediated rejection (c-aABMR) contributes significantly to late renal allograft failure. Non-invasive biomarkers of c-aABMR are currently not available but could be valuable for early detection. In this study the activation profiles of relevant immune cell populations in peripheral blood of patients with c-aABMR were evaluated as potential biomarker.
Methods: The peripheral blood mononuclear cells of the kidney transplant recipients included were used for flow cytometric analysis. A panel of monoclonal antibodies was used designed to characterize both the specific cell type (T and B cells, γδ T cells, NK cells and monocytes) and their activation status. Cases with biopsy proven c-aABMR (c-aABMRpos, N=25) were compared to matched controls (c-aABMRneg, N=25).
Results: No significant differences were found in the total percentage and distribution of NK cells, B cells and T cells. There was however a higher percentage of monocytes present in c-aABMRpos cases (19.5% vs. 14.4%, $p<0.05$). Additionally, differences were found in activation status of circulating monocytes, NK cells and γδ T cells. The c-aABMRpos cases had a significantly higher percentage of monocytes expressing the activation marker CD38 ($p=0.04$) as well as higher expression of CD38 on NK cells ($p=0.02$). CD16 (Fcγ III receptor) expression on NK cells was significantly higher in c-aABMRpos cases (MFI 56965 vs. 34345, $p<0.01$) but significantly lower in γδ T cells (MFI 837 vs. 1277, $p=0.02$). Although statistically significant, these differences were not sufficient to readily identify patients with c-aABMR.
Conclusions: Cases with c-aABMR express a different CD16 and CD38 expression profile on circulating NK cells, γδ T cells and monocytes. Increased CD16 expression on circulating NK cells suggest that an interaction with antibodies on renal endothelial cells has taken place.

Using a cardiac-output guided hemodynamic therapy algorithm reduces intra-operative fluid administration in LDKT with large donor-recipient size mismatch

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Background: A living donor kidney transplantation (LDKT) in young children requires a substantial increase in cardiac output (CO) to maintain good perfusion of the relatively large kidney. To achieve this, intra-operative hemodynamic therapy protocols commonly advise liberal fluid administration guided by high target central venous pressure (CVP) and arterial blood pressure (ABP). However, ABP and CVP are known to poorly estimate CO or organ blood flow. Such therapy may lead to good renal outcomes, but inherits the risk of severe fluid overload. Goal of our study was, first, to evaluate the feasibility of using a gold standard CO monitor for children, the transpulmonary thermodilution (TPTD) technique. Second goal was to evaluate whether a CO-guided hemodynamic therapy algorithm could induce a reduction in fluid administration, while achieving increased target CO and ABP.
Methods: Twelve consecutive LDKT recipients were studied. Heart rate (HR), ABP and CVP were measured continuously. A thermistor tipped catheter was inserted in the left arteria femoralis which was used to measure perioperative CO by TPTD measurements (PiCCO device, Pulsion). A CO-guided hemodynamic therapy algorithm steered hemodynamic management. Data on patient characteristics, fluid administration and vasoactive medication were collected. Hemodynamic values were obtained before (t0), during (t1) and after (t2) transplantation and were analyzed with repeated measurements ANOVA.
Results: Recipients were 3.2 (1.6-4.9) yrs of age and 14.1 (10.4-18) kg bodyweight. R/D weight ratio was 0.18 (0.11-0.28). No complications related to the TPTD-CO monitor were reported. Between t0 and t2, indexed CO increased with 31% (95% CI=15-48%). HR appeared to be the main contributor to the augmented CO and increased with 22% (95% CI=9-34%). Increase in indexed SV (stroke volume) was non-significant. MAP increased with 66% (95% CI=34-98%). Between t0 and t1, CVP did not change despite fluid administration. Mean fluid administration reduced from 166 ml/kg in the first two to 59 ml/kg (!) in the last ten patients. All kidneys showed diuresis shortly after reperfusion. Patient and graft survival were 100%.
Conclusions: In LDKT in young children TPTD-CO monitoring is a safe technique to guide hemodynamic therapy. Using a CO-guided hemodynamic therapy algorithm reduces intra-operative fluid administration while achieving increased CO and ABP and preserving good renal outcome. This might prevent fluid overload and subsequent tissue edema.

Transplanting kidneys from hepatitis C virus positive donors: new possibilities

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Background: The scarcity of kidneys for transplantation results in a high mortality rate for waitlisted patients. In comparison with long-term dialysis, kidney transplantation results in better patient survival. However, many kidneys from donors infected with the Hepatitis C Virus (HCV) are being discarded. In this era, a sustained virologic response can be achieved with Direct Acting Antivirals (DAAs). The aim of this systemic review was to examine the consequences and new possibilities of transplanting kidneys from HCV positive donors to HCV negative recipients (D+/R-).
Methods: We searched Pubmed for studies related to transplantations of kidneys from HCV infected donors into HCV negative recipients. We analysed the quality, characteristics and results of these studies. Our primary outcome measurement was the difference in patient survival between the D+/R- group and a control group of HCV negative donors transplanting to HCV negative recipients (D-/R-). Furthermore, as secondary outcome measurements we focussed on graft survival, HCV transmission and cause of death of the recipients.
Results: As a result of our study selection, we included six articles. Patient survival was worse in the D+/R- group in comparison with the D-/R- group. However, the D+/R- group had higher survival rates compared to waitlisted controls (68% respectively 43% ($p<0.001$)). Graft survival was lower in the D+/R- group compared to the D-/R- group. HCV transmission varied between 62-100%, depending on the rate of viral load testing. One study reported a sustained virologic response of 100% within 30 days with the use of DAAs. Moreover, the most common cause of death were infection and cardiovascular disease. Liver disease was more often reported in the D+/R- group, with an overall incidence of approximately 5-6%.
Conclusions: We conclude that HCV negative recipients have a worse patient and graft survival when transplanted with a kidney from an HCV infected donor. However, despite the high likelihood of viral transmission, acceptance of a kidney from an HCV infected donor could result in superior patient survival compared to remaining on the waiting list. A sustained virologic response could be achieved with DAA treatment. At last, further research is necessary to examine the long-term outcomes.

Timing of ureteric stent removal and occurrence of urological complications after kidney transplantation: A systematic review and meta-analysis

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Background: Implanting a ureteric stent during ureteroneocystostomy reduces the risk of urinary leakage and ureteral stenosis after kidney transplantation (KTx), but it may also predispose to urinary tract infections (UTI). The aim of this study is to determine a more definite moment for ureteric stent removal after KTx.
Methods: Searches were performed in EMBASE, MEDLINE Ovid, Cochrane CENTRAL, Web of science and Google scholar. All aspects of the Cochrane Handbook for Interventional Systematic Reviews are followed and is written based on the PRISMA-statement. Articles discussing JJ-stents and their time of removal in relation to outcome were included. Studied outcome measures were UTI, urinary leakage, ureteral stenosis and re-intervention.
Results: 1043 articles were identified, of which 14 articles were included. Meta-analysis showed a significant reduction of UTI when stents were removed within three weeks (OR 0.52, p = 0.008). Regarding incidence of urinary leakage, there is no significant difference between early and late stent removal (OR 0,928, p= 0,898). No meta-analysis could be performed on the outcome of ureteral stenosis, because of the lack data.
Conclusions: Based on our results, earlier stent removal after KTx (earlier than 3 weeks) is associated with a decreased incidence of UTI and does not show a higher incidence of urinary leakage compared to later removal (later than 3 weeks). We recommend that the routine removal of ureteric stents implanted during kidney transplantation should be performed around three weeks postoperatively.

Increased number of intragraft FOXP3+ T cells is strongly correlated with decreased graft survival in chronic-active antibody-mediated rejection

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Background: Chronic-active antibody-mediated rejection (c-aABMR) is the most important cause of late renal allograft failure. However, renal inflammation and rate of loss of renal allograft function vary substantially. Surprisingly, little is known about the type of immune cell infiltrates in the kidney during c-aABMR and whether this correlates with graft survival. In this study, various immune cell subpopulations in renal biopsies of patients with c-aABMR were quantitatively characterized and correlated with allograft survival.
Methods: Multiplex immunofluorescent staining was performed on 20 cases of biopsy-proven c-aABMR. The stainings were designed to identify T cell subsets (CD3, CD8, Foxp3 and granzyme B), macrophages (CD68 and CD163), B cells (CD20) and NK cells (CD57). The number of positive cells were counted in the glomeruli (cells/glomerulus) and the tubulo-interstitial (TI) compartment (cells/HPF).
Results: $CD3^+$ T cells were the dominant cell type in both glomeruli and the TI compartment. The glomeruli had a mean total of 5.5 $CD3^+$ cells, 62% being $CD8^+$ T cells. Forty-six percent of $CD8^+$ T cells were positive for granzyme B. Macrophages had a mean of 4 cells per glomerulus, of which 68% were pro-fibrotic M2 macrophages ($CD68^+$ $CD163^+$).
The TI compartment showed a mean of 116 $CD3^+$ cells per HPF, of which 46% were $CD4^+$ and 54% $CD8^+$. Macrophage count was 21.5 per HPF with 39% being of M2 type ($CD68^+CD163^+$). $CD20^+$ cells were sporadically present in glomeruli, whereas 45% of biopsies showed B cell aggregates in the TI compartment. NK cells were rarely present in the glomeruli and scarcely in the TI compartment.
Remarkably, decreased graft survival was significantly associated with increased numbers of $CD3^+$ $FoxP3^+$ cells in the TI compartment ($p=0.004$) and a trend towards increased amount of macrophages ($CD68^+$) in the TI compartment ($p=0.08$).
Conclusions: Renal allograft biopsies with c-aABMR have differential compartmentation of infiltrating immune cells with a predominance of $CD8^+$ T cells. Interestingly, increased numbers of $FoxP3^+$ T cells in the TI compartment are associated with inferior allograft survival.

Management of portal vein anastomotic stenosis after pediatric liver transplantation: evaluation of single center experience

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Background: Late onset portal vein anastomotic stenosis (PVAS) is a frequent complication in pediatric liver transplantation. For clinical relevant PVAS percutaneous transluminal angioplasty (PTA) is the first treatment option. When PTA is not feasible or not successful to obtain portal vein patency, a surgical Meso-portal shunt (MPS) can be performed. Our aim was to evaluate the clinical and biochemical characteristics of pediatric patients with post-transplant PVAS and the results of our management of these patients.
Methods: We retrospectively studied all patients aged ≥18 years that underwent a therapeutic intervention procedure between 2014 and 2018, either PTA or MPS after pediatric liver transplantation including living and deceased liver donors. We evaluated primary patency of the PTA and MPS and secondary patency after the complete therapeutic intervention process.
Results: PVAS was diagnosed by ultrasound and/ or CT-scan prior to the first intervention. At our center, 18 (11%) of 165 patients underwent a therapeutic intervention procedure for PVAS after liver transplantation. Of the patients with PVAS, 72% had biliary atresia as the primary diagnosis, 72% were transplanted under 1 year of age and 67% received a living donor graft. All PVAS patients presented with splenomegaly. Thrombocyte counts were below 150 in only 67% of PVAS patients before the first intervention. Of all PVAS patients 44% had at least one episode of a gastro-intestinal bleeding. In 12 patients endoscopy was performed and all had esophageal varices. The median post-procedural follow-up time was 1.4 years. Twelve patients underwent a primary PTA, of whom one patient underwent two PTA's and one patient three PTA's in total. 10 patients received a MPS of whom four patient had MPS after PTA. Primary patency was 67% for the first PTA, 0% for the second and third and patency after MPS was 80%. Secondary patency was 89% for the complete therapeutic approach.
Conclusions: In 11% of our cohort of pediatric transplantation patients portal vein anastomotic stenosis is a significant problem especially in recipients with biliary atresia, transplantation below 1 years of age and after living donor transplantation. Based on our results we do not support a second PTA if the first PTA fails. Our combined treatment strategy with PTA and MPS has a good clinical outcome with a secondary patency of 89%.

A temporary portocaval shunt and initial arterial perfusion in orthotopic liver transplantation

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Background: The use of a temporary portocaval shunt (TPCS), as well as the order of reperfusion (initial arterial reperfusion (IAR) vs. initial portal reperfusion (IPR)), in orthotopic liver transplantation (LT), is controversial, and therefore still under debate.
Methods: Aim of this study was to evaluate outcome for the four possible combinations (TPCS with IAR (A+S+), TPCS with IPR (A-S+), no-TPCS with IAR (A+S-), no-TPCS with IPR (A-S-)), in a center-based cohort study, including liver transplantations from both donation after brain death (DBD) and donation after circulatory death (DCD). Primary outcome was peroperative blood loss and secondary outcomes were operative time, incidence of non-anastomotic biliary strictures (NAS), patient- and graft survival. Between January 2005 and May 2017 all orthotopic, first liver transplantations performed in our institution were included into the four groups mentioned.
Results: The A+S+ group consisted of significant more DCD- LT (p=0.005). Since the introduction of A+S+, a significant decrease in peroperative transfusion of red blood cells (RBCs) was seen (p<0.001), as well as significant decrease in number of recipients who did not need any transfusion of RBCs (p<0.001). Multivariate analysis showed labMELD (p<0.001) and IAR (p=0.014) to be independent confounders on transfusion of RBCs. No statistical difference was seen in operative time, nor in 1-year incidence of NAS, 1-year patient- and graft survival, even though A+S+ consisted of significant more DCD-LT.
Conclusions: In conclusion, the introduction of TPCS and IAR in our clinic has led to significant less peroperative blood loss, without increasing operative time and seems to be a reasonable, alternative surgical strategy.

Risk Predictive Strategy to Optimize Pancreas Donor Selection

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Background: The discrepancy between the number of patients on the waiting list and the number of donor pancreata for transplantation needs extension of accepting criteria for pancreas allografts. We investigated ways to safely increase the number of suitable pancreas allografts by expanding donor BMI and age criteria.
Methods: The current pancreas donor selection in the Netherlands was analysed and compared to the potential pancreas donors if extended criteria donors would have been used. Risk assessment was done by in-depth analysis of all donor reports and calculation of the PDRI. An additional method to approach a more adequate number of potential donors in extended age criteria was to select donors without Diabetes Mellitus, BMI <30 kg/m^2 and who donated their liver and at least one kidney, suggesting to have a general medical condition being sufficient to potentially also donate their pancreas.
Results: Between January 1st 2014 and December 31st 2017, 405 of 1273 donors were reported as potential whole pancreas donor. Of these 405 reported donors 93 (23%) pancreata were eventually transplanted as whole organ. Extending BMI criteria up to BMI ≤35 kg/m^2 results in an 6% increase of pancreas donors reported. If age criteria would be increased by 5 years, it could result in an additional 21% potential DBD donors and 53% potential DCD donors reported. The PDRI of these extended criteria donors was in 31% of the cases below the upper limit of currently accepted and transplanted pancreas allografts. In respectively 45% and 64% of all potential DBD and DCD donors no absolute contra-indications were found by in-depth analysis of the donor report.
Conclusions: Selected older donors have similar risk parameters as compared to current pancreas donors, except for age itself. The PDRI seems not to reflect the actual increased risk in higher aged donors. It demands validation and adjustment for these extended criteria donors. Expanding BMI criteria does not result in a significant increase of potential donor pancreata. However, by extending age criteria, this study shows an acceptable risk predictive strategy to optimize pancreas donor selection and to meet the increasing waiting list.

Risk Factors for Thrombosis and Bleeding in Pediatric Liver Transplantation in an Era of Routine Postoperative Antithrombotic Therapy

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Background: Hepatic artery thrombosis (HAT) and portal vein thrombosis (PVT) are serious causes of morbidity and mortality after pediatric liver transplantation. In order to reduce the number of thrombotic complications, routine antithrombotic therapy, consisting of 1 week heparin followed by 3 months acetylsalicylic acid, was implemented in our pediatric liver transplant program in 2003. The aim of this study is to evaluate the incidence of bleeding and thrombotic complications since the implementation of routine antithrombotic therapy and to identify risk factors for these complications.

Methods: A retrospective cohort study including all 200 pediatric primary liver transplantations performed between 2003-2016. Uni- and multivariate logistic regression analysis, the Kaplan-Meier method and Cox regression analysis were used to evaluate recipient outcome.

Results: Fifty-six (28%) full size and 144 (72%) partial grafts from 161 (80%) deceased and 39 (20%) living donors were transplanted. HAT occurred in 15 (7.5%), PVT in 4 (2.0%) and venous outflow thrombosis in 2 (1.0%) recipients. Intra-operative vascular interventions (OR 14.4 (3.7-55.7)), recipient age (OR 0.81 (0.69-0.95)) and donor age (OR 0.96 (0.93-0.99)) were associated with post-transplant thrombosis. Clinically relevant bleeding occurred in 37%. Risk factors for post-transplant bleeding were high recipient age (OR 1.08 (1.02-1.15)), high Child-Pugh scores (OR 1.14 (1.02-1.28)) and intra-operative blood loss (OR 1.003 (1.001-1.006)). Both post-transplant thrombotic (HR 3.4 (1.4-8.5); *P*=0.009) and bleeding complications (HR 2.5 (1.2-5.2); *P*=0.015) increased mortality.

Conclusions: In 200 consecutive pediatric liver transplant recipients receiving routine post-operative antithrombotic therapy we report low incidences of post-transplant vascular complications. Post-transplant routine antithrombotic therapy seems to be valuable for pediatric liver transplant care. The identified risk factors for bleeding and thrombotic complications may facilitate a more personalized approach to antithrombotic therapy.

Elevated plasma levels of cell-free DNA during orthotopic liver transplantation are associated with activation of coagulation

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Background: Patients undergoing liver transplantation have complex changes in their hemostatic system, and the net effect of these changes appears a 'rebalanced' hemostatic profile. Recently, neutrophil extracellular traps (NETs) were discovered. Upon activation, neutrophils expel DNA, histones and granular proteins such as neutrophil elastase extracellularly, that together form web-like structures called NETs. NETs were first described in the context of pathogen entrapment and killing. Increasing evidence suggests a crucial role for NETs, and their main component cell-free DNA in activation of coagulation. As liver transplantation is associated with substantial (hepatocyte) cell death and intrahepatic neutrophil accumulation, NETs might play an important role in the hemostatic balance during liver transplantation. The aim of this study was to determine whether formation of NETs occurs during liver transplantation and examine their association with activation of coagulation.

Methods: Twenty-one patients undergoing a liver transplantation were included in this study. Plasma samples were obtained at four time points during transplantation and up to 6 days after transplantation. Patient plasma levels of cell-free DNA, nucleosomes and myeloperoxidase (MPO)-DNA complexes (markers for NETs) were determined using enzyme-linked immunosorbent assays and compared with plasma levels in healthy controls. Moreover, markers for activation of coagulation were assessed in the plasma samples. Post-reperfusion liver biopsies were stained for neutrophil elastase.

Results: Perioperative increases of plasma levels of markers for NETs were found with levels of cell-free DNA and nucleosomes that peaked after reperfusion, and MPO-DNA complexes that peaked during the anhepatic phase. Cell-free DNA and nucleosome levels, but not MPO-DNA levels (which is the most specific marker of NETs), were associated with markers for activation of coagulation. Immunostainings of post-reperfusion liver biopsies were suggestive for intrahepatic NET formation.

Conclusions: This study indicates that NET formation occurs during liver transplantation. However, the majority of circulating DNA appears to be derived from cell death within the graft and not from formation of NETs. Elevated plasma levels of cell-free DNA and nucleosomes, and not MPO-DNA, were associated with activation of coagulation and might contribute to the complex hemostatic rebalance during liver transplantation.

Recall of living kidney donors for long-term follow-up is worthwhile

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Background: Since 50 years, the number of living kidney donors increased considerably. We encourage donors to participate in yearly control visits after donation. However, long-term follow-up data of living kidney donors are scarce.
With the aim to decrease the amount of missing data, we encouraged donors, by a letter, to visit the general practitioner (GP) for a control visit.
Methods: From 1968 until 2012, 1029 living kidney donors are registered in our center. Numbers specified per period are 134, 304 and 591 donors between 1968 to 1992 (period 1), 1993 to 2002 (period 2) and 2003 to 2012 (period 3), respectively. In 2017, we analyzed follow-up data collected during the last five years, showing available data in 22%, 19% and 52% of the donors for period 1, 2 and 3, respectively. Mean rate for the whole group was 38%. Because of this disappointing result, we started this project.
We included donors without follow-up data registered for at least 5 years. They received a letter with an appeal to visit their GP. Also, a declaration of consent to register their data in our database, a note for the GP and a self-addressed envelope was attached. In case of no response within 3 months, a recall letter was sent. The last data were received until 9 months after starting the project.
Results: 635 of the 1029 donors met the inclusion criteria and got a letter. We received follow-up data from 293 donors, resulting in a overall response rate of 46%. The average age of the responders was 67 years (range 38-88 years). The average follow-up time after kidney donation was 17 years (range 6-49 years).
From 193 donors (30%), we didn't receive any reaction. The calculated average age of these non-responders was 63 years (range 30-98 years). The calculated average follow-up time was 18 years (range 6-49 years).
The remaining group of 149 donors (24%) is heterogeneous; no follow-up was received because of not willing to participate, death, rehousing or no data received by the GP.
Conclusions: Before starting this project, the percentage of follow-up data (till 5 years ago) registered in our database was 38%. As a result of this project, this percentage increased to a mean of 67% and specified for period 1, 2 and 3 percentages are now 49%, 57% and 76%, respectively.
This follow-up project demonstrates that it's worthwhile to recall donors who did not send data for more than 5 years. The follow-up data will eventually contribute to a better understanding of long-term follow-up.

Ex-vivo normothermic perfusion of a porcine kidney with three different perfusion solutions

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Background: In the Netherlands, hypothermic machine perfusion (HMP) is clinically used to preserve deceased donor kidneys. Normothermic machine perfusion (NMP) could comprise an even better kidney preservation strategy and also provides the opportunity for interventions. At this time, a suitable perfusion solution has to be established for NMP. The purpose of this study was to evaluate three different perfusion solutions and determine which solution is the most suitable for NMP.
Methods: Porcine kidneys and autologous blood were obtained from a local slaughterhouse. Warm ischaemia time was standardised at 20 min and subsequent HMP with UW-MP at 2-3 hours. Next, kidneys underwent NMP at 37°C during 7 hours, with 3 different perfusion solutions (n=5 per group). Perfusion solution 1 consisted of 350 ml red blood cells (RBCs), 500 ml Williams' Medium E and bovine serum albumin. Perfusion solution 2 consisted of 350 ml RBCs, 250 ml of NaCl, human albumin and several electrolytes. The third perfusion solution was based on a British clinical NMP medium and consisted of 120 ml RBCs, 120 ml SAG-M, 290 ml Ringers lactate, mannitol, dexamethasone and sodium bicarbonate. Vital parameters were monitored during NMP and perfusate and urine samples were taken regularly. Biopsies were taken to assess renal histology. Thiobarbituric acid reactive substances (TBARS) and N-Acetyl-β-D Glucosaminidase (NAG) levels were measured in the perfusate samples.
Results: During perfusion all kidneys were functional and produced urine. Flow rates in group 1 and 2 were similar. The flow increased during the first hour and decreased to 250 ml/min after 7 hours of NMP. Group 3 started off with a lower flow but reached the same values as the other two groups after 7 hours. In all groups, histology showed glomerular dilatation, tubular dilatation and necrosis; consistent with ischemic injury in this donation after circulatory death model. TBARS were significantly higher in group 1 when compared to group 2 ($p < 0.005$) and group 3 ($p < 0.005$). NAG levels after 7 hours of NMP were significantly lower in group 2 in comparison with group 1 ($p = 0.02$) and group 3 ($p = 0.01$).
Conclusions: In conclusion, perfusion of porcine kidneys with three different perfusion solutions proved feasible. However, the group 2 perfusate, based on human albumin and a balanced electrolyte composition, showed the lowest levels of injury markers, indicating that this perfusate is probably most suitable for normothermic machine perfusion of a porcine kidney.

Mucosal Associated Invariant T cells in patients with recurrent urinary tract infection exhibit an activated and cytotoxic profile

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Background: Mucosal associated invariant T (MAIT) cells are innate-like T-cells involved in the antibacterial response by recognizing bacterial riboflavin metabolites. They comprise ~ 10% of the T-cell population in human blood, are highly abundant at mucosal barrier sites and respond to a wide range of bacteria. Urinary tract infection (UTI) is a common complication after renal transplantation and can, especially in case of frequent recurrence, lead to damage of the allograft and eventually allograft failure. Although animal studies have indicated that MAIT cells play a role in the defense against UTI, there are currently no human data on the role of MAIT cells in (recurrent) UTI.
Methods:
We used a fluorescently-labelled MR1-tetramer in conjunction with 14-color flowcytometry to identify and characterize MAIT cells in blood from women with recurrent urinary tract infections (RUTI) (n=10) and in healthy controls (n=10).
Results: There was no significant difference in the amount of MAIT cells between RUTI patients and healthy controls. Characterization of MAIT cells revealed that in RUTI patients, the percentage of MAIT cells expressing the proliferation marker Ki67 was significantly higher ($p<0.01$), just as the percentage of MAIT cells expressing the cytotoxic markers granzyme B, granzyme K and perforin (respectively $p<0.01$, $p<0.01$, $p<0.05$). The percentage of MAIT cells expressing the transcription factors T-bet and Eomes was also significantly higher among the RUTI patients (respectively $p<0.001$ and $p<0.01$), which is in line with the cytotoxic profile of these cells.
Conclusions: MAIT cells in blood from women with RUTI display an activated and cytotoxic profile. This suggests that MAIT cells are involved in the defense against uropathogens. Currently it is unclear whether MAIT cells are able to migrate to the urogenital tract or whether also (lower) UTI may be accompanied by ascending bacteria and bacterial metabolites, which would lead to activation of MAIT cells in the bloodstream. Further research is warranted to determine what the exact role is of MAIT cells during UTI, also in renal transplant recipients with R(UTI).

The effect of preceding respiratory viral infection towards bronchiolitis obliterans syndrome development in lung transplant recipients

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Background: Lung transplant recipients are continuously exposed to respiratory viral infections. Bronchiolitis obliterans syndrome (BOS) is the major cause of morbidity and mortality post- transplantation. To identify if preceding (cumulative) respiratory viral infections contribute to BOS onset, a retrospective study of lung transplant recipients treated for ongoing care in the X centre and X hospital, from 2004 to 2013 was conducted.
Methods: Approaches for modelling recurrent events are discussed. Secondly, the association between the first viral event and outcomes were assessed using Cox proportional hazards regression with time-dependent covariates.
Results: Results: 852 viral specimens were collected from 113 total patients with 81 patients producing 316 virus positive specimens in 285 episodes of community acquired respiratory viral infection. Overall, the risk of BOS was not elevated by viral infection (HR 1.33 [0.692, 2.57], p=0.387).
Conclusions: Conclusions: Respiratory viral infections occur in the majority of lung transplant recipients with and without BOS but was not associated with chronic rejection and mortality during the study period in this cohort.
Key words: Lung transplantation, bronchiolitis obliterans syndrome, Polymerase chain reaction, community acquired respiratory infections.

How reliable are HLA antibody detection assays under immunosuppressive regimen?

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Background: Precise and accurate assessment of donor-specific HLA antibodies (DSA) is a crucial step prior to transplantations to reduce the risk for antibody mediated rejection (AMR), as well as to screen for the development of *de novo* DSA post-transplantation. However, immunosuppressive reagents used for desensitization of highly immunized patients or for the treatment of AMR can interfere with antibody detection assays leading to misinterpretation of the test results. Therefore, we examined the effect of two commonly used agents, Intravenous immunoglobulin (IVIG) and Rituximab, on Luminex mixed screen and single antigen (SA) assays and on flow- and CDC- crossmatches.
Methods: IVIG and Rituximab were added to patients' sera or negative and positive control sera. Also, sera from patients treated with either agents were included. Sera were tested with Luminex mixed and SA, flow and CDC crossmatch assays.
Results: In vitro treatment of negative sera with IVIG (dilution 1:10) resulted in increased MFI value of certain beads in both Luminex SA and mixed assays, creating a broad pattern of false positive specificities. This pronounced pattern of reactivity was reproducible with four different IVIG batches. Similar patterns were observed when patient's sera were analyzed shortly after IVIG treatment although sera before IVIG infusion were negative. Spiking IVIG in the positive control serum did not affect the Luminex assay results. Further, testing the IVIG effect on CDC crossmatches using 3 different cells, did not show any difference with untreated sera. On the other hand, Rituximab treatment of negative serum had no effect on the Luminex assay results, but gave false positive reactions in unseparated CDC and B cell flow crossmatches, again using three different samples of cells.
Conclusions: Our results indicate the presence of HLA antibody specificities in negative sera treated with IVIG when tested with Luminex assays, but no induction of false positive crossmatches, probably either because antibodies are not complement-fixing or the titer is not high enough for CDC reaction. Furthermore, in line with previous findings, our data revealed the interference of Rituximab with crossmatch assays, but not with Luminex bead assays, so the latter ones can be safely used to monitor the effect of Rituximab therapy. Further investigation is required to test for other medications and to develop strategies to eliminate the interference of each medication or therapy on antibody detection assays.

Lower urinary tract dysfunction is still underestimated in pediatric kidney transplants despite underlying cause of renal failure

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Background: Pediatric kidney graft survival has been significantly improved over the years with a current mean survival of 15-20 years. Several factors, like lower urinary tract dysfunction, are associated with a negative graft survival. Its prevalence however is largely unknown in the pediatric population. This study evaluates the prevalence of lower urinary tract dysfunction in our transplanted children. Results were compared between children with a nephrologic versus urologic origin of chronic kidney failure.
Methods: A single centre analysis of all pediatric kidney transplants performed between 2005 and 2018. Characteristics of donor and recipient, origin of kidney failure, voiding-, drinking-, and bowel habits were documented and evaluated using frequency voiding charts, standardized medical forms and uroflowmetry. Lower urinary tract dysfunction was defined as an expected bladder capacity for age (EBC) >130%, residual urinary volumes >10% of EBC, recurrent urinary tract infections, abnormal daytime voiding pattern (less than 4 times or over 11 times), intermittent uroflowmetry and concomitant occurrence of constipation according to the Rome III classification.
Results: A total of 65 pediatric transplants are currently still under close pediatric follow-up and were available for evaluation (male:female = 39:26). Five patients were not yet potty trained. Overall lower urinary tract dysfunction was present in 32 out of 65 patients (49%) and significantly more present in the urologic group (N=12, 75%) versus the nephrologic group (N=20, 46%), p=0.044. Mean maximum bladder capacity was not significantly different between the groups, respectively 403ml in the nephrogenic group and 450ml in the urologic group, p=0.58. In both groups mean daytime voiding frequency was 7 times (2-13) with an abnormal pattern in four patients. A significant residual volume of urine and intermittent flowmetry were not different between the groups, respectively 38% (N=6/16) in the urologic group versus 18% (N=9/49) in the nephrogenic group, p=0.198. Overall constipation was rarely seen (N=3). Recurrent urinary tract infections were present in 13 nephrogenic patients (30%) versus 6 urologic patients (40%), p=0.643.
Conclusions: Lower urinary tract dysfunction is as common in the nephrologic patients as in the urologic patients. This emphasizes a thorough evaluation and treatment if indicated in all kidney transplanted patients in order to optimize transplant survival.

The effects of an IL-21 receptor antagonist on the alloimmune response in a humanized skin transplant mouse model

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Background: After solid organ transplantation, the presence of a mixed pattern rejection with features of T cell-mediated rejection (TCMR) and antibody-mediated rejection (ABMR) is increasingly recognized. Treatment of these mixed type rejections is challenging since the majority of current immunosuppressive agents are directed towards either T-cell or B-cell mediated processes. The pleiotropic cytokine interleukin 21 (IL-21) is involved in regulating the expansion and effector function of a broad range of leucocytes, including CD4+ T cells, CD8+ T cells and B cells. In transplantation, the role of IL-21R signaling is acknowledged in several studies. However, the exact role of this cytokine in the process of allograft rejection is currently unknown. Here, we hypothesize that blockade of the IL-21 receptor (IL-21R) in a humanized skin transplant mouse model with T and B cell reconstitution prevents rejection of the human skin.

Methods: Immunodeficient Balb/c IL2rγ$^{-/-}$ Rag2$^{-/-}$ mice were transplanted with human skin followed by adoptive transfer of human allogeneic splenocytes. Control animals were treated with a PBS vehicle (*n*=7) while the other group was treated with a humanized anti-IL-21R antibody (αIL-21R; *n*=8). Mice were sacrificed 30 days after cellular infusion in order to assess for evidence of skin rejection and inflammation at a single time point.

Results: In control animals, human skin allografts were infiltrated with lymphocytes and developed a thickened epidermis with increased expression of the inflammatory markers Keratin 17 (Ker17) and Ki67. In mice treated with a humanized anti-IL-21R antibody (αIL-21R), these signs of allograft reactivity were significantly reduced. Of note, treatment with αIL-21R blocked phosphorylation of STAT3 and attenuated the process of T and B cell reconstitution after adoptive cellular transfer, which may contribute to the observed reduction in graft inflammation.

Conclusions: These findings demonstrate a promising role for blockade of IL-21 signaling to improve transplant outcomes.

Predictors of symptomatic lymphocele after kidney transplantation

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Background: Symptomatic lymphocele (SL) is a frequent post-operative surgical complication after kidney transplantation. It may lead to pain and discomfort, but can also cause transplant malfunction or even secondary graft loss. We therefore investigated a large cohort for possible risk factors for SL.
Methods: All transplant patients of a single centre were retrospectively analysed for SL between January 2010 and December 2017. SL group was compared with a control group from the same cohort.
Results: 45 out of 1003 transplanted patients developed a SL (incidence 4.5%; 95%CI: 3.6%-5.8%). There was a six-fold higher overall mortality in the SL group (1.5% vs. 8.9%, p=0.000). SL developed more in older patients (48 years vs. 57 years, p=0.017), in those with a PD catheter (14% vs. 22%, p=0.007) and in ADKDP as primary diagnosis (15% vs 31%, p=0.001). Surgical predictors for SL were venous anastomosis on the external iliac vein (5.4% vs. 11%, p=0.021), concomitant PD catheter removal (14% vs. 18%, p=0.014), perfusion defects (7.3% vs. 20%, p=0.000), longer operating time (165min ± 0:41 vs. 156min ± 0:33, p=0.012), splint >7 days (0.6% vs. 2.2%, p=0.009), JJ stenting (11% vs. 22%, p=0.000), drain requirement at discharge (1.3% vs. 6.7%, p=0.000), low initial drain production (359ml ± 533ml vs. 147ml ± 188ml, p=0.011) and ureteral obstruction (4.2% vs. 18%, p=0.000). Opening the peritoneum (6.4% vs. 0%, p=0,000), re-operation for post-operative bleeding (2.5% vs. 0%, p=0.03) and previous nephrectomy (10% vs 0%, p=0.03) seem protective for developing SL.
Conclusions: Despite finding multiple heterogeneous predictors for SL, a common denominator relate to surgical management of the retro-peritoneal space and the ureter. Hopefully, this will lead to measures that can prevent SL from developing.

Whole Body CT Imaging in Post-Mortem Donor Screening

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Background: To increase the number of suitable organs for transplantation, it is current practice to include extended criteria donors. By extending age criteria, not only organ quality decreases but the risk of malignancy increases. Our aim was to analyze the effect of a preoperative computed tomography (CT) scan on identifying malignancies and to perform a systematic literature search on radiologic screening of potential post-mortem donors.
Methods: We included all patients reported as post-mortem organ donor in the Netherlands between January 1st, 2013 and December 31st, 2016. Donor reports were analyzed to identify results of radiologic investigations or (suspected) malignancies found during MOD procedures. We compared findings between the conventional donor screening protocol and donor screening including a CT-scan. Studies were excluded for our systematic review if they were not describing post-mortem donor screening by imaging or if they were not available in English.
Results: Chest or abdominal CT-scans were performed in 17% and 18% of the 1375 reported donors respectively. Screening by chest CT-scan versus chest X-ray resulted in 1.3% and 0.2% thoracic malignancies found respectively. During MOD procedures no thoracic malignancies were found in patients screened by chest CT compared to 0.2% malignancies in the chest X-ray group. Screening by abdominal CT-scan resulted in 0.4% malignancies, compared to 0.1% in the abdominal ultrasound (US) group. During MOD procedures, 0.8% and 1.6% malignancies were found in the abdominal CT-scan and US groups respectively. Based on selection criteria 3 articles were further analyzed. Two prospective cohort studies evaluated CT-scanning in post-mortem donor screening. The studies reported in 8% and 11% of the cases a (possible) malignancy and in 4% and 11% of the cases the MOD procedure was cancelled because of an active malignancy. The third study evaluated diagnostic imaging of potential lung donors and its clinical relevance. In 7% of the patients a (possible) malignancy was reported.
Conclusions: CT-scanning decreased the percentages of perioperative detection of tumors, from 0.2% to 0% for thoracic imaging and from 1.6% to 0.8% for abdominal imaging. Another possible advantage of extended screening is to enhance the pre-operative planning by providing additional information on (aberrant) anatomy. In conclusion, it could decrease the risk of donor derived malignancies and prevent about 2-3 unnecessary MOD procedures per year in the Netherlands.

Post-transplant obesity is associated with poor long-term survival after liver transplantation

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Background: Short-term survival after orthotopic liver transplantation (OLT) has improved over the past decades, but long-term survival remains impaired. The effects of obesity on long-term survival after OLT remain controversial. Because pre-transplant body mass index (BMI) can be confounded by for example ascites, we hypothesized that post-transplant BMI at 1 year could be a predictor of long term survival.
Methods: In a single-center retrospective cohort study 370 adult OLT recipients were included. Baseline BMI was set at 1 year post-transplantation to represent a stable condition. Patients were stratified into 3 BMI categories: normal weight with BMI<25 kg/m^2 (n=184), overweight with 25≤BMI≤30 kg/m^2 (n=136), and obese with BMI>30 kg/m^2 (n=50). Survival analyses were performed according to Kaplan-Meier with log-rank testing, followed by Cox proportional-hazards regression analyses.
Results: After a median follow-up of 12.3 years (interquartile range 8.4-17.5 years), 132 (35.6%) patients deceased. As a continuous variable, higher BMI was inversely associated with 15 year overall survival (HR = 1.07, 95% CI: 1.02-1.12, *P* = 0.002), independent of age, sex, and total body muscle mass measured by urinary creatinine excretion rate. Obese OLT recipients had a significantly decreased 15 years survival of 56%, when compared to 75% survival rate of normal weight OLT recipients (HR = 1.80, 95% CI: 1.07-3.03, *P* = 0.026).
Conclusions: Post-transplant BMI is inversely associated with long-term survival after OLT. Obesity at 1 year post-transplantation is associated with poor survival, which may offer potential interventional strategies (i.e. dietary advice and lifestyle modification) to improve long-term survival of obese OLT recipients.

The inhibitory effect of tacrolimus and sirolimus on the differentiation of T cells into follicular helper-like T cells

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Background: The effect of immunosuppressive drugs on the generation of T follicular helper (Tfh) cells, specialized in supporting B cell differentiation, is largely unknown. We examined whether the calcineurin inhibitor tacrolimus (TAC) and the mTOR inhibitor sirolimus (SRL) inhibit differentiation of Tfh cells and impact subsequent B cell functions.
Methods: Isolated naïve T cells were polarized to Tfh-like cells in the presence of TAC or SRL. To demonstrate the functionality of the generated Tfh cells we co-cultured these cells with isolated B cells in the presence of alloantigen, and analyzed the Tfh-like cells for B cell help function. Tfh-like cells were defined as $CD4^+CXCR5^+$T cells, which also express PD-1 and ICOS.
Results: Both TAC and SRL significantly inhibited the differentiation into Tfh-like cells. Therapeutic concentrations of TAC and SRL markedly reduced the percentage of $CD4^+CXCR5^+PD\text{-}1^+$ and $CD4^+CXCR5^+ICOS^+$ Tfh cells compared to controls. In addition, the T cells grown in the presence of TAC and SRL expressed less IL-21 and were less potent in providing B cell help. Tfh dependent alloantigen activated B cell proliferation and differentiation into plasma cells and transitional B cells was inhibited by both TAC and SRL.
Conclusions: TAC and SRL inhibited the differentiation of naïve T cells into functional Tfh-like cells, a finding that can be extrapolated to immunosuppressive regimens in transplant patients.

Exploring TTV as a potential biomarker of infection in renal transplant recipients

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Background: Torque teno virus (TTV) is an ubiquitous, non-pathogenic and highly prevalent virus. TTV load has been proposed as a biomarker of immunity, for instance in solid organ transplant recipients. In kidney transplantation (KTx) patients, over immunosuppression increases the risk of infection, for instance with BK polyomavirus (BKPyV), whereas under-immunosuppression might result in allograft rejection. The aim of this study was to explore whether TTV loads can predict BKPyV viremia in KTx recipients.
Methods: Development of BKPyV viremia was retrospectively assessed in a cohort of 389 Dutch KTx recipients, with one-year follow up. BKPyV as well as TTV viral load were determined using real-time PCR in plasma and serum samples taken at baseline, and 1.5, 3, 6, and 12 months after KTx. Survival analysis was performed in R software v. 3.5.1.
Results: During follow-up, 105 (27%) recipients developed BKPyV viremia. TTV detection increased from 84% at baseline (mean 2.2 * 10^3 TTV copies/ml) to 97% 3 months after transplantation (8.3* 10^6 copies/ml). KTx recipients who already tested TTV positive prior to KTx had a 2-fold increased risk (HR of 2.0; CI: 1.0-4.0) for developing BKPyV viremia. Longitudinal TTV loads in association with development of BKPyV are currently being analyzed.
Conclusions: TTV positivity and load correspond to risk of BK viremia in KTx recipients. Further evaluation of TTV as a potential biomarker of infection in KTx recipients is needed.

Islet allo-autotransplantation: allogeneic pancreas transplantation followed by transplant pancreatectomy and islet transplantation

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Background: Simultaneous pancreas/kidney (SPK) transplantation is an important treatment option for patients with type 1 diabetes (T1D) and end stage renal disease (ESRD). In up to 10% of cases, allograft pancreatectomy is needed, after which the donor pancreas is normally discarded. But after pancreatectomy of the endogenous pancreas due to benign pancreatic disease, islet isolation and autotransplantation are regularly performed. We report on a novel treatment option for patients who require allograft pancreatectomy: islet allo-autotransplantation.
Methods: A 39 year old woman with T1D and ESRD who had received an SPK transplantation required emergency allograft pancreatectomy due to bleeding at the anastomosis. 478,587 IEQ of islets were isolated from the removed pancreas allograft and infused into the portal vein. The patient recovered fully. After 3 months stable glycemic control without hypoglycemia with only low dose long acting insulin was achieved. Maximal stimulated C-peptide during a mixed meal test was 3.22 nmol/L and HbA1c was 32.7 mmol/mol Hb (5.3%).
Conclusions: When a pancreas transplant is lost, rescue beta cell therapy by islet allo-autotransplantation allows the possibility to optimise glycemic control without additional HLA allo-antigen exposure.

Multiple non-HLA antibodies are significantly increased in chronic-active antibody-mediated rejection

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Background: Chronic-active antibody mediated rejection (c-aABMR) is characterized by continuous inflammation at the level of the microvascular endothelium. Although donor-specific anti-HLA antibodies play an important role in this process, in many cases these antibodies cannot be detected. In recent years the presence of non-HLA antibodies has emerged as a possible prominent contributing factor in c-aABMR. We therefore investigated whether specific non-HLA antibodies are increased in patients with c-aABMR.
Methods: Fifty-six patients with a for-cause renal biopsy showing c-aABMR (n=35) or interstitial fibrosis and tubular atrophy (IFTA) (n=21) were included between June 2015 and January 2018. Pre-transplantation sera (t=0) and sera at time of biopsy (t=1) of these patients were tested against 14 proteins highly expressed in the kidney using a multiplex non-HLA assay. The assay tested for the presence of autoantibodies against agrin, APMAP, ARHGDIB, ARHGEF6, endorepelin, AT1R, ETAR, LMNB1, LPLUNC1, PECR, Pla2R1, PRKCZ, Tubb4B, and vimentin.
Results: A significant increase in signal-to-background-ratios (STBR) was detected over time (t=0 vs. t=1) against autoantibodies against agrin (p=0.002), ARHGEF6 (p=0.015), AT1R (p<0.001), ETAR (p=0.031), PECR (p=0.027), Tubb4B (p=0.032), vimentin (p=0.018) and ARHGDIB (p=0.011) in patients with c-aABMR. Similarly, patients with IFTA also demonstrated a significant increase in STBR for agrin, AT1R, PECR, Pla2R, Vimentin, ARHGDIB and Tubb4B autoantibodies between t=0 and t=1. However, autoantibodies against ARHGDIB, APMAP, endorepelin and Tubb4B were significantly increased at t=1 in patients with c-aABMR compared to the IFTA group. The STBR in patients with c-aABMR vs. IFTA was 3.40 vs. 1.46 (p=0.006) for anti-ARHGDIB, 1.50 vs. 1.06 (p=0.007) for anti-APMAP, 1.30 vs. 1.06 (p=0.033) for anti-endorepelin and 1.71 vs. 1.15 (p=0.007) for anti-Tubb4B.
Conclusions: After transplantation, renal transplant patients showed a significant increase in various autoantibodies. Moveover, STBR for autoantibodies against ARHGDIB, APMAP, endorepelin and Tubb4B were significantly increased in patients with c-aABMR.

Outcome after transplantation of liver grafts from diabetic donors: a national multicenter study

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Background: As the incidence of diabetes mellitus (DM) continues to grow, an increased number of potential deceased organ donors with DM can be expected. Outcome after transplantation of livers from deceased, diabetic organ donors, however, is not well documented. We aimed to analyze outcomes after transplantation of livers from diabetic donors and compare donors with type I or type II DM.
Methods: All transplant procedures of liver grafts from diabetic donors, performed in one of the three liver transplant centers in the Netherlands between 2006–2016, were included. A matched control group of transplantations with non-diabetic liver grafts was selected using a 1:2 matching for year of transplantation, retransplantation, and balance at risk score. Outcome parameters were 90-day, 1-year, and 3-year graft and patient survival rates, incidence of primary non-function (PNF), hepatic artery thrombosis (HAT), and non-anastomotic biliary strictures (NAS).
Results: A total of 69 transplantations of liver grafts from diabetic donors were identified and matched with 138 non-diabetic donor liver transplants. Of diabetic donors, 22 had type I and 37 had type II DM (data was missing for 10 cases). Moreover, 11/69 were donation after circulatory death donors (DCD) and 58/69 donation after brain death donors. Graft and patient survival rates were significantly lower in recipients of livers from a diabetic donor, compared to recipients of non-diabetic livers. Graft survival at 90-day, 1 and 3 years was 88.4%, 84.1%, and 78.3%, for livers from diabetic donors versus 96.4%, 91.3%, and 89.1% for non-diabetic donors. Interestingly, NAS occurred less often in recipients of the diabetic liver group (4.3% vs. 14.6%, p=0.032), whereas HAT occurred more frequently in these recipients (8.7% vs. 2.2%, p=0.030). There were no differences in outcome after transplantation of livers from donors with type I or type II DM. Noteworthy, transplantation of livers from diabetic DCD donors resulted in very favorable outcomes with 91% 3-year graft survival, 100% 3-year patient survival, no PNF or HAT, and only 1/11 recipients developed NAS.
Conclusions: Overall outcome after transplantation of livers from deceased donors with DM is inferior compared to transplantation of liver grafts from non-diabetic donors. However, transplantation of livers from selected DCD donors with DM had a favorable outcome and diabetes in a DCD donor should, therefore, not be considered a contraindication for liver donation.

Altruistic liver donation in the Netherlands

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Background: Living donor liver transplantation (LDLT) in the pediatric program was started in our centre in 2004 because of a growing shortage of suitable postmortal donor liver grafts. Altruistic liver donation is controversial and in some countries not allowed. In 2010 the first potential altruistic donor in our center was screened. It took 6 months to agree on donation, mainly because of ethical concerns, but after extensive screening no contraindications for donation were found. The liver was accepted for a child who did not have a parent suitable for donation. This procedure was successfully performed anonymously. Despite preoperative concerns we also saw an advantage for the parents who repeatedly reported their gratitude that they both could take care of their sick child. This study aims to compare outcome between altruistic non-directed and related living liver donation.
Methods: Donor and recipient parameters were collected from our prospectively maintained living donor database.
Results: So far, 60 LDLT procedures were performed. Six procedures (10%) were performed in altruistic donors. Median follow up was 267 days. Altruistic donors were significantly older than related donors (50 vs 34 yrs old). Previously 5 out of 6 donors already donated a kidney anonymously, but the liver donation did not have impact on their kidney function. Complication rate was statistically similar in both altruistic (0% gr 3 Clavien Dindo) and related donors (4%). Recipient outcome was also similar in both groups.
Conclusions: This study shows that the donor and recipient outcome after altruistic non-directed left lateral liver donation is good without increased risks in donor or recipient, despite the fact that the donor is older and has a more extensive medical history.

Cost-effectiveness of a home-based educational programme on renal replacement therapies: A proof-of-principle study

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Background: Living donor kidney transplantation (LDKT) is the optimal treatment for most patients with end-stage renal failure (ESRD). Unfortunately, a significant number of these patients cannot find a living donor kidney. Previous research showed that our home-based programme increases knowledge on renal replacement therapies, increases discussing this knowledge with the social network of the patients, and increases LDKT. In this pilot study effects and costs of this intervention are evaluated and compared to the baseline in a state-transition model: A proof-of-principle study.
Methods: The parameters used in the model are the intervention effects, transition probabilities, incidence rates, health-stage related costs and quality adjusted life years (QALYs). Costs and QALY-data were obtained from the literature. Costs of the educational programme at the out-patient transplantation clinic of the Erasmus Medical Center were estimated. Transition probabilities and incidence rates were estimated from the database of all ESRD-patients in the Netherlands from 1990-2007.
Results: The pilot data suggests that the home-based educational programme offers both better effects and lower costs for ESRD patients compared to standard care from the second year onwards: an incremental cost-effectiveness ratio (ICER) of -€27.163 after year 2, indicating that after two years €27.163 is saved for every QALY gained. After ten years the ICER is €-29.906.
Conclusions: This proof-of-principle study demonstrates that the home-based education programme is dominant in terms of cost-effectiveness compared to standard care; after two years there is a gain in overall health with lower costs. However, the data used in the model is outdated and more recent parameters are warranted. The programme is now nationally implemented to evaluate the cost-effectiveness. Based on this proof-of-principle pilot, cost-effectiveness will be assessed using programme effects, programme costs and QALYs of the national implementation project across centers. Incidence rates and transition probabilities also have to be calculated with the most recent data to make a comprehensive cost-effectiveness analysis.

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