NEDERLANDSE **TRANSPLANTATIE** VERENIGING

Bootcongres 2020

Wetenschappelijke voorjaarsvergadering

Nederlandse Transplantatie Vereniging

4 en 5 maart 2020

Theaterhotel De Oranjerie te Roermond

georganiseerd in samenwerking met

Maastricht UMC

Maastricht UMC+

Inhoudsopgave

Algemene informatie

Schematisch overzicht programma woensdag 10

Schematisch overzicht programma donderdag 12

Informatie NTV

Welkom op het Bootcongres in Roermond!

Een nieuw decennium: nieuwe kansen en uitdagingen voor zowel orgaandonatie als orgaan-transplantatie.

Dit bootcongres zit vol inspirerende verhalen wat wij kunnen leren van ervaringen binnen en buiten de transplantatie wereld. De 'Lessons to be Learned' begint al in de openingssessie, waarin we horen van een andere organisatie hoe deze omgaat met samenwerking onder tijdsdruk in complexe situaties om een goed resultaat te bereiken.

Vanaf 1 juli 2020 geldt de nieuwe donorwet (actief donorregistratie). Leidt deze wet tot gewenste gevolgen? Orgaandonatie (en orgaantransplantatie) zal zeker in de publicitaire belangstelling staan. De NTS is gestart met een campagne om de bevolking voor te lichten over de wet. Hij geldt voor iedereen van 18 jaar en ouder die ingeschreven staat in een Nederlandse gemeente. Daardoor heeft deze wet ook gevolgen voor bijzondere doelgroepen, die eerder niet betrokken waren bij donatie. Wat de praktische gevolgen zijn en hoe hiermee om te gaan is nog niet breed bekend, niet bij de doelgroepen en hun begeleiders, maar ook niet bij professionals betrokken bij orgaandonatie. Je hoort hier meer over in dit congres.

Dag 2 staat grotendeels in het teken van donoren, nabestaanden en getransplanteerden. Te vaak vergeten we wat we van hen kunnen leren. 's Ochtends delen een altruïstische donor en een nabestaande van een orgaandonor hun indrukwekkende persoonlijke verhalen. Een professional die bij deze orgaandonatie na euthanasie betrokken was, vertelt ons haar ervaringen.

Hoewel we mogen dromen dat door de nieuwe wet er geen tekort aan donororganen zal zijn, moeten we reëel zijn en aandacht houden voor momenteel niet gebruikte potentiële organen. Niet primair uit onwil, maar omdat we rondom orgaandonatie te maken hebben met een delicate balans tussen technische mogelijkheden en maatschappelijke acceptatie. Hartdonatie bij DCD donoren is hier een voorbeeld van en wordt vanuit verschillende kanten belicht.

Na transplantatie gaat veel aandacht uit naar de functie van een orgaan. Tijdens dit congres hoort iedereen het laatste nieuws op technisch, medisch en verpleegkundig gebied tijdens de presentaties van de ingezonden abstracts. Maar wat is de rol van de getransplanteerde? Zij staan centraal en het is de bedoeling dat zij hun levensdoel kunnen bereiken met de minste beperking. Er is daarom speciaal een sessie die zich toespitst op de (elektronische) hulpmiddelen die ter beschikking komen om de patiënt te betrekken als partner in zijn behandeling en over de (potentiele) uitkomstmaten die de patiënt in deze belangrijk vindt.

Een getransplanteerde is momenteel een actieve partner in zijn behandeling. Hij/zij kan zelf veel bijdragen aan zijn eigen gezondheid en toekomst. Herstel na transplantatie vergt van de patiënt een actieve houding, waaronder vaak verandering van levensstijl. Hierbij is steun en begeleiding nodig. De afsluitende lezing laat zien hoe belangrijk een ondersteunend team is voor een topsporter om zijn doel te bereiken. Herstel na transplantatie is ook een vorm van topsport en onze patiënten verdienen daarbij onze ondersteuning. Ik wens U een boeiend Bootcongres met veel "Lessons to be learned".

Namens het lokale organisatiecomité,
Maarten Christiaans, Maastricht UMC

Organisatiecommissie Bootcongres 2020

Vanuit het Maastricht UMC
Maarten Christiaans
Wim de Jongh
Marielle Gelens
Emily Doyle
Tineke Wind
Jorinde van Laanen
Noud Peppelenbosch
Monique Mullens
Philip Ulrichts
Christien Voorter
Burcu Duygu

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
Emma Bocxe

Accreditatie is aangevraagd bij de volgende verenigingen:

Nederlandse Vereniging voor Heelkunde	12
Nederlandse Vereniging voor Immunologie	10
Nederlandse Internisten Vereniging	
Nederlandse Vereniging voor Kindergeneeskunde	11
Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose	12
Nederlandse Vereniging van Maag-Darm-Leverartsen	
Nederlandse Vereniging voor Thoraxchirurgie	

V&VN, kwaliteitsregister algemeen	12
V&VN, kwaliteitsregister, deskundigheidsgebied Dialyse	12
V&VN, verpleegkundig specialisten register	12
Nederlandse Associatie van Physician Assistants	12

Theaterhotel De Oranjerie

Kloosterwandplein 12-16
6041 JA Roermond
Website: www.theaterhotelroermond.nl

Bereikbaarheid met openbaar vervoer

Vanaf treinstation Roermond loopt u in 5 minuten naar De Oranjerie.
- Loop het stationsgebouw uit richting het Stationsplein.
- Steek het Stationsplein over en loop de Kruisherenstraat in.
- Sla rechtsaf naar de Joep Nicolasstraat.
- Vervolg uw weg, De Oranjerie bevindt zich aan de linkerkant.

Bereikbaarheid met de auto

Indien u met een navigatiesysteem of routeplanner het hotel wilt bereiken, voert u dan 'Achter de Oranjerie 1' in als adres. U komt dan uit bij de Q-Park garage 'De Oranjerie' die direct achter ons hotel gelegen is. Dit is ook de beste plek om uw auto te parkeren.

Parkeermogelijkheden

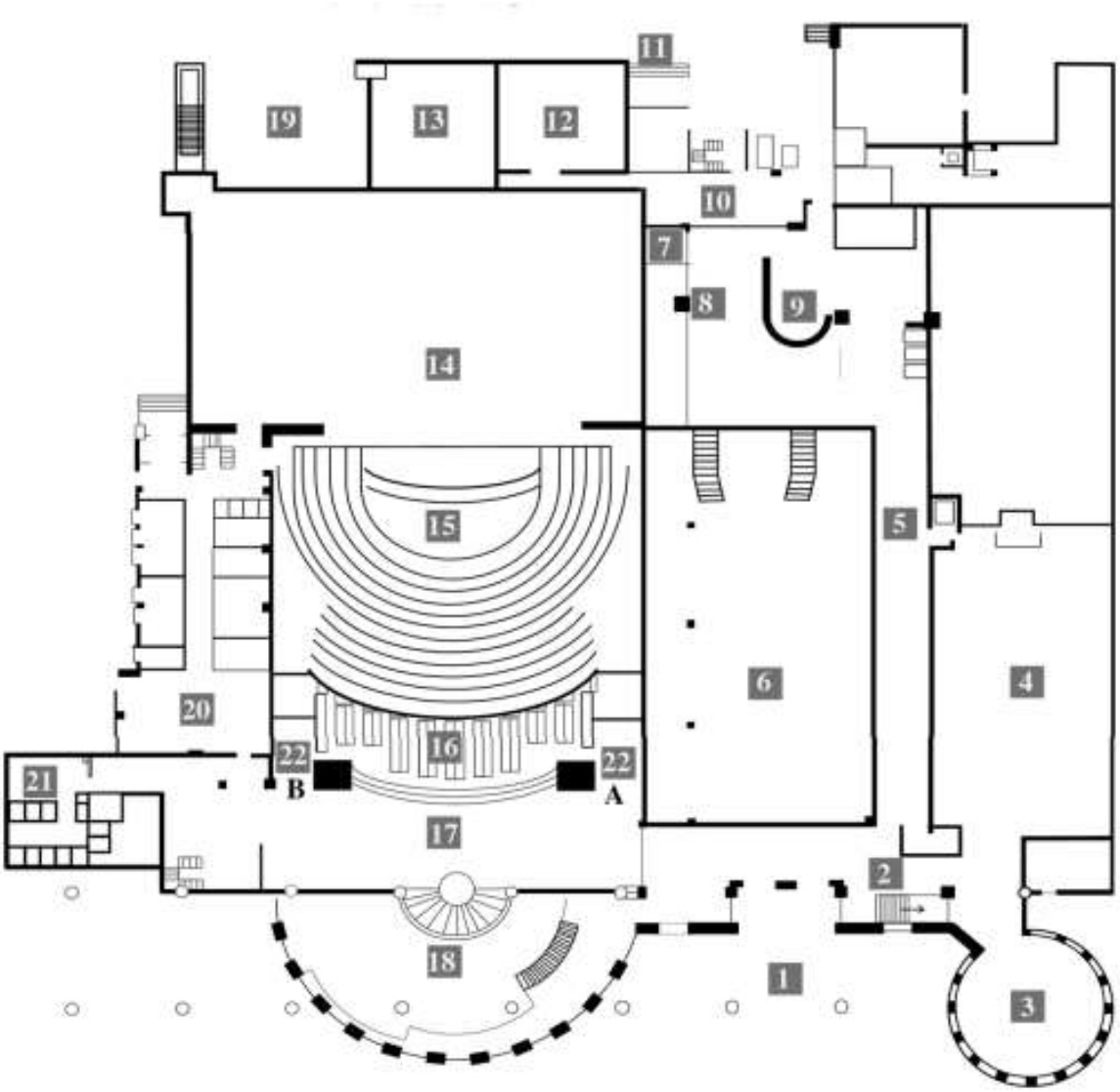
De dichtstbijzijnde parkeergarage is Q-Park De Oranjerie (6041 JX Roermond). Vanaf de parkeergarage kunt u lopend naar de hoofdingang van Theaterhotel De Oranjerie. Een dagkaart bij Q-park kost € 14,00, u kunt deze ook bij de receptie van De Oranjerie (contact) kopen voor € 7,50. Open 24/7.

WiFi

In het Theaterhotel De Oranjerie is een openbaar WiFi-netwerk beschikbaar waarop u kunt inloggen:
Netwerk: Oranjerie-Free-WiFi
Wachtwoord is niet nodig

Plattegrond zalen

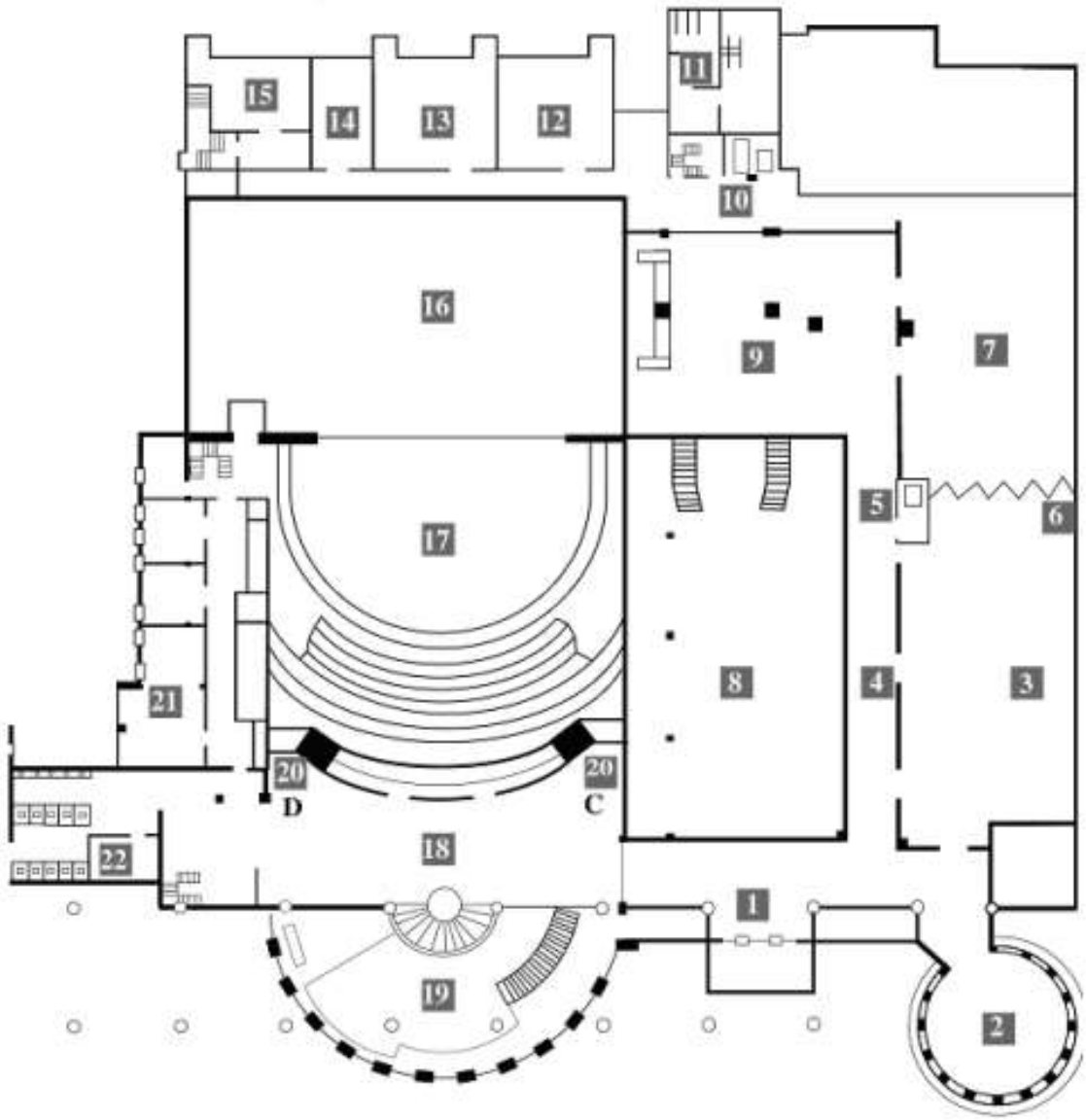
Begane grond



Voor het Bootcongres zijn de volgende congreszalen in gebruik:

Kloosterzaal, begane grond (nummer 3)
De Theaterzaal, begane grond (nummer 15-16, te bereiken via nummer 22)
Salle de Fête, begane grond (nummer 6)

1ste verdieping



Voor het Bootcongres zijn de volgende congreszalen in gebruik:

De Theaterzaal, 1ste verdieping (nummer 17, te bereiken via nummer 20)
Joep Nicolas zaal, 1ste verdieping (nummer 7)
Leo Franssen zaal,1ste verdieping (nummer 3)
Toon Hermans Foyer, 1ste verdieping (nummer 18)

Inleveren presentaties

Wij verzoeken sprekers zo spoedig mogelijk na aankomst de presentatie in te leveren in de Kloosterzaal op de begane grond (nummer 3 op de plattegrond).

Ophangen posters

De posters graag ophangen in de Toon Hermans Foyer op de 1ste verdieping (nummer 18 op de plattegrond). Daar staan (genummerde) posterborden gereed, materiaal om de posters te bevestigen is aanwezig. Deelnemers worden verzocht de posters pas te verwijderen na de laatste pauze op donderdag 5 maart.

Tijdstip en locatie van de maaltijden

Woensdag

Lunch	13.00 – 14.00 uur in de foyer
Lopend buffet	19.30 – 22.00 uur in ECI Cultuurfabriek
Feest	22.00 – 01.00 uur in ECI Cultuurfabriek

Avondprogramma
ECI Cultuurfabriek
ECI 13, 6041 MA Roermond
www.ecicultuurfabriek.nl

Parkeergelegenheid ECI Cultuurfabriek:
– Dr. Bärstraat, voorkant ECI (na 18:00 gratis)
– Hockeyveld Concordia Burgemeester Geuljanslaan 1 (gratis, 5 min. lopen)
– Parkeergarage Roercenter Roersingel 13 (betaald, 5 min. lopen)

Vanaf het station van Roermond is het ongeveer een kwartier lopen naar de ECI cultuurfabriek. Het is ook mogelijk om de bus te pakken. Vanaf station Roermond kun je Arriva Stadsbus 1 richting Herten nemen tot de bushalte Bisschop Lindanussingel. Vanaf hier is het nog ongeveer 5 minuten lopen naar de ECI cultuurfabriek.

Donderdag

Lunch:	12.30 – 13.30 uur in de foyer

Vergaderingen tijdens Bootcongres

Woensdag 4 maart 2020

Ledenvergadering Nederlandse Transplantatie Vereniging 17.40-18.40 uur
Locatie: Theaterhotel De Oranjerie, Joep Nicolas zaal, 1ste verdieping (nummer 7 op de plattegrond)

Woensdag 4 maart 2020
Schematisch overzicht programma

Woensdagochtend	**Theaterzaal**		
09.00 – 09.30	Ontvangst met koffie		
09.30 – 11.00 09.35 10.35	**Plenaire sessie I** *voorzitters: Maarten Christiaans / Marlies Reinders* Opening congres door voorzitter LOC en NTV 'Lessons to be learned' acuut handelen in een complexe organisatie Luitenant-kolonel M. Hilali, Ministerie van Defensie **Prijsuitreikingen** Astellas Transplantatie Research Prijs 2020 Chiesi prijs 2020 – Beste Idee in Transplantatie Novartis Transplantation Awards 2020		
11.00 – 11.30	Koffiepauze		
11.30 – 13.00	**Plenaire sessie II** *voorzitters: Tineke Wind / Lili Guo* Thema: Nieuwe Wet Orgaan Donatie: Consequenties voor speciale bevolkingsgroepen 11.30 Nichon Jansen, senior beleidsmedewerker/onderzoeker, NTS- Verschillen tussen de huidige en de nieuwe WOD 12.00 Erica Baarends, onderzoeker afdeling Kwaliteit, Audit & Inspectie, Koraal - Toepassing nieuwe WOD in de verstandelijk gehandicaptenzorg 12.30 Best Abstracts		
13.00 – 14.00	Lunch met gemodereerde postersessies		
Toon Hermans Foyer	**Postersessie I**: Klinisch *Moderator: Arjan van Zuilen*	**Postersessie 2**: Basaal *Moderator: Karin Boer*	**Postersessie 3**: Klinisch *Moderator: Dorottya de Vries*

Schematisch overzicht programma
Woensdag 4 maart 2020

Woensdagmiddag	Theaterzaal	Joep Nicolas zaal	Leo Franssen zaal
14.00 – 15.30	**Parallelle sessie III**: klinische abstracts *Voorzitters: Bianca Zomer / Azam Nurmohamed*	**Parallelle sessie IV**: basale abstracts *Voorzitters: Burcu Duygu / Henny Otten*	**Parallelle sessie V**: verpleegkundige en donatie abstracts *Voorzitters: Monique Mullens / Louise Maasdam*
15.30 – 16.00	Koffiepauze		
16.00 – 17.30	**Parallelle sessie VI**: klinische abstracts *Voorzitters: Marielle Gelens / Luuk Hilbrands*	**Parallelle sessie VII**: klinische/basale abstracts *Voorzitters: Carla Baan / Cyril Moers*	**Parallelle sessie VIII**: Young Professionals *Voorzitters: Dorottya de Vries*
17.40 – 18.40		Ledenvergadering NTV	
19.30 – 01.00	Avondprogramma in ECI cultuurfabriek		
01.00	Einde programma		

Schematisch overzicht programma
Donderdag 5 maart 2020

Donderdagochtend	**Theaterzaal**	**Joep Nicolas zaal**
07.30 – 09.00	Ontvangst en registratie	
08.00 – 09.00		**Onderwijssessie** *Voorzitters: Martin Hoogduijn / Coby Annema*
09.00 – 10.30	**Plenaire sessie IX** *Voorzitters: Wim de Jongh / Rianne van Zoggel* Thema: Ervaringen bij bijzondere orgaandonaties 09.00 Peter Keijsers, nierdonor 09.30 Anita Kempener, nabestaande 10.00 Najat Tajaate, anesthesist-intensivist, Zuyderland MC	
10.30 – 11.00	Koffiepauze	
	Theaterzaal	**Joep Nicolas zaal**
11.00 – 12.30	**Parallelle sessie X**: Medisch Ethische Commissie van de NTV *Voorzitters: Tineke Wind / Marion Siebelink* Thema: DCD hartdonatie: hardnodig? 11.00 Dr. Michiel E. Erasmus, thoraxchirurg, UMCG 11.20 Dr. Mike Bos, ethicus 11.40 Dr. Michiel Erasmus, thoraxchirurg, UMCG Dr. Hans. Sonneveld, intensivist, Isala Ziekenhuis	**Parallelle sessie XI**: *Voorzitters: Dr. Marja Ho-Dac – Pannekeet / Marielle Gelens* Thema: Naar waarde- en data driven transplantatiezorg
12.30 – 13.30	Lunch met gemodereerde postersessies	
Toon Hermans Foyer	**Postersessie IV**: Donatie / Verpleegkundig *Moderator: Marjo van Helden*	**Postersessie V**: Klinisch / Verpleegkundig *Moderator: Annelies de Weerd* **Postersessie VI**: Basaal *Moderator: Elena Kamburova*

Schematisch overzicht programma
Donderdag 5 maart 2020

Donderdagmiddag	Theaterzaal	Joep Nicolas zaal	Leo Franssen zaal
13.30 – 15.00	**Parallelle sessie XII**: Klinische/basale abstracts *Voorzitters: Arnold van der Meer / Frederike Bemelman*	**Parallelle sessie XIII**: *Voorzitters: Emilie Doyle / Laura Bruinenberg* Thema: Wensen en grenzen rondom donatie Door LWTC	**Parallelle sessie XIV**: Klinische abstracts *Voorzitters: Jan-Stephan Sanders / Arjan van Zuilen*
15.00 – 15.30	Koffiepauze		
	Theaterzaal		
15.30 16.15	**Plenaire sessie XV** *Voorzitters: Maarten Christiaans / Marlies Reinders* 'Lessons to be learned' personalisatie van voeding bij topsport J. Lacroix, manager Daily Fresh Food G. Rietjens, inspanningsfysioloog UM M. Bisselink, chefkok Daily Fresh Food **Prijsuitreikingen** Presentatie NTV innovatie in transplantatie onderwijs winnaar 2019 LWTV Innovatie-Kwaliteitsprijs 2020, gevolgd door presentatie winnaar 2019 NTV wetenschapsprijs 2020 Jon van Rood proefschrift prijs 2020, gevolgd door presentatie winnaar 2020		
16.45	Sluiting congres		

Plenaire sessie I – Openingssessie **Theaterzaal**

09.00 Ontvangst en registratie

Voorzitters: *Dr. Maarten Christiaans, voorzitter LOC, internist-nefroloog, MUMC*
Prof. dr. Marlies Reinders, voorzitter NTV, internist-nefroloog, LUMC

09.30 Opening

09.35 **'Lessons to be learned' acuut handelen in een complexe organisatie**
Luitenant-kolonel M. Hilali, Ministerie van Defensie

10.40 Astellas Transplantatie Research Prijs 2020
Uitgereikt door Vincent Sloos, Astellas

Voordracht winnaar prijs 2019: Identifying drugs to prevent hypoxia-induced epithelial injury in liver and lung transplantation using a novel organoid model.
F.J.M. Roos, promovendus, Erasmus MC

10.47 Chiesi-prijs Beste Idee in Transplantatie 2020
Uitgereikt door Niels van Dijk, Chiesi

10.55 Novartis Transplantation Awards 2020
Uitgereikt door Dr. Arjan van Zuilen, internist-nefroloog UMCU en voorzitter Novartis Transplant Advisory Board

11.00 Koffie- / theepauze

Plenaire sessie II **Theaterzaal**

Thema: **Nieuwe Wet Orgaan Donatie: Consequenties voor speciale bevolkingsgroepen**

Voorzitters: *Dr. Tineke Wind, transplantatiecoördinator, MUMC*
Msc. Lili Guo, beleidsadviseur Min. van Volksgezondheid, Welzijn en Sport

11.30 Verschillen in de huidige en de nieuwe WOD
Dr. Nichon Jansen, senior beleidsmedewerker/onderzoeker, NTS

12.00 Toepassing nieuwe WOD in de verstandelijk gehandicaptenzorg
Dr. Erica Baarends, onderzoeker afdeling Kwaliteit, Audit & Inspectie, Koraal

Best abstracts
Voordrachten in het Nederlands, 7 minuten presentatie en 3 minuten discussie.

12.30 Long-term survival of lung transplant recipients transplanted from ICU. A multicentre study (p.32)

C.T. Gan[1], M.E. Hellemons[2], M.E. Erasmus[3], J. Droogh[4], D. Dos Reis Miranda[5], R.A.S. Hoek[2], W. van der Bij[1], E.A.M. Verschuuren[1], [1]Dept. of Pulmonary diseases and tuberculosis, lung-transplantation, UMCG, Groningen, The Netherlands. [2]Dept. of Pulmonary diseases, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Thorax Surgery, UMCG, Groningen, The Netherlands. [4]Intensive Care, UMCG, Groningen, The Netherlands. [5]Intensive Care, Erasmus MC, Rotterdam, The Netherlands.

12.40 The Renin-Angiotensin System is present and functional in human ipsc-derived kidney organoids (p.33)

A.S. Shankar[1], Z. Du[1], H. Tejeda Mora[1], T.P.P. van den Bosch[2], S.S. Korevaar[1], I.M. van den Berg – Garrelds[4], J. Gribnau[3], M. Clahsen-van Groningen[2], C.C. Baan[1], A.H.J. Danser[4], E.J. Hoorn[1], M.J. Hoogduijn[1], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, [2]Dept. of Pathology, [3]Dept. of Developmental Biology, [4]Dept. of Internal Medicine, Division of Pharmacology & Vascular Medicine, Erasmus MC, Rotterdam, The Netherlands.

12.50 Promising results of kidney transplantation from donors following euthanasia (p.34)

J. Bollen, Dept. of Anesthesiology, MUMC, Maastricht, The Netherlands.

13.00 Lunch en gemodereerde postersessies

Postersessie 1 – Klinische abstracts **Toon Hermans Foyer**

Tijd: 13.00 – 13.25

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

Moderator: Arjan van Zuilen, nefroloog, UMCU

1. Pharmacokinetics of tacrolimus in paediatric renal transplantation recipients during adolescence (p.35)

F.H.M. Prince[1], J.I. Roodnat[2], R.F. van der Wouden[1], E.A.M. Cornelissen[3], A.H. Bouts[4], C.C. Baan[5], A.C.S. Hokken-Koelega[6], T. van Gelder[7], K. Cransberg[8], [1]Dept. of Pediatric Nephrology, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Nephrology, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Pediatric Nephrology, Radboudumc - Amalia kinderziekenhuis, Nijmegen, The Netherlands. [4]Dept. of Pediatric Nephrology, Amsterdam UMC, Emma kinderziekenhuis, Amsterdam, The Netherlands. [5]Dept. of Transplantation, Erasmus MC, Rotterdam, The Netherlands. [6]Dept. of Pediatric Endocrinology, Erasmus MC - Sophia Kinderziekenhuis, Rotterdam, The Netherlands. [7]Dept. of Nephrology & Clinical Pharmacology, Erasmus MC, Rotterdam, The Netherlands. [8]Dept. of Pediatric Nephrology, Erasmus MC - Sophia Kinder-ziekenhuis, Rotterdam, The Netherlands.

2. A population pharmacokinetic model not predict the optimal starting dose of tacrolimus in pediatric renal transplant recipients in a prospective study; lessons learned and model improvement (p.36)

L.M. Andrews[1], B.C.M. de Winter[1], E.A.M. Cornelissen[2], H. de Jong[3], D.A. Hesselink[4], M.F. Schreuder[2], R.J.M. Bruggemann[5], T. van Gelder[1], K. Cransberg[3], [1]Pharmacy, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Pediatric Nephrology, Radboudumc, Nijmegen, The Netherlands. [3]Dept. of Pediatric Nephrology, Erasmus MC, Rotterdam, The Netherlands. [4]Dept. of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. [5]Pharmacy, Radboudumc, Nijmegen, The Netherlands.

3. Design of the OPTIMIZE study. OPen label multicenter randomized Trial comparing standard IMmunosuppression with tacrolimus and mycophenolate mofetil with a low exposure tacrolimus regimen In combination with everolimus in de novo renal trans-plantation in Elderly patients. (p.37)

S.E. de Boer[1], J.S.F. Sanders[1], F.J. Bemelman[2], A.W. Gomes Neto[1], L. Hilbrands[3], D. Kuypers[4],

S.A. Nurmohamed[5], H. Bouwsma[6], A.P.J. de Vries[6], A.D. van Zuilen[7], D.A. Hesselink[8], S.P. Berger[1], [1]Dept. of Nephrology, UMCG, Groningen, The Netherlands. [2]Dept. of Nephrology, Amsterdam UMC, loc. AMC, Amsterdam, The Netherlands. [3]Dept. of Nephrology, Radboudumc, Nijmegen, The Netherlands. [4]Dept. of Nephrology, UZ Leuven, Leuven, Belgium. [5]Dept. of Nephrology, Amsterdam UMC, loc. VUmc, Amsterdam, The Netherlands. [6]Dept. of Nephrology, LUMC, Leiden, The Netherlands. [7]Dept. of Nephrology, UMCU, Utrecht, The Netherlands. [8]Dept. of Nephrology, Erasmus MC, Rotterdam, The Netherlands.

4. LCP-tacrolimus in daily practice. tolerability and intrapatient variability (p.38)
K.L.W. Bunthof[1], A.D. van Zuilen[2], J.W. van der Heijden[3], L.B. Hilbrands[1], [1]Dept. of Nephrology, Radboudumc, Nijmegen, The Netherlands. [2]Dept. of Nephrology, UMCU, Utrecht, The Netherlands. [3]Dept. of Nephrology, Amsterdam UMC, loc. VUmc, Amsterdam, The Netherlands.

5. Gastro-intestinal complaints in stable renal transplant recipients on tacrolimus and mycophenolate mofetil. (p.39)
Z. al Fatly[1], J.A. van Gestel[2], M.J. Verschragen[3], M.G.H. Betjes[1], A.E. de Weerd[3], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, [2]Dept. of Internal Medicine, [3]Dept. of Internal Medicine, Division of Nephrology & Transplantation, Erasmuc MC, Rotterdam, The Netherlands.

Postersessie 2 – Basale abstracts — Toon Hermans Foyer

Tijd: 13.00 – 13.25

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

Moderator: Dr. ing. Karin Boer, onderzoeker, Erasmus MC

6. Normothermic perfusion of porcine ex vivo livers to study hepatic pharmacokinetic processes (p.40)
L.J. Stevens[1], J. Dubbeld[1], J.B. Doppenberg[1], B. van Hoek[2], C.A.J. Knibbe[3], W.H.J. Vaes[4], E. van de Steeg[5], I.P.J. Alwayn[1], [1]Dept. of Surgery, LUMC, Leiden, The Netherlands. [2]Dept. of Gastroenterology & Hepatology, LUMC, Leiden, The Netherlands. [3]Systems Biomedicine and Pharmacology, Leiden Academic Centre for Drug Research (LACDR), Leiden, The Netherlands. [4]Dept. of Microbiology & Systems biology, The Netherlands Organization for Applied Scientific Research (TNO), Zeist, The Netherlands. [5]Dept. of Microbiology & Systems biology, Leiden Academic Centre for Drug Research (LACDR), Leiden, The Netherlands.

7. A tool for combined analysis of transcriptome and T cell receptor repertoire at the single cell level to characterize low frequent donor-specific hypo-responsive CD137-expressing T cells (p.41)
N.H.R. Litjens[1], A.W. Langerak[2], A.C.J. van der List[1], M. Klepper[1], M. de Bie[2], Z. Azmani[3], A.T. den Dekker[3], R.W.W. Brouwer[3], M.G.H. Betjes[1], W.F.J. van IJcken[3], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Immunology, The Netherlands. [3]Center for Biomics, The Netherlands.

8. Porcine precision-cut kidney slices as an ex vivo model to evaluate the effect of a ketogenic diet on mitochondrial function (p.42)
L.A. van Furth, H. Maassen, L.H. Venema, P. Olinga, H.G.D. Leuvenink, Dept. of Surgery, UMCG, Groningen, The Netherlands.

9. Hydrogen sulphide-induced hypometabolism in human-sized porcine kidneys (p.43)
H. Maassen[1], K.D.W. Hendriks[2], L.H. Venema[1], R.H. Henning[2], H.S. Hofker[1], H. van Goor[3], H.G.D. Leuvenink[1], A.M. Coester[1], [1]Dept. of Surgery, [2]Dept. of Clinical Pharmacy and Pharmacology, [3]Dept. of Pathology & Medical Biology, UMCG, Groningen, The Netherlands.

Postersessie 3 – Klinische abstracts **Toon Hermans Foyer**

Tijd: 13.00 – 13.25

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

Moderator: Dr. Dorottya de Vries, chirurg, LUMC

10. Effect of portal hypertension and surgical technique on perioperative blood loss in liver transplantation. (p.44)
L.C. Pietersen[1], E. Sarton[2], C.S.P. van Rijswijk[3], M. Tushuizen[4], H. Putter[5], H.D. Lam[6], A.G. Baranski[6], I.P.J. Alwayn[1], A.E. Braat[1], B. van Hoek[4], [1]Dept. of Surgery, LUMC, Leiden, The Netherlands. [2]Dept. of Anesthesiology, The Netherlands. [3]Dept. of Radiology, The Netherlands. [4]Dept. of Gastroenterology & Hepatology, LUMC, Leiden, The Netherlands. [5]Dept. of Medical Statistics, The Netherlands. [6]Dept. of Surgery, The Netherlands.

11. Oxygenated Hypothermic Machine Perfusion of the pancreas followed by Controlled Oxygenated Rewarming to sub-normothermia for viability testing (p.45)
L.J.M. Habets[1], J.B. Doppenberg[2], I.P.J. Alwayn[1], M.A. Engelse[2], V.A.L. Huurman[1], [1]Dept. of Transplant Surgery, LUMC, Leiden, The Netherlands. [2]Dept. of Internal Medicine, LUMC, Leiden, The Netherlands.

12. Diabetic nephropathy alters circulating long noncoding RNA levels that normalize following simultaneous pancreas-kidney transplantation (p.46)
K.E. Groeneweg[1], Y.W. Au[2], C. van Kooten[2], J.W. de Fijter[1], M.E.J. Reinders[1], A.J. van Zonneveld[2], R. Bijkerk[2], [1]Dept. of Internal Medicine, Division of Nephrology, LUMC, Leiden, The Netherlands. [2]Dept. of Nephrology & Transplantation, LUMC, Leiden, The Netherlands.

13. Intraoperative indocyanine green plasma disappearance rate as predictor for retransplantation in liver transplantation (p.47)
L.C. Pietersen[1], W.M. Nijboer[1], H. Putter[2], B. van Hoek[3], A.E. Braat[1], I.P.J. Alwayn[1], M. Reekers[4], [1]Dept. of Surgery, LUMC, Leiden, The Netherlands. [2]Dept. of Medical Statistics, The Netherlands. [3]Dept. of Gastroenterology & Hepatology, LUMC, Leiden, The Netherlands. [4]Dept. of Anesthesiology, The Netherlands.

Parallel sessie III – Klinische abstracts **Theaterzaal**

Voorzitters: Bianca Zomer, internist-nefroloog, MUMC
Dr. Azam Nurmohamed, internist-nefroloog, Amsterdam UMC

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

14.00 The efficacy of therapeutic anticoagulation in pancreas allograft thrombosis according the CPAT grading system (p.48)
S.A. Simonis[1], B.M. de Kok[2], J.C. Korving[2], W.H. Kopp[1], A.G. Baranski[1], V.A.L. Huurman[1], P.J.M. van der Boog[3], M.N.J.M. Wasser[2], A.E. Braat[1], [1]Dept. of Surgery, LUMC, Leiden, The Netherlands. [2]Dept. of Radiology, LUMC, Leiden, The Netherlands. [3]Dept. of Nephrology, LUMC, Leiden, The Netherlands.

14.10 Normothermic machine perfusion is a feasible preservation technique and a promising strategy for donor kidneys in the Eurotransplant Senior program (ESP). (p.49)
E. Rijkse[1], J. de Jonge[1], H.J.A.N. Kimenai[1], M.J. Hoogduijn[2], R.W.F. de Bruin[1], M.W.F. van den Hoogen[2], J.N.M. IJzermans[1], R.C. Minnee[1], [1]Dept. of Surgery, Division of HPB & Transplant

Surgery, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands.

14.20 Detrimental consequences of early graft loss after kidney transplantation. conclusions from a nationwide evaluation. (p.50)

M.J. de Kok[1], A.F. Schaapherder[1], J.W. Mensink[1], A.P. de Vries[2], M.E. Reinders[2], C. Konijn[3], F.J. Bemelman[4], J. van de Wetering[5], A.D. van Zuilen[6], M.H. Christiaans[7], M.C. Baas[8], S.A. Nurmohamed[9], S.P. Berger[10], R.J. Ploeg[11], I.P. Alwayn[1], J.H. Lindeman[1], [1]Dept. of Surgery & Leiden Transplant Center, LUMC, Leiden, The Netherlands. [2]Dept. of Internal Medicine, Division of Nephrology & Leiden Transplant Center, LUMC, Leiden, The Netherlands. [3]Dutch Transplant Foundation, Dutch Transplant Foundation, Leiden, The Netherlands. [4]Dept. of Internal Medicine, Division of Nephrology, Amsterdam UMC, loc. AMC, Amsterdam, The Netherlands. [5]Dept. of Internal Medicine, Division of Nephrology, Erasmus MC, Rotterdam, The Netherlands. [6]Dept. of Internal Medicine, Division of Nephrology, University Medical Center Utrecht, Utrecht, The Netherlands. [7]Dept. of Internal Medicine, Division of Nephrology, MUMC, Maastricht, The Netherlands. [8]Dept. of Internal Medicine, Division of Nephrology, Radboudumc, Nijmegen, The Netherlands. [9]Dept. of Internal Medicine, Division of Nephrology, Amsterdam UMC, loc. VUmc, Amsterdam, The Netherlands. [10]Dept. of Internal Medicine, Division of Nephrology, UMCG, Groningen, The Netherlands. [11]Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, United Kingdom.

14.30 Limited Survival Benefit of Living versus Deceased Donor Kidney Transplantation in Elderly Recipients. (p.51)

E. Tegzess[1], A.W. Gomes Neto[1], R.A. Pol[2], S.E. de Boer[1], J.S.F. Sanders[1], S.P. Berger[1], [1]Dept. of Internal Medicine, Division of Nephrology, [2]Dept. of Surgery, UMCG, Groningen, The Netherlands.

14.40 The impact of donor organ extraction time on pancreas graft survival (p.52)

M. Leemkuil[1], F. Messner[2], S. Benjamens[1], J.F. Krendl[2], H.G.D. Leuvenink[1], C. Margreiter[2], R.A. Pol[1], [1]Dept. of Surgery, UMCG, Groningen, The Netherlands. [2]Dept. of Surgery, Medical University Innsbruck, Innsbruck, Austria.

14.50 Double J or percutaneous single J-uretic stent after renal transplantation; Differences in urologic complication (p.53)

M.A.C.J. Gelens[1], J.H.H. van Laanen[2], A.G. Peppelenbosch[2], M.H.L. Christiaans[3, 4], [1]Dept. of Nephrology, [2]Dept. of Vascular Surgery, [3]Dept. of Internal Medicine, Division of Nephrology, MUMC+, Maastricht, The Netherlands.

15.00 Transplanting Livers From Hepatitis C Virus Positive Donors; Is It Worth The Risk? (p.54)

J.W. Mensink[1], B. van Hoek[2], B. Schaefer[3], M.D. van Rosmalen[4], I.P.J. Alwayn[2], A.E. Braat[5], [1]Dept. of Transplant Surgery, NTS/LUMC, Leiden, The Netherlands. [2]Transplantation Center, LUMC, Leiden, The Netherlands. [3]Policy & Organ Center, Nederlandse Transplantatie Stichting, Leiden, The Netherlands. [4]Dept. of Organ Allocation, Eurotransplant, Leiden, The Netherlands. [5]Dept. of Transplant Surgery, LUMC, Leiden, The Netherlands.

15.10 The transition of frailty state after kidney transplantation (p.55)

E.E. Quint[1], L. Schopmeyer[1], L.B.D. Banning[1], C. Moers[1], M. El Moumni[2], G.J. Nieuwenhuijs-Moeke[2], S.P. Berger[3], S.J.L. Bakker[3], R.A. Pol[1], [1]Dept. of Surgery, [2]Dept. of Anesthesiology, [3]Dept. of Internal Medicine, UMCG, Groningen, The Netherlands.

15.30 Koffie- / theepauze

Parallel sessie IV – Basale abstracts **Joep Nicolas zaal**

Voorzitters: *Dr. Burcu Duygu, moleculair bioloog, MUMC*
Dr. Henny Otten, medisch immunoloog, UMCU

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

14.00 Uncensored immune profiling in kidney transplantation. towards individualized immunosuppressive treatment (p.56)
E.G. Kamburova[1], R.L. Smeets[2], W.B.L. Alkema[3], I. Joosten[4], L.B. Hilbrands[1], H. Koenen[4], M.C. Baas[1], [1]Dept. of Nephrology, [2]Dept. of Laboratory Medicine, [3]Center for Molecular and Biomolecular Informatics, [4]Dept. of Laboratory Medicine, Laboratory of Medical Immunology, Radboudumc, Nijmegen, The Netherlands.

14.10 Potential protective effects of doxycycline on renal degradome during hypothermic machine perfusion and reperfusion (p.57)
L.L. van Leeuwen[1], L.H. Venema[1], H.G.D. Leuvenink[1], B.M. Kessler[2], [1]Dept. of Surgery, UMCG, Groningen, The Netherlands. [2]Nuffield Dept. of Medicine, University of Oxford, Oxford, United Kingdom.

14.20 Increased development of microthrombi and fibrin depositions in deceased donor kidney transplantation (p.58)
T.A.J. van den Berg[1], M.C. van den Heuvel[2], J. Wiersema-Buist[1], J. Adelmeijer[1], S.J.L. Bakker[3], H. van Goor[2], T. Lisman[1], R.A. Pol[4], [1]Dept. of Surgery, Research Laboratory, [2]Dept. of Pathology, [3]Dept. of Internal Medicine, Division of Nephrology, [4]Dept. of Surgery, UMCG, Groningen, The Netherlands.

14.30 Generation of human monoclonal HLA-DR antibodies for verification of HLA-DR eplets. (p.59)
C.S.M. Kramer, M.E.I. Franke-van Dijk, K.H. Bakker, M. Uyar-Mercankaya, G.E. Karahan, D.L. Roelen, F.H.J. Claas, S. Heidt, Dept. of Immunohematology & Blood Transfusion, LUMC, Leiden, The Netherlands.

14.40 Unbiased multiparameter analysis identifies increased immunosenescence of alloreactive CD8+ T cells in association with donor-specific hyporesponsiveness (p.60)
A.C.J. van der List, N.H.R. Litjens, M. Klepper, M.G.H. Betjes, Dept. of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands.

14.50 The small-molecule BCL6-inhibitor 79-6 suppresses follicular T helper cell differentiation and plasma blast formation (p.61)
R. Kraaijeveld, D.A. Hesselink, C.C. Baan, Dept. of Internal Medicine, Division of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands.

15.00 Mesenchymal stromal cell treatment during ex vivo normothermic machine perfusion of donor kidneys - a porcine autotransplantation study (p.62)
M.B.F. Pool[1], S. Lohmann[2], K.M. Rozenberg[3], M. Eijken[2], R.J. Ploeg[3], J. Hunter[3], C. Moers[1], A. Krarup Keller[4], U. Moldrop[4], H.G.D. Leuvenink[1], B. Jespersen[2], [1]Dept. of Surgery, UMCG, Groningen, The Netherlands. [2]Dept. of Renal Medicine, Aarhus Hospital, Aarhus, Denmark. [3]Nuffield Dept. of Surgical Sciences, Oxford Biomedical Research Centre, Oxford, United Kingdom. [4]Dept. of Urology, Aarhus Hospital, Aarhus, Denmark.

15.10 Anti-rejection therapy does not eliminate donor-reactive IFN-γ and IL-21 producing cells (p.63)
N.M. van Besouw[1], D. Reijerkerk[1], A. Mendoza-Rojas[1], M.C. Clahsen-van Groningen[2], D.A. Hesselink[1], C.C. Baan[1], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, [2]Dept. of Pathology, Erasmus MC, Rotterdam, The Netherlands.

15.20 Immunosuppression affects circulating follicular regulatory T cells in kidney transplant recipients (p.64)
C.C. Baan[1], Q. Niu[2], A. Mendoza Rojas[1], M. Dieterich[1], T. van Gelder[3], D.A. Hesselink[1], N.M. van Besouw[1], [1]Dept. of Internal Medicine, [2]Dept. of Laboratory Medicine, [3]Dept. of Internal Medicine & Clinical Pharmacology, Erasmus MC, Rotterdam, The Netherlands.

15.30 Koffie- / theepauze

Parallel sessie V – Donatie en Verpleegkundige abstracts **Leo Franssen zaal**

Voorzitters: *Monique Mullens, research verpleegkundige, MUMC*
Louise Maasdam, verpleegkundig specialist, Erasmus MC

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

14.00 Renal functional reserve predicts long-term kidney function in living donors (p.65)
M.H. de Borst[1], J. van der Weijden[1], M. van Londen[1], S.J.L. Bakker[1], G. Navis[1], I.M. Nolte[2], S.P. Berger[1], [1]Dept. of Nephrology, [2]Dept. of Epidemiology, UMCG, Groningen, The Netherlands.

14.10 Posttraumatic Growth in liver transplant recipients. result of a prospective cohort study (p.66)
C. Annema[1], A. Venema[2], H.J. Metselaar[3], B. van Hoek[4], R.J. Porte[5], A.V. Ranchor[6], [1]Dept. of Health Sciences, Division of Nursing research, UMCG, Groningen, The Netherlands. [2]Dept. of Nursing, UMCG, Groningen, The Netherlands. [3]Dept. of Gastroenterology & Hepatology, Erasmus MC, Rotterdam, The Netherlands. [4]Dept. of Gastroenterology & Hepatology, LUMC, Leiden, The Netherlands. [5]Dept. of Surgery, Division of HPB & Liver Transplantation, UMCG, Groningen, The Netherlands. [6]Dept. of Health Psychology, UMCG, Groningen, The Netherlands.

14.20 Validation of the Model for End-stage Liver Disease sodium score in the Eurotransplant region. (p.67)
B.F.J. Goudsmit[1], H. Putter[2], J. de Boer[3], S. Vogelaar[3], B. van Hoek[4], A.E. Braat[5], [1]Dept. of Transplant Surgery, LUMC / Eurotransplant, Leiden, The Netherlands. [2]Biomedical data sciences, [3]Allocation, Eurotransplant, [4]Dept. of Gastroenterology & Hepatology, [5]Dept. of Transplant Surgery, LUMC, Leiden, The Netherlands. ELIAC Collaboration

~~14.30~~ ~~The effect of mannitol on kidney function after kidney transplantation. a systematic review and meta-analysis (p.68)~~
~~*S.C. van de Laar, G.N. Schouten, J.N.M. IJzermans, R.C. Minnee, Dept. of Surgery, Division of HPB & Transplant Surgery, Erasmus MC, Rotterdam, The Netherlands.*~~

14.30 Exploring health literacy and self-management after kidney transplantation. a prospective cohort study. (p.68)
L. Maasdam[1], R. Timman[2], M. Cadogan[1], M. Tielen[1], M.C. de Haan[1], W. Weimar[1], E.K. Massey[1], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Psychiatry, Divison of Medical Psychology & Psychotherapy, Erasmus MC, Rotterdam, The Netherlands.

14.40 Participation of compatible kidney donor-recipient pairs in the Dutch Kidney Exchange Program (KEP). an exploration of the decision-making process (p.69)

M. de Klerk, E. Massey, J. van de Wetering, Dept. of Nephrology, Erasmus MC, Rotterdam, The Netherlands.

14.50 Directed deceased donation in the Netherlands? An exploration (p.70)
L. Dijkhuizen, Legal Department, Dutch Transplantation Foundation, Leiden, The Netherlands.

15.30 Koffie- / theepauze

Parallel sessie VI – Klinische abstracts **Theaterzaal**

Voorzitters: *Dr. Marielle Gelens, nefroloog, MUMC*
Prof. dr. Luuk Hilbrands, nefroloog, Radboudumc

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

16.00 Steroid withdrawal is safe in pediatric kidney recipients (p.71)
L. Oomen[1], L.L. de Wall[2], E.A.M. Cornelissen[3], W.F.J. Feitz[2], C.M.H.H.T Bootsma-Robroeks[3], [1]Dept. of Pediatrics, [2]Dept. of Pediatric Urology, [3]Dept. of Pediatric Nephrology, Radboudumc, Nijmegen, The Netherlands.

16.10 Active knowledge building and group learning is limited in online sources for patients on renal transplantation (p.72)
C.W. van Klaveren[1], P.G.M. de Jong[2], R.A. Hendriks[2], F. Luk[1], A.P.J. de Vries[1], P.J.M. van der Boog[1], M.E.J. Reinders[1], [1]Dept. of Internal Medicine, Division of Nephrology & Leiden Transplant Center, [2]Center for Innovation in Medical Education, LUMC, Leiden, The Netherlands.

16.20 The management of aorto-iliac vascular disease in candidates for kidney transplantation. a worldwide survey among transplant surgeons (p.73)
E. Rijkse[1], H.J.A.N. Kimenai[1], F.J.M.F. Dor[2], J.N.M. IJzermans[1], R.C. Minnee[1], [1]Dept. of Surgery, Division of HPB & Transplant Surgery, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Surgery, Imperial College, London, United Kingdom.

16.30 Mental health of unspecified anonymous living kidney donors after donation. (p.74)
W. Zuidema[1], I. Ismail[2], J. van de Wetering[1], I. van Raalten[2], W. Weimar[1], E.K.J. Massey[1], [1]Dept. of Internal Medicine, [2]Dept. of Psychiatry, Erasmus MC, Rotterdam, The Netherlands.

16.40 Chronic Diarrhea in Renal Transplant Recipients. a Metagenomic Study of Gut Microbiota Composition and Functionality (p.75)
J.C. Swarte[1], R.M. Douwes[1], R. Gacesa[2], S. Hu[2], H.J.M. Harmsen[3], R.K. Weersma[2], S.J.L. Bakker[4], [1]Dept. of Internal Medicine, [2]Dept. of Gastroenterology & Hepatology, [3]Dept. of Microbiology, [4]Dept. of Internal Medicine, Division of Nephrology, UMCG, Groningen, The Netherlands.

16.50 The effect of being overweight on surgical complications after living kidney donation (p.76)
L.B. Westenberg[1], M. van Londen[2], S.J.L. Bakker[2], R.A. Pol[3], [1]Dept. of Surgery, [2]Dept. of Internal Medicine, Division of Nephrology, [3]Dept. of Surgery & Transplant surgery, UMCG, Groningen, The Netherlands.

17.00 Metabolic Acidosis is associated with increased risk for graft failure and premature death in stable Renal Transplant Recipients (p.77)
A.W. Gomes Neto[1], M.C.J. Osté[1], E. van den Berg[1], A. Post[1], J.S.F. Sanders[1], S.P. Berger[1], J.J. Carrero[2], G.J. Navis[1], S.J.L. Bakker[1], [1]Dept. of Internal Medicine, Division of Nephrology, UMCG, Groningen, The Netherlands. [2]Dept. of Clinical Science, Intervention & Technology, Division of Renal Medicine, Karolinska Instituut, Solna, Sweden.

17.10 Robotic-assisted laparoscopic donornephrectomy. Initial results and comparison with the hand-assisted laparoscopic technique. (p.78)
M.M. Idu[1], M. Willems[1], K. van de Pant[2], F. Bemelman[2], [1]Dept. of Vascular & Transplant Surgery, Amsterdam UMC, loc. AMC, Amsterdam, The Netherlands. [2]Dept. of Nephrology, Amsterdam UMC, loc. AMC, Amsterdam, The Netherlands.

17.20 Prolonged organ extraction time negatively impacts kidney transplantation outcome (p.79)
H. Maassen[1], C. Moers[1], H. van Goor[2], H.G.D. Leuvenink[1], H.S. Hofker[1], [1]Dept. of Surgery, [2]Dept. of Pathology & Medical Biology, UMCG, Groningen, The Netherlands.

17.40 Ledenvergadering NTV in Joep Nicolas zaal

19.30 Avondprogramma in ECI Cultuurfabriek

Parallel sessie VII – Basale- en Klinische abstracts **Joep Nicolas zaal**

Voorzitters: *Prof. dr. Carla Baan, onderzoeker, Erasmus MC*
Dr. Cyril Moers, chirurg, UMCG

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

16.00 Preformed donor specific antibodies in CDC-XM negative living unrelated male to female spousal kidney transplantations are associated with an increased risk of acute antibody-mediated rejection (p.80)
K.E. Groeneweg[1], F. van der Toorn[1], D.L. Roelen[2], F.H.J. Claas[2], S. Heidt[2], M.E.J. Reinders[1], J.W. de Fijter[1], D. Soonawala[1], [1]Dept. of Internal Medicine, Division of Nephrology, [2]Dept. of Immunohematology & Blood Transfusion, LUMC, Leiden, The Netherlands.

16.10 The effect of different mean arterial pressures on renal function during ex vivo normothermic machine perfusion of porcine kidneys. Towards optimal conditions. (p.81)
T.M. Huijink[1], L.H. Venema[1], J.L. Hillebrands[2], S.P. Berger[3], H.G.D. Leuvenink[1], [1]Dept. of Surgery, [2]Dept. of Pathologie & Medical Biology, [3]Dept. of Nephrology, UMCG, Groningen, The Netherlands.

16.20 PROlonged normothermic machine PERfusion of human discarded donor kidneys. first results of the PROPER study (p.82)
A.S. Arykbaeva[1], D.K. de Vries[1], J.B. Doppenberg[1], V.A.L. Huurman[1], R.C. Minnee[2], C. Moers[3], R.A. Pol[3], H.G.D. Leuvenink[3], R.J. Ploeg[1], I.P.J. Alwayn[1], [1]Dept. of Surgery, LUMC, Leiden, The Netherlands. [2]Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Surgery, UMCG, Groningen, The Netherlands.

16.30 Magnetic resonance imaging to assess renal flow distribution during ex vivo normothermic machine perfusion - It takes time to obtain cortical perfusion (p.83)
R. Schutter[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, UMCG, Groningen, The Netherlands.

16.40 What is the clinical relevance of HLA-C antibodies detected by luminex single antigen bead assays? (p.84)
G.E. Karahan, K. Bakker, S. Brand-Schaaf, D. Roelen, F.H.J. Claas, S. Heidt. Dept. of Immuno-hematology & Blood Transfusion, LUMC, Leiden, The Netherlands.

16.50 Why should we pursue abdominal Normothermic Regional Perfusion in Donation after Circulatory Death donors. A critical appraisal (p.85)

F.E.M. van de Leemkolk[1], I.J. Schurink[2], O.M. Dekkers[3], G.C. Oniscu[4], I.P.J. Alwayn[1], R.J. Ploeg[5], J.J. de Jonge[2], V.A.L. Huurman[1], [1]Dept. of Surgery, LUMC, Leiden, The Netherlands. [2]Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Clinical Epidemiology, LUMC, Leiden, The Netherlands. [4]Edinburgh Transplant Centre, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom. [5]Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, United Kingdom.

17.00 Reparative effect of mesenchymal stromal cells on endothelial cells after ischemic and inflammatory injury (p.86)
J.M. Sierra Parraga[1], A. Merino[1], M. Eijken[2], R. Ploeg[3], B. Moller[2], B. Jespersen[4], C. Baan[1], M. Hoogduijn[1], [1]Dept. of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark. [3]Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, United Kingdom. [4]Dept. of Renal medicine, Aarhus University Hospital, Aarhus, Denmark.

17.10 Influence of pregnancy on eGFR slope in kidney transplant recipients (p.87)
M.C. van Buren[1], M. Gosselink[2], H. van Hamersvelt[3], H. Groen[4], M. de Jong[5], A.T. Lely[2], J. van de Wetering[1], [1]Dept. of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Obstetrics, WKZ birth center, UMCU, Utrecht, The Netherlands. [3]Dept. of Nephrology, Radboudumc, Nijmegen, The Netherlands. [4]Dept. of Epidemiology, UMCG, Groningen, The Netherlands. [5]Dept. of Nephrology & Transplantation, UMCG, Groningen, The Netherlands.

17.40 Ledenvergadering NTV

19.30 Avondprogramma in ECI Cultuurfabriek

Parallel sessie VIII – Young professionals sessie **Leo Franssen zaal**

Thema: **Ballen in de lucht**

Voorzitter: *Dorottya de Vries, transplantatiechirurg, LUMC*

16.00 "Sweat and non-sweat", over sport, bewegen en motivatie.
Dr. Sijbrand Hofker, chirurg UMC Groningen
Prof. dr. Anton Scheurink., neuro endocrinoloog, UMC Groningen

17.30 Einde programma

17.40 Ledenvergadering NTV in Joep Nicolas zaal

19.30 Avondprogramma in ECI Cultuurfabriek

Onderwijssessie **Joep Nicolas zaal**

Voorzitters: *Dr. Martin Hoogduijn. onderzoeker, Erasmus MC*
Dr. Coby Annema, verpleegkundig onderzoeker, UMCG

08.00 Zijn er grenzen aan donoren en acceptoren?
Diederik Kimenai, transplantatiechirurg, Erasmus MC

08.30 Wat is het traject dat een transplantatie patiënt doorloopt?
Marjo van Helden, verpleegkundig specialist, Radboudumc

Plenaire sessie IX – Ervaringen bij bijzondere orgaan donaties **Theaterzaal**

Voorzitters: *Wim de Jongh, transplantatie coördinator, MUMC*
Rianne van Zoggel, transplantatie coördinator, Radboudumc

09.00 Een bijzondere altruïstische donor
Peter Keijsers, donor

09.30 Van thuis naar ziekenhuis: een bijzondere donatie
Anita Kempener, nabestaande

10.00 Orgaan Donatie na Euthanasie met thuissedatie
Najat Tajaate, anesthesist-intensivist, Zuyderland MC

10.30 Koffie- / theepauze

Parallel sessie X – Medisch Ethische Commissie NTV **Theaterzaal**

Thema: **DCD hartdonatie: hardnodig?**

Voorzitters: *Dr. Tineke Wind, transplantatie coördinator, MUMC*
Dr. Marion Siebelink, onderzoeker, UMCG

11.00 Overzicht DCD hartdonatie
Dr. Michiel E. Erasmus, thoraxchirurg, UMCG

11.20 Ethische aspecten van DCD hartdonatie
Dr. Mike Bos, ethicus

11.40 Pro/con discussie – Ethiek van DCD hartdonatie
Pro: Dr. Michiel Erasmus, thoraxchirurg, UMCG
Con: Dr. Hans. Sonneveld, anaesthesioloog-intensivist, Isala Ziekenhuis, Zwolle

12.30 Lunch en gemodereerde postersessies

Parallel sessie XI **Joep Nicolas zaal**

Voorzitters: *Dr. Marielle Gelens, nefroloog, MUMC*
Dr. Marja Ho-Dac – Pannekeet, directeur NVN

Thema: **Waardegedreven zorg:**
hoe maken we onze transplantatiezorg (nog) beter?

11.00 Introductie waardegedreven zorg voor de nefrologie
Prof. dr. Willem Jan Bos, LUMC, internist-nefroloog St Antonius Nieuwegein
internist-nefroloog, LUMC

Patient-gerapporteerde uitkomsten in de nefrologie (en Tx).
Dr. Yvette Meuleman, Gezondheidspsycholoog
Senior onderzoeker en docent op de Klinische Epidemiologie
afdeling van het Leids Universitair Medisch Centrum

Patientparticipatie in niertransplantatie
Drs. Sumit Gokoel, arts-onderzoeker, afd. Nierziekten, LUMC

Transplantatie Centrum Dashboard
Dr. Aiko de Vries, nefroloog, LUMC

Naar een output gedreven nationaal kwaliteitssysteem
Dr. Marc ten Dam, nefroloog, CWZ, voorzitter PVC

Reflecterende samenvatting directeur NVN, *Dr. Marja Ho-Dac – Pannekeet*
en opening plenaire Q&A

12.30 Lunch en gemodereerde postersessies

Postersessie 4 – Donatie en Verpleegkundige abstracts **Toon Hermans Foyer**

Tijd : 12.30 – 12.55

Moderator: *Marjo van Helden, verpleegkundig specialist, Radboudumc*

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

14. National implementation of the Kidney Team at Home educational intervention (p.88)
S. Redeker[1], S.Y. Ismail[1], R. Timman[1], J.J. van Busschbach[1], W. Weimar[2], E.K. Massey[2], [1]Dept. of Medical Psychology & Psychotherapy, [2]Dept. of Nephrology, Erasmus MC, Rotterdam, The Netherlands.

15. Vervallen

16. Reasons for disapproval of potential living kidney donors (p.89)
P.H.M.M. Dooper[1], A. Rasing[1], D.B. Pilzecker[1], C.W. Hooghof[1], E.M. van Ommen[1], F.C.H. d' Ancona[2], H.L. Langenhuijsen[2], X. Zhu[2], M. van der Jagt[3], M. Warle[3], H.J. Kloke[1], [1]Dept. of Nephrology, [2]Dept. of Urology, [3]Dept. of Surgery, Radboudumc, Nijmegen, The Netherlands.

17. Vervallen

18. Mate van arbeidsparticipatie na levertransplantatie en determinanten van invloed, een

single centrum retrospectieve studie. (p.90)
A.M. van den Burg, R.A. de Man, L.C. Elshove, Dept. of Gastroenterology & Hepatology, Erasmus MC, Rotterdam, The Netherlands.

Postersessie 5 – Klinische en Verpleegkundige abstracts — Toon Hermans Foyer

Tijd : 12.30 – 12.55

Moderator: Annelies de Weerd, internist-nefroloog, Erasmus MC

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

19. The association between pre-transplant SIPAT-score and transplant related outcomes in lung and liver transplant patients. a retrospective cohort study. (p.91)
T.W. Norder[1], L.S. Derksen[2], C. Oosterhoff[3], A. Hoogendoorn[1], C.T. Gan[1], A.P. van den Berg[3], W. van der Bij[1], J.H. Annema[4], [1]Dept. of Pulmonary diseases and tuberculosis, lungtransplantation, UMCG, Groningen, The Netherlands. [2]Dept. of Clinical Health Sciences, UMCU, Utrecht, The Netherlands. [3]Dept. of Gastroenterology & Hepatology, Liver transplantation, UMCG, Groningen, The Netherlands. [4]Dept. of Health Sciences, UMCG, Groningen, The Netherlands.

20. Plasma mitochondrial DNA levels and damage correlate with post-transplant renal allograft function (p.92)
M. Trefna[1], G.J. Nieuwenhuijs-Moeke[2], Z. Hijazi[1], M.A.J. Seelen[3], F.H. Hoogstra-Berends[1], R.H. Henning[1], [1]Dept. of Clinical Pharmacy and Pharmacology, [2]Dept. of Anesthesiology, [3]Dept. of Nephrology, UMCG, Groningen, The Netherlands.

21. Low Protein Intake is Associated with Severe Fatigue in Stable Outpatient Renal Transplant Recipients (p.93)
A.W. Gomes Neto[1], M. Geelink[1], R.M. Douwes[1], I.M. Vliet[2], A. Post[1], J.G.M. Rosmalen[3], M.L. Joustra[3], S.P. Berger[1], G.J. Navis[1], S.J.L. Bakker[1], [1]Dept. of Internal Medicine, Division of Nephrology, [2]Dept. of Dietetics, [3]Interdisciplinary Center for Psychopathology and Emotion Regulation, UMCG, Groningen, The Netherlands.

22. No clear influence of non-adherence on tacrolimus intra-patient variability in stable kidney transplant recipients (p.94)
S.R.M. Gokoel[1], T.C. Zwart[2], D.J.A.R. Moes[2], P.J.M. van der Boog[1], J.W. de Fijter[1], [1]Dept. of Nephrology, [2]Dept. of Clinical Pharmacy & Toxicology, LUMC, Leiden, The Netherlands.

23. Walk & Talk, a program to stimulate an active lifestyle after kidney transplantation (p.95)
J.W. van der Heijden[1], E.A. Hartman[2], A. van den Berg[3], C. Schrauwers[1], [1]Dept. of Nephrology, Amsterdam UMC, loc. VUmc, Amsterdam, The Netherlands. [2]Dept. of Dietetics, Amsterdam UMC, Amsterdam, The Netherlands. [3]Service/design/innovation, Ideate, Amersfoort, The Netherlands.

Postersessie 6 – Basale abstracts **Toon Hermans Foyer**

Tijd : 12.30 – 12.55

Moderator: *Dr. Elena Kamburova, postdoctoraal onderzoeker, Radboudumc*

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

24. Impact of immunosuppressive drugs on endothelial barrier (p.96)
S.A. Nurmohamed[1], D. Ootes[2], P.L. Hordijk[2], M.G. Vervloet[1], J.W. van der Heijden[1], J.S.M. van Bezu[2], [1]Dept. of Nephrology, [2]Dept. of Physiology, Amsterdam UMC, loc. VUmc, Amsterdam, The Netherlands.

25. High tacrolimus intra-patient variability is associated with elevated anti-donor reactivity after kidney transplantation (p.97)
A. Mendoza Rojas[1], P. de Kuiper[1], D. Reijerkerk[1], M.L. Mccahery[1], M.C. Clahsen-van Groningen[2], T. Gelder[3], D.A. Hesselink[1], C.C. Baan[1], N.M. van Besouw[1], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, [2]Dept. of Internal Medicine, Division of Pathology, [3]Dept. of Internal Medicine & Clinical Pharmacology Unit, Erasmus MC, Rotterdam, The Netherlands.

26. Nanoparticle Release by Extended Criteria Donor Kidneys During Normothermic Machine Perfusion (p.98)
W.W. Woud[1], A. Merino[1], M.J. Hoogduijn[1], K. Boer[1], M.W.F. van den Hoogen[2], C.C. Baan[1], R.C. Minnee[2], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, [2]Dept. of Surgery, Division of HPB & Transplant Surgery, Erasmus MC, Rotterdam, The Netherlands.

27. Circulating cell-free nucleosomes as marker of graft integrity in kidney transplantation patients (p.99)
J.G.H.P. Verhoeven, C. Baan, M. Herzog, D.A. Hesselink, K. Boer, Dept. of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands.

28. Phenotyping circulating endothelial cells as a marker for transplant kidney damage (p.100)
H. Tejeda-Mora[1], W. Verschoor[1], R.C. Minnee[2], K. Boer[1], D.A. Hesselink[1], M.W.F. van den Hoogen[1], L.J.W. van der Laan[2], C.C. Baan[1], M.J. Hoogduijn[1], [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, [2]Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands.

Parallel sessie XII – Klinische en Basale abstracts **Theaterzaal**

Voorzitters: *Dr. Arnold van der Meer, transplantatie immunoloog, Radboudumc*
Prof. dr. Frederike Bemelman, nefroloog, Amsterdam UMC, loc AMC

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

13.30 Peripheral blood analysis by flow cytometry and gene expression profiling in long-term renal transplant recipients with squamous cell carcinoma (p.101)
S. Bezstarosti[1], M.J. Bottomley[2], J. Hester[2], F. Issa[2], [1]Dept. of Immunohematology & Blood Transfusion, LUMC, Leiden, The Netherlands. [2]Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, United Kingdom.

13.40 Donor blood composition is a risk factor for biliary injury in donation after circulatory death liver transplantation (p.102)
O.B. van Leeuwen[1], M. van Reeven[2], D. van der Helm[3], J.N.M. IJzermans[2], I.P.J. Alwayn[4], B. van

Hoek[3], W.G. Polak[2], T. Lisman[1], V.E. de Meijer[1], R.J. Porte[1], [1]Dept. of Surgery, UMCG, Groningen, The Netherlands. [2]Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Gastroenterology & Hepatology, LUMC, Leiden, The Netherlands. [4]Dept. of Surgery, LUMC, Leiden, The Netherlands.

13.50 Model-based estimation of iohexol plasma clearance for renal function evaluation in the renal transplant setting (p.103)
T.C. Zwart[1], A.G.J. Engbers[2], R.E. Dam[3], P.J.M. van der Boog[3], J.W. de Fijter[3], H.J. Guchelaar[1], A.P.J. de Vries[3], D.J.A.R. Moes[1], [1]Dept. of Clinical Pharmacy and Toxicology, [2]Division of Systems Biomedicine and Pharmacology, [3]Dept. of Internal Medicine, Division of Nephrology & Leiden Transplant Center, LUMC, Leiden, The Netherlands.

14.00 HLA Selected Allogeneic Mesenchymal Stromal Cell Therapy in Renal Transplantation. the Neptune study, a phase I open-label single-center study (p.104)
G.J. Dreyer[1], K.E. Groeneweg[1], S. Heidt[2], D.L. Roelen[2], M. van Pel[2], H. Roelofs[2], V.A.L. Huurman[3], I.M. Bajema[4], D.J.A.R. Moes[5], W.E. Fibbe[2], F.H.J. Claas[2], C. van Kooten[1], T.J. Rabelink[1], J.W. de Fijter[1], M.E.J. Reinders[1], [1]Dept. of Internal Medicine, Division of Nephrology, [2]Dept. of Immuno-haematology and Blood Transfusion, [3]Dept. of Transplant Surgery, [4]Dept. of Pathology, [5]Dept. of Clinical Pharmacy and Toxicology, LUMC, Leiden, The Netherlands.

14.10 Population pharmacokinetics of meltdose tacrolimus (Envarsus®) in stable adult liver transplant recipients (p.105)
M. Biewenga[1], L.C. Martial[2], B.N. Ruijter[3], J.J. Swen[2], D.J.A.R. Moes[2], B. van Hoek[3], [1]Dept. of Gastroenterology & Hepatology, LUMC, Leiden, The Netherlands. [2]Dept. of Clinical Pharmacy and Toxicology, [3]Transplantation Center, LUMC, Leiden, The Netherlands.

14.20 Real-time visualization of cortical renal perfusion using laser speckle contrast imaging (p.106)
H. Maassen[1], W. Heeman[1], J. Calon[2], H. van Goor[3], H.G.D. Leuvenink[1], G. van Dam[1], E.C. Boerma[4], [1]Dept. of Surgery, UMCG, Groningen, The Netherlands. [2]Visual Intelligence, ZiuZ Visual Intelligence, Gorredijk, The Netherlands. [3]Dept. of Pathology & Medical Biology, UMCG, Groningen, The Netherlands. [4]Intensive Care, MCL, Leeuwarden, The Netherlands.

14.30 Enhancing ex vivo perfusion of the liver by restoring positive pressure in the inferior caval vein. (p.107)
I.J. Schurink, F.H.C. de Goeij, J.N.M. IJzermans, L.J.W. van der Laan, J. de Jonge. Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands.

15.00 Koffie- / theepauze

Parallel sessie XIII – Land. Werkgroep Transplantatiecoördinatoren Joep Nicolas zaal

Thema: Wensen en grenzen rondom donatie

Voorzitters: *Emily Doyle, transplantatiecoördinator, MUMC*
Laura Bruinenberg, transplantatiecoördinator, UMCG

13.30 Kind donor: pro-con stellingen
Natascha Moret, transplantatiecoördinator, Erasmus MC

14.15 Virologie: Hepatitis B
Annelies Kraal, transplantatiecoördinator, UMCG

14.30 Virologie: Drugs gebruik
Marion van den Hoeven, transplantatiecoördinator, LUMC

14.45 Dankbrieven: pro-con stellingen
Janneke Vervelde, verpleegkundig specialist, LUMC

15.00 Koffie- / theepauze

Parallel sessie XIV– Klinische abstracts **Leo Franssen zaal**

Voorzitters: *Dr. Jan-Stephan Sanders, internist-nefroloog, UMCG*
Dr. Arjan van Zuilen, internist-nefroloog, UMCU

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

13.30 Prognostic factors for graft function in peadiatric kidney transplant (p.108)
L. Oomen[1], L.L. de Wall[2], E.A.M. Cornelissen[3], W.F.J. Feitz[2], C.M.H.H.T Bootsma-Robroeks[3], [1]Dept. of Pediatrics, [2]Dept. of Pediatric Urology, [3]Dept. of Pediatric Nephrology, Radboudumc, Nijmegen, The Netherlands.

13.40 Medication-Related Problems in liver transplant patients in the Netherlands. the role of the clinical pharmacist in the outpatient setting (p.109)
M.B. Mulder[1], S.D. Borgsteede[2], S. Darwish Murad[3], H.J. Metselaar[3], N.G.M. Hunfeld[1], [1]Hospital Pharmacy, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Clinical Decision Support, Stichting Health Base, Houten, The Netherlands. [3]Dept. of Hepatology, Erasmus MC, Rotterdam, The Netherlands.

13.50 Therapeutic window for ribavirin therapy in transplant recipients with chronic hepatitis E virus infection (p.110)
M.B. Mulder[1], R.A. de Man[2], N. Kamar[3], G. Durmaz[1], J. de Bruijne[4], T. Vanwolleghem[5], A.A. van der Eijk[6], T. van Gelder[7], D.A. Hesselink[8], B.C.M. de Winter[1], [1]Hospital Pharmacy, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Hepatology, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Nephrology & Transplantation, CHU Rangueil, Toulouse, France. [4]Dept. of Gastro-enterology, UMCU, Utrecht, The Netherlands. [5]Dept. of Gastroenterology & Hepatology, Universitair Ziekenhuis Antwerpen, Antwerpen, Belgium. [6]Dept. of Virology, [7]Dept. of Internal Medicine & Hospital Pharmacy, [8]Dept. of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands.

14.00 Resting energy expenditure in cystic fibrosis patients decreases after lung transplantation, which improves validity of prediction equations for energy requirement (p.111)
F.M. Hollander-Kraaijeveld[1], A.S. van Lanen[2], N.M. de Roos[2], H.G.M. Heijerman[3], E.A. van de Graaf[3], [1]Dept. of Dietetics, UMCU, Utrecht, The Netherlands. [2]Division of Human Nutrition and Health, Wageningen University & Research, Wageningen, The Netherlands. [3]Dept. of Pulmonology, Division of Heart and Lungs, UMCU, Utrecht, The Netherlands.

14.10 Survival prediction models in liver transplantation - comparisons between Cox models and machine learning techniques (p.112)
G. Kantidakis[1], H. Putter[2], C. Lancia[3], J.D. de Boer[4], A.E. Braat[4], M. Fiocco[2], [1]Dept. of Statistics, EORTC, Brussels, Belgium. [2]Biomedical data sciences, [3]Mathematical Institute, [4]Dept. of Surgery, LUMC, Leiden, The Netherlands.

14.20 Minor negative effects of calcineurin inhibitor based immunosuppression on pregnancy outcomes after renal transplantation in the Netherlands (p.113)
L.M. Koenjer[1], J.R. Meinderts[2], A.T. Lely[3], M.F.C. de Jong[2], O.W.H. van der Heijden[1], R.G. van

der Molen[4], H.W. van Hamersvelt[5], [1]Dept. of Obstetrics & Gynaecology, Radboudumc, Nijmegen, The Netherlands. [2]Dept. of Nephrology, UMCG, Groningen, The Netherlands. [3]Dept. of Obstetrics & Gynaecology, UMCU, Utrecht, The Netherlands. [4]Dept. of Immunology, Radboudumc, Nijmegen, The Netherlands. [5]Dept. of Nephrology, Radboudumc, Nijmegen, The Netherlands.

14.30 Prevalence and Predictors of Sensory Polyneuropathic Signs and Symptoms in Kidney Transplant Recipients (p.114)

S. Nolte[1], J.M.G. Hofman[1], A.W. Gomes-Neto[2], B.T.A. de Greef[3], J.W.J. Elting[4], M.F. Eisenga[2], M. van Londen[2], S.J.L. Bakker[2], I.M. Nolte[5], C.G. Faber[3], J.S.F. Sanders[2], D.J. Touw[6], G.A.T. Lesman-Leegte[1], S.P. Berger[2], G. Drost[1], [1]Dept. of Neurosurgery, UMCG, Groningen, The Netherlands. [2]Dept. of Nephrology, UMCG, Groningen, The Netherlands. [3]Dept. of Neurology, MUMC+, Maastricht, The Netherlands. [4]Dept. of Neurology, UMCG, Groningen, The Netherlands. [5]Dept. of Epidemiology, UMCG, Groningen, The Netherlands. [6]Dept. of Clinical Pharmacy and Pharmacology, UMCG, Groningen, The Netherlands.

14.40 Induction therapy determines graft and patient survival in ABO-incompatible kidney transplantation. (p.115)

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[6], A.D. van Zuilen[6], F.J. Bemelman[7], M.S. van Sandwijk[7], S.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, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Nephrology, Radboudumc, Nijmegen, The Netherlands. [3]Dept. of Nephrology, LUMC, Leiden, The Netherlands. [4]Dept. of Nephrology, UMCG, Groningen, The Netherlands. [5]Dept. of Nephrology, MUMC, Maastricht, The Netherlands. [6]Dept. of Nephrology, UMCU, Utrecht, The Netherlands. [7]Dept. of Nephrology, Amsterdam UMC, loc. AMC, Amsterdam, The Netherlands. [8]Dept. of Nephrology, Amsterdam UMC, loc. VUmc, Amsterdam, The Netherlands.

14.50 Testosterone levels and the development of posttransplantation diabetes mellitus in male renal transplant recipients (p.116)

S.P. Stam[1], M.F. Eisenga[1], A. van der Veen[2], J.J. van Zanden[3], I.P. Kema[2], A.P. van Beek[4], S.J.L. Bakker[1], [1]Dept. of Internal Medicine, Division of Nephrology, U [2]Dept. of Laboratory Medicine, [3]Dept. of Clinical Chemistry, [4]Dept. of Internal Medicine, Division of Endocrinology, UMCG, Groningen, The Netherlands.

15.00 Koffie- / theepauze

Plenair sessie XV – Afsluitende sessie **Theaterzaal**

Voorzitters: *Dr. Maarten Christiaans, nefroloog, MUMC*
Prof. dr. Marlies Reinders, internist-nefroloog, LUMC

15.30 **'Lessons to be learned' personalisatie van voeding bij topsport**

Jorg Lacroix, manager marketing en Communicatie, Daily Fresh Food
Dr. Gerard Rietjens, inspanningsfysioloog, UM
Marcel Bisselink, chefkok, Daily Fresh Food

Prijsuitreikingen

16.15 Presentatie NTV innovatie in transplantatie onderwijs prijs 2019
3D model van niertransplantatie
Dr. Dorottya de Vries, chirurg, LUMC

16.25 LWTV Innovatie-Kwaliteitsprijs 2020
Uitgereikt door Dr. Coby Annema, bestuurslid

Presentatie winnaar LWTV Innovatie-Kwaliteitsprijs 2019
Longfunctiecontrole na longtransplantatie middels een smart peak-flowmeter
Joke Smit, UMCG

16.35 NTV Wetenschapsprijs 2020
Uitgereikt door Prof. dr. Marlies Reinders, voorzitter NTV

16.45 Jon J van Rood proefschrift prijs 2020
Uitgereikt door Dr. Dave Roelen, immunoloog, LUMC

gevolgd door presentatie winnaar 2020

17.00 Sluiting congres

Long-term survival of lung transplant recipients transplanted from ICU: a multicentre study

C.T. Gan[1], M.E. Hellemons[2], M.E. Erasmus[3], J. Droogh[4], D. Dos Reis Miranda[5], R.A.S. Hoek[2], W. van der Bij[1], E.A.M. Verschuuren[1]. [1]Dept. of Pulmonary diseases and tuberculosis, lungtransplantation, UMCG, Groningen, The Netherlands. [2]Dept. of Pulmonary diseases, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Thorax Surgery, UMCG, Groningen, The Netherlands. [4]Intensive Care, UMCG, Groningen, The Netherlands. [5]Intensive Care, Erasmus MC, Rotterdam, The Netherlands.

Background: Lung transplantation (LTx) from ICU in patients with respiratory failure remains debated. Specifically in patients without an active lung transplant listing status. We compared long-term survival in patients transplanted from ICU with patients transplanted electively from the waiting list.
Methods: In this retrospective multicentre study patients from the University Medical Center Groningen and the Erasmus Medical Center Rotterdam were included from April 2004-December 2018 with a single, bilateral or heart- lung transplantation, and stratified by LTx from ICU or electively. Survival was assessed by Wilcoxon rank-tests. Parameters between groups were compared by Mann-Whitney *U*-test.
Results: A total of 595 patients had a single (n = 110), bilateral (n = 475) or heart-lung transplant (n = 10), 70 were transplanted from ICU (4 single and 66 bilateral LTx). Thirty-one out of 70 had no previous waiting list status and were assessed and listed for LTx on ICU. Patients transplanted from ICU were younger [ICU vs Elective; 49.8 (17.8-66.2) vs 54.3 (12.5-69.2) years, p<0.01]. Mechanical support was either mechanical ventilation n = 41 (58.6%), ECMO n = 29 (41.4%) or a combination. The length of stay on ICU pre-transplant was 25.5 (1-110) days. Patients electively transplanted stayed shorter on ICU [ICU; 18 (0-192) days vs. Elective; 5 (0-242) days, p < 0.001] and total hospital time after LTx was shorter [ICU; 52 (17-230) days vs. Elective; 32 (1-286) days, p <0.001]. One-year survival in the elective group (90.8%) and the group transplanted from ICU (90.9%) was not different. Long-term survival of patients transplanted from ICU was not different from the elective group. In addition, patients transplanted from ICU with a previous listing status compared to patients assessed, listed and transplanted from ICU had comparable long-term survival.
Conclusions: In this large multicentre Dutch cohort LTx from the ICU results in similar long-term outcome in comparison with elective lung transplantation**.** In addition, long-term survival in patients without an active lung transplant waiting list status and therefore assessed, listed and transplanted from ICU had good comparable long-term outcome.

The Renin-Angiotensin System is present and functional in human ipsc-derived kidney organoids

A.S. Shankar[1], Z. Du[1], H. Tejeda Mora[1], T.P.P. van den Bosch[2], S.S. Korevaar[1], I.M. van den Berg - Garrelds[1], J. Gribnau[3], M. Clahsen-van Groningen[2], C.C. Baan[1], A.H.J. Danser[4], E.J. Hoorn[1], M.J. Hoogduijn[1]. [1]Dept. of Internal Medicine, Division of Nephrology & Transplantation, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Pathology, Erasmus MC, Rotterdam, The Netherlands. [3]Dept. of Developmental Biology, Erasmus MC, Rotterdam, The Netherlands. [4]Dept. of Internal Medicine, Division of Pharmacology & Vascular Medicine, Erasmus MC, Rotterdam, The Netherlands.

Background: Renin production in the adult kidney dictates salt, blood pressure and fluid volume homeostasis. The lack of suitable human models to study the RAS and the regulation of renin hampers deeper investigation into the relevance of this system. Recently protocols for the *in vitro* generation of kidney organoids from human induced pluripotent stem cells (iPSC) have been developed.
Methods: We wanted to examine whether the hormonal function of the kidney can be emulated in this *in vitro* model.
Results: To confirm that we could successfully generate kidney organoids, single cell sequencing analysis (SC-seq) of a kidney organoid after 25 days of culture was performed. Differentiated kidney-specific cell populations consisting of podocytes, proximal tubular cells, distal tubular cells, stromal cells and a small cluster of endothelial cells were revealed. Subsequently, these presence of these cell types was confirmed *in situ* using immunohistochemistry. Second, components of the RAS were expressed in kidney organoids. Angiotensinogen mRNA increased 100-fold from day 1 to day 7 and was shown to be primarily present in proximal tubuli, while 75-fold increase in angiotensin receptor type 1 and 10-fold increase type 2 mRNA during differentiation could be attributed to expression in the stromal cell cluster. During kidney organoid differentiation renin-producing cells appear in this stromal cluster, which contains cells characteristic of pericytes and mesenchymal stem cells. The addition of the cyclic AMP-elevating agent forskolin to the culture for 24 hours further increased the mRNA expression of renin up to 1000-fold ($p<0.05$). Moreover, the use of an enzyme-kinetic assay revealed a 20-fold ($p<0.05$) increased renin activity in the forskolin-treated kidney organoids. Analysis of the medium harvested from forskolin-treated kidney organoid cultures exhibited a similar significant increase of renin activity, confirming secretion of functional renin by the kidney organoids. Immunostaining confirmed the presence of renin-producing cells which could be observed in the stromal compartment in close association with glomerular and tubular cells. Lastly, kidney organoids were subcutaneously implanted in immune deficient mice($IL2Ry^{-/-}$ $RAG2^{-/-}$DKO) and harvested after 1 month follow-up. Implantation led to vascularisation and further maturation, as demonstrated by the presence of glomerular and tubular structures using immunohistochemistry. When stimulation with forskolin was performed on explanted kidney organoids, there was a significant 10-fold increase of functional renin secreted into the supernatant.
Conclusions: Therefore, kidney organoids have the ability to maintain kidney-specific hormonal production after implantation. This may have beneficial implications for future use in transplantation and kidney regeneration. Furthermore, the kidney organoid model can provide novel insights into the regulation of renin in an *in vitro* setting.

Promising results of kidney transplantation from donors following euthanasia

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Background: to examine the quality of kidneys transplanted following organ donation after euthanasia, compared to kidneys transplanted following other types of deceased donation.
Organ donation after euthanasia is performed in Belgium, the Netherlands and Canada while the number of countries that allow physician assisted death is increasing. So far, the quality of kidneys donated and transplanted following euthanasia had not been investigated.
Methods: Data from all kidney transplantations from deceased organ donors in the Netherlands from 2012 to 2017 were obtained. Postoperative graft function and death-censored graft and recipient survival of kidneys from donors after euthanasia were compared with the results of kidneys donated after circulatory (DCD) and brain death (DBD).
Results: 73 kidneys transplanted following donation after euthanasia were compared with 1212 transplanted after DBD, and 1234 transplanted after DCD in the period 2012-2017. The incidence of immediate graft function in kidneys from donor after euthanasia was 70%, similar to DBD kidneys (74%, P= 0.56) and higher than other DCD kidneys (44%, P<0.001). The incidence of primary non-function was 7% and did not differ between donor types. Death-censored graft survival was 93% and recipient survival was 95% at 1 year after transplantation, was comparable to DBD and DCD kidneys.
Conclusions: Kidney transplantation following donation after euthanasia is associated with good short-term and medium term clinical outcomes, and is comparable to DBD and DCD kidneys. Outcome is not an obstacle in the implementation of organ donation after euthanasia in countries where the legal and ethical requirements have been met.

Pharmacokinetics of tacrolimus in paediatric renal transplantation recipients during adolescence

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Background: Adolescents have a higher risk of kidney transplant failure, regardless of the age at transplantation. The effects of changing hormonal parameters may influence the pharmacokinetics. In this study we investigated the relation between pubertal development and pharmacokinetic properties of tacrolimus among children after kidney transplantation.
Methods: This pharmacokinetics study is embedded in the prospective multicenter observational Adolesce-NT study. Kidney transplant recipients aged between 8 and 30 years were enrolled between 2012 and 2018. The study contains a pre-transplant and a post-transplant patient group at time of inclusion. The tacrolimus levels measured from 6 months till 1 year after transplantation in the pre-transplant group and from inclusion till 1 year later in the post-transplant group were used to calculate the variability. The levels at the beginning of the study period were used to calculate the dose adjusted trough level.
Exclusion criteria: no informed consent, pubertas praecox, treatment with rituximab or ATG and no tacrolimus. Our primary outcome parameters are the dose-adjusted trough level and the intrapatient variability. We compared these pharmacokinetic parameters to puberty staging and gender, and corrected for confounders (including eGFR, steroid use, CYP3A4 and CYP3A5 polymorphisms) with linear regression analysis.
Results: 25 patients were included in the pre-transplant and 35 patients in the post-transplant group. When corrected for confounders, we found a significant correlation between puberty staging and the dose-adjusted trough level ($p= 0.017$). There was a linearly increase of the dose-adjusted trough levels by increasing age. The dose-adjusted trough level seemed to increase with a higher rate for females compared to males. We found no significant relation between the intrapatient variability and stages of puberty ($p=0.122$) or gender ($p=0.287$).
Conclusions: Our results indicate that the same trough level is reached with lower relative doses of tacrolimus with progression of adolescence and for females. We did not find a relationship between variability as a measure of adherence and pubertal development. As we aim to include more patients and add data on drug compliance, future evaluations will provide more information.

A population pharmacokinetic model not predict the optimal starting dose of tacrolimus in pediatric renal transplant recipients in a prospective study; lessons learned and model improvement

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Background: Multiple clinical, demographic and genetic factors affect the pharmacokinetics of tacrolimus in children, yet in daily practice a uniform body-weight based starting dose is used. It can take weeks to reach the target tacrolimus predose concentration (C0). This study was done to investigate whether adaptation of the tacrolimus starting dose according to a validated dosing algorithm increases the proportion of pediatric kidney transplant recipients being within the target tacrolimus predose concentration range (10-15 ng/mL) at first steady state.
Methods: This was a multi-center, single arm, prospective trial with a planned interim analysis after 16 patients, in which the tacrolimus starting dose was based on bodyweight, *CYP3A5* genotype and donor status (living *vs.* deceased donor). After five doses the tacrolimus predose concentration was determined and the dose adjusted accordingly.
Results: At the interim analysis, 31% of children had a tacrolimus predose concentration within the target range. As the original dosing algorithm was poorly predictive of tacrolimus exposure, the clinical trial was terminated prematurely. Next, the original model was improved by including the data of the children included in this trial, thereby doubling the number of children in the model building cohort. *CYP3A5* genotype, hematocrit and creatinine influenced the tacrolimus clearance. A new starting dose model was developed in which *CYP3A5* genotype was incorporated. Both models were successfully internally and externally validated.
Conclusions: The weight-normalized starting dose of tacrolimus should be higher in patients with a lower bodyweight and in those who are *CYP3A5* expresser.

Design of the OPTIMIZE study: OPen label multicenter randomized Trial comparing standard IMmunosuppression with tacrolimus and mycophenolate mofetil with a low exposure tacrolimus regimen In combination with everolimus in de novo renal transplantation in Elderly patients

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Background: In 2015, more than 30% of the kidney transplant recipients in the Netherlands were above 65 years of age. Elderly patients are less prone to rejection, and death censored graft loss is less observed amongst them. Elderly do have increased rates of malignancies and infection-related mortality. Poor renal function in elderly patients may be related to both pre-existing kidney damage (due to older donor age) and to increased susceptibility to toxicity of calcineurin inhibitors (CNI's). Hence, it is essential to shift the focus from prevention of rejection to preservation of graft function and prevention of over-immunosuppression in the elderly. The OPTIMIZE study tests the hypothesis that reduced CNI exposure in combination with everolimus will lead to better kidney function, a reduced incidence of complications and improved quality of life for kidney transplant recipients aged 65 years and older, compared to the standard immunosuppressive regimen.
Methods: This open label, randomized, multicenter, clinical trial will include 374 elderly patients (≥65 years) and consists of two strata. Stratum A includes elderly recipients of a kidney from an elderly deceased donor and stratum B includes elderly recipients of a kidney from a living donor *or* from a deceased donor < 65 years. In each stratum, subjects will be randomized to the standard, tacrolimus-based immunosuppressive regimen (arm 1) or an adapted immunosuppressive regimen with reduced CNI exposure in combination with everolimus (arm 2). The primary endpoint is "successful transplantation", defined as survival with a functioning graft and an eGFR ≥30 ml/min per 1.73 m^2 in stratum A and ≥45 ml/min per 1.73 m^2 in stratum B, after 2 years. Secondary endpoints include rejection, immunosenescence, frailty, co-morbidities and quality of life and will be analyzed in both the complete study population and the separate strata. Also, a cost-effectiveness analysis will be done.
Results: Thus far, 11 participants are enrolled in the first center. Four other centers will start at the end of 2019, and the last two will start in the beginning of 2020.
Conclusions: The OPTIMIZE study will help to determine the optimal immunosuppressive regimen after kidney transplantation for elderly patients and the cost-effectiveness of this regimen. It will also provide knowledge about immunosenescence and outcome after kidney transplantation in elderly recipients.

LCP-tacrolimus in daily practice: tolerability and intrapatient variability

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Background: Tacrolimus is one of the most widely used immunosuppressive drugs in kidney transplantation. LifeCyclePharma (LCP)-tacrolimus is an extended-release, MeltDose formulation of tacrolimus (Envarsus), which is registered for clinical use. Studies demonstrate greater bioavailability and flatter concentration-time curves with similar efficacy compared to other tacrolimus formulations. We aimed to evaluate the differences in side effects and variability in trough levels in patients who have been converted to Envarsus on clinical indication.
Methods: We initiated a non-interventional prospective registry. Patients from three Dutch university medical centers are followed for 2 years after conversion. Collected data include side effects, doses and trough levels of Envarsus, and serum creatinine during follow up. Intrapatient variability of tacrolimus trough levels is expressed as the coefficient of variation.
Results: 27 patients (15 male, 12 female) were included for analysis. Former formulations of tacrolimus were advagraf (n=22), prograft (n=4) or other (n=1). The interval between kidney transplantation and start of Envarsus was 19.1 months (SD 24.3 months) and 23/27 patients were converted to Envarsus because of side effects. Most common side effects were tremors (n=15), psychological complaints (n=8) and headache (n=3), which disappeared in 11, 6 and 1 patients, respectively. New side effects appeared in 9 patients. 2 patients were converted because of unstable trough levels and had stable levels of tacrolimus when using Envarsus. Tacrolimus intrapatient variability (IPV) in the study cohort ranged from 16.4 to 55%, with a mean IPV of 31.5% (SD 8.9%).
Conclusions: Most tacrolimus-associated side effects disappeared after conversion from other tacrolimus formulations to Envarsus. Intrapatient variability in this registry was high compared to the intrapatient variability of tacrolimus levels reported in previous studies.

Gastro-intestinal complaints in stable renal transplant recipients on tacrolimus and mycophenolate mofetil

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Background: Gastro-intestinal complaints are frequently reported in renal transplant recipients. In a nested cohort study of a randomized weaning trial, we were able to systematically investigate the burden of gastro-intestinal complaints and the effect of mycofenoalte mofetil (MMF) on these complaints in stable renal transplant recipients.
Methods: Low immunological risk renal transplant recipients (HLA mismatches <4 and PRA <5%) were randomized, 6 months after transplantation, to either continue tacrolimus with MMF (TAC/MMF), or to reduce MMF until discontinuation at month 9 (TACmono). Patients filled in the Gastro-intestinal Symptom Rating Scale questionnaire (AstraZeneca, 1995) during outpatient visits at month 6, 12 and 15. This questionnaire makes use of a seven-graded Likert scale, in which 1 represents the most positive option and 7 the most negative one. The questions cover 5 dimensions (abdominal pain, reflux, indigestion, constipation and diarrhea).
Results: Of the 121 included patients, 2 discontinued MMF prior to randomization due to diarrhea. Of the 79 randomized patients, 72 patients completed all questionnaires (34 TACmono and 38 TAC/MMF). Mean age was 59 years with 72% male. At month 6, BMI was 28 kg/m^2, eGFR 55 ml/min/1,73m^2 and daily dose MMF 1200 mg and TAC 5,8 mg, with trough levels of 2.1 mg/L and 7.4 ug/L respectively.
Abdominal pain, reflux , indigestion and constipation did not differ between the groups and over time. Mean scores at month 6 were 1,8, 1,3, 1,8 and 1,7 respectively. At month 15 these scores were 1,6, 1,3, 1,8 and 1,8 respectively. Diarrhea, over time, was significantly more frequent with continuation of MMF (p =0,024).
Conclusions: Stable renal transplant recipients with immunological low risk experience mild gastro-intestinal complaints. Moreover, mycophenolate mofetil on top of tacrolimus causes more diarrhea in comparison to tacrolimus monotherapy.

Normothermic perfusion of porcine ex vivo livers to study hepatic pharmacokinetic processes

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Background: Good prediction of human pharmacokinetics during preclinical drug development is hampered by the lack of translational *in vitro* and *in vivo* models, especially regarding prediction of hepatic clearance and biliary excretion. On top of this, an increasing number of newly developed drugs are subjective to enterohepatic circulation, enhancing the difficulty to predict plasma profiles after oral and intravenous administration, also since these drugs are more prone to cause a drug-drug interaction. We therefore aim to develop a preclinical model to investigate hepatic clearance, biliary excretion and DDI by utilizing normothermic machine perfusion (NMP) on porcine livers.

Methods: Porcine livers were procured from a slaughterhouse. Two livers underwent NMP using the LiverAssist machine. Blood gas analyses were performed hourly. A bolus of atorvastatin was administered at t=0 and at t=120 minutes a subsequent bolus of atorvastatin was co-administered with rifampicin. Samples from the perfusate and bile were taken at prespecified times and bilirubin as endogenous marker for OATP1B1/B3 function was measured. After 360 minutes, indocyanine green (ICG) was administered to study the liver functionality.

Results: Warm and cold ischemia times were 16±4 min and 142±23 min respectively. In both livers atorvastatin was rapidly cleared within 30 min from circulation after the first dose with a C_{max} of 38.9 ± 3.54 ng/mL. Upon co-administration with rifampicin, the atorvastatin plasma levels increased showing a C_{max} of 230.0 and 56.7 ng/mL and the area under the curve ratio (AUCR) was 6.8 and 1.7, respectively, indicating DDI. We hypothesize that the discrepancy in C_{max} and AUCR can be attributed to measured differences in flow, resistance and genetic differences in transport and metabolism of the pigs. In both livers, upon administration of rifampicin, the biliary bilirubin concentration decreased while bilirubin in the circulation increased, suggesting inhibition of the OATP1B1/B3 transporters. At the end of the experiment, in both livers, ICG was rapidly cleared ($t_{½}$ 6 min) from the circulation and excreted in the bile demonstrating good functionality and viability of the porcine liver after 6 h of NMP.

Conclusions: We have demonstrated the feasibility of applying NMP of porcine livers to study hepatic clearance, biliary excretion and DDI, and will further explore the potential of this model by studying other drugs and DDIs in comparison to clinical data.

A tool for combined analysis of transcriptome and T cell receptor repertoire at the single cell level to characterize low frequent donor-specific hypo-responsive CD137-expressing T cells

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Background: Single cell transcriptomics is a powerful tool for in-depth characterization of a heterogeneous pool of T cells and this assay can be combined with TRA/TRB T cell receptor (TCR-) repertoire analysis. The aim of this study was to evaluate the potential of this combined assay to eventually unravel mechanisms of donor-specific hypo-responsiveness in stable kidney transplant recipients 3-5 years after transplantation.
Methods: For this purpose, we carefully selected T cell lines with defined TRA/TRB clonotypes as well as clinical samples enriched for T cells, possessing a complex TCR repertoire. Low cell numbers of the different samples were dispensed in a Wafergen chip, messenger (m)RNA was isolated and cDNA prepared on the iCell 8 system. Two assays were performed on each single cell cDNA preparation, one for the TRA/TRB TCR-repertoire and one for the 5' ends of transcripts. The 5' libraries were sequenced on an Illumina HiSeq2500 sequencer, whereas the TRA/TRB TCR libraries were sequenced on an Illumina MiSeq system.
Results: On average 225 cells/sample were dispensed in a chip and 77% of the cells could be used for analysis of either TRA/TRB clonotype or transcriptome. The correct TRA/TRB clonotype was determined for on average 98.1% of the cells of the cell-lines. The TRA/TRB TCR-repertoire of the clinical samples was more complex than that of the cell-lines. The TRB clonotype distribution of the clinical samples was positively correlated to that obtained by flow cytometry-based approach (R=0.80). Transcriptome (5-prime) analysis revealed expression of on average 2351 unique genes/cell for the cell-lines and 770 genes/cell for the clinical samples.
Conclusions: In conclusion, combined single cell analysis of transcriptome and TRA/TRB clonotype can be applied to low frequent T cell populations. Complex TRA/TRB TCR-repertoires (clinical samples) can be distinguished from T cell lines having only one TRA/TRB clonotype. Moreover, samples with particular TRA/TRB clonotypes can now be analyzed in more depth in parallel with their transcriptome. This new technology now paves the way for in-depth analysis of pathways underlying donor-specific hypo-responsiveness in stable kidney transplant recipients through characterizing donor-reactive CD137-expressing T cells.

Porcine precision-cut kidney slices as an ex vivo model to evaluate the effect of a ketogenic diet on mitochondrial function

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Background: Kidneys derived from Donation after Circulatory Death (DCD) donors suffer from ischemic injury. When reperfusion occurs, the formation of Reactive Oxygen Species (ROS) contributes to the development of ischemia reperfusion injury (IRI). The major site of production and the major target of ROS are the mitochondria. Preoperative dietary restriction and fasting are known to be protective against renal IRI. During fasting or a ketogenic diet, the metabolic substrate switches from glucose to fatty acids, which then becomes the main source of adenosine triphosphate (ATP) production. Precision-cut kidney slices (PCKS) is an ex vivo model to evaluate intra- and extracellular mechanisms. Here, we aim to evaluate the effect of a ketogenic diet on mitochondrial function using PCKS.
Methods: Porcine kidneys were obtained at a local abattoir and prepared for hypothermic machine perfusion (HMP). After 30 min of WIT, kidneys were flushed and placed on HMP and preserved for 3 hours with UW-CS. Thereafter PCKS were made and incubated at 37°C with 80% oxygen. The incubation medium of the control group consisted RPMI 1640 medium, which contains 2 mg/mL glucose. The experimental groups consisted RPMI 1640 medium without glucose, supplemented with 2 mg/mL (±)-sodium 3-hydroxybutyrate (BHB) or 1,5 mg/mL SMOFlipids®. Directly after slicing and after 24, 48 or 72 hours of incubation, tissue and medium samples were taken to analyse for different mitochondrial, oxidative stress and injury markers.
Results: After 72 hours of incubation in ketogenic culture medium all slices are vital. Improved mitochondrial function in both the experimental groups are observed compared to the control group. More in-depth analysis are ongoing.
Conclusions: A ketogenic culture environment seems to conserve PCKS by stabilizing mitochondria thereby protecting against IRI.

Hydrogen sulphide-induced hypometabolism in human-sized porcine kidneys

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Background: Since the start of organ transplantation, hypothermia-forced hypometabolism has been the cornerstone in organ preservation. Cold preservation showed to protect against ischemia, although post-transplant injury still occurs and further improvement in preservation techniques is needed. We hypothesize that hydrogen sulphide can be used as such a new preservation method, by inducing a reversible hypometabolic state in human sized kidneys during normothermic machine perfusion.
Methods: Porcine kidneys were connected to an ex-vivo isolated, oxygen supplemented, normothermic blood perfusion set-up. Experimental kidneys (n=5) received a 85mg NaHS infusion of 100 ppm and were compared to controls (n=5). As a reflection of the cellular metabolism, oxygen consumption, mitochondrial activity and tissue ATP levels were measured. Kidney function was assessed by creatinine clearance and fractional excretion of sodium. To rule out potential structural and functional deterioration, kidneys were studied for biochemical markers and histology.
Results: Hydrogen sulphide strongly decreased oxygen consumption by 61%, which was associated with a marked decrease in mitochondrial activity/function, without directly affecting ATP levels. Renal biological markers, renal function and histology did not change after hydrogen sulphide treatment.
Conclusions: In conclusion, we showed that hydrogen sulphide can induce a controllable hypometabolic state in a human sized organ, without damaging the organ itself and could thereby be a promising therapeutic alternative for cold preservation under normothermic conditions in renal transplantation.

Effect of portal hypertension and surgical technique on perioperative blood loss in liver transplantation

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Background: Liver cirrhosis can cause portal hypertension (PH) by increased intrahepatic vascular resistance and therefore increased perioperative bleeding risk. The hepatic venous pressure gradient (HVPG) is the gold standard for measuring PH. In orthotopic liver transplantation (LT), the beneficial use of a temporary portocaval shunt (TPCS) and initial arterial reperfusion (IAR) is contradictory. The aim of this study was to evaluate the effect of TPCS and IAR on perioperative transfusion requirement of packed red blood cells (RBC) in patients with PH (PH group) and without PH (no-PH group).
Methods: Between January 2005 and May 2017 all orthotopic, first LTs (n=214) performed in a single center were retrospectively analyzed. A multivariate analysis was performed to determine the predictors for blood loss.
Results: A TPCS decreased significantly the number of transfusion of RBCs ($p=0.01$) in the no-PH group, while IAR decreases the number of transfusion of RBCs ($p<0.001$) in the PH group. In conclusion, in patients without PH, a TPCS results in less perioperative transfusion of RBCs, whereas in patients with PH, IAR results in less perioperative transfusion of RBCs.
Conclusions: These surgical techniques, on indication or combined, should be considered as surgical options in LT.

Oxygenated hypothermic machine perfusion of the pancreas followed by controlled oxygenated rewarming to sub-normothermia for viability testing

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Background: Pancreas transplantation is the treatment of choice in a selected group of patients with type 1 diabetes. Machine preservation techniques have the potential of increasing organ quality and utilization, by allowing vitality and functionality assessment while reconditioning the pancreas. A protocol for a novel combination of consecutive preservation techniques in pancreata was established and tested.
Methods: Two human pancreata disregarded for clinical use were used for this experiment. The superior mesenteric artery, splenic artery and pancreatic duct were identified and cannulated on the backtable. Furthermore, an anastomosis was created between the distal splenic artery and vein. The pancreata endured f static cold storage respectively followed by preservation applying 2h of Hypothermic Machine Perfusion (HMP), 1h Controlled Oxygenated Rewarming (COR) and 1h of sub-Normothermic Machine Perfusion (sNMP) using a Kidney Assist perfusion machine. Belzer UW MPS was used for HMP, and perfusate solutions for COR-sNMP differed between the experiments. Respectively DMEM and Williams-E medium combined with Albumin was used. Biopsies were taken for histologic examination using HE A previously published scoring system (grade 0 – 2) was used focusing on edema, vacuolization and acinar integrity loss.
Results: During perfusion, the human pancreata demonstrated stable perfusion parameters. The experimental vascular anastomosis between the Splenic Artery and Splenic Vein increased total flow marginally. Temperature was consistently 5ºC during HMP in one pancreas, while the other remained 10ºC (40 ml/min vs. 15 ml/min). Laboratory analyses of pancreatic fluid collected from the pancreatic duct showed high contents of amylase. pH levels were 7.34 and 7.6 at the end of sNMP, lactate climbed in both cases to 2.63 and 4.79 mmol/L. from 2.43 and 4.33 mmol/L. Grade 2 edema was observed in both pancreata.
Conclusions: Consecutive techniques of machine perfusion were deemed technically feasible. However, further alterations to the protocol are required for preventing extensive formation of edema. Future perfusion experiments will focus on providing a stable sNMP perfusion environment for assessment of flow and viability parameters, which might ultimately lead to an increase in pancreas graft utilization.

Diabetic nephropathy alters circulating long noncoding RNA levels that normalize following simultaneous pancreas-kidney transplantation

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Background: Simultaneous pancreas kidney transplantation (SPKT) replaces kidney function and restores endogenous insulin secretion in patients with insulin-dependent diabetes mellitus and its vascular complication diabetic nephropathy (DN). Circulating long noncoding RNAs (lncRNAs) have emerged as promising biomarkers in (cardio)vascular disease and may provide insight into pathogenesis. Here, we aimed to identify lncRNAs that are associated with DN and vascular injury in the context of SPKT.
Methods: We first performed a pilot study of 40.173 lncRNAs in plasma of healthy controls and patients with DN. Based on these results, as well as on a literature based-selection of vascular injury related lncRNAs, we assessed 14 candidate lncRNAs in plasma samples of DN (n=14), SPKT (n=35), healthy controls (n=15) and renal transplant recipients (KTx; n=13). DN patients were also studied longitudinally before and 1, 6 and 12 months after SPKT. Markers of vascular injury angiopoietin-2 and soluble thrombomodulin(sTM) were measured using ELISA, while angiogenic microRNAs were assessed using RT-qPCR.
Results: Out of 14 selected lncRNAs, we found MALAT1 and LIPCAR to be significantly higher in patients with DN compared with healthy controls, while we found a similar trend for LNC-EPHA6. SPKT caused MALAT1, LIPCAR and LNC-EPHA6 to normalize to levels of healthy controls (p=0.012). The longitudinal study demonstrated that MALAT1, LNC-EPHA6 and LIPCAR levels significantly declined within one month after SPKT (p=0.01, p=0.01 and p=0.04, respectively). In addition, we observed a strong association between MALAT1, LNC-EPHA6 and LIPCAR and the vascular injury marker sTM and a subset of angiogenic microRNAs (miR-27a, miR-130b, miR-152 and miR-340).
Conclusions: Specific circulating lncRNAs associate with DN and vascular injury and normalize after SPKT. As such, lncRNAs are potentially interesting biomarkers for disease progression in DN and may provide insight into the underlying pathophysiology.

Intraoperative indocyanine green plasma disappearance rate as predictor for retransplantation in liver transplantation

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Background: Liver transplantation (LT) is the treatment of choice for end-stage liver disease and hepatocellular cancer. In case of irreversible graft failure, retransplantation is the only viable treatment option. Early detection of postoperative graft failure may help for timely listing for retransplantation. Unfortunately, no such simple and specific early predictor of graft failure is yet available. The aim of this study was to evaluate whether poor initial function of the liver could be predicted by intraoperative indocyanine green plasma disappearance rate (ICG-PDR) as measured by the need for one-month retransplantation in LT.
Methods: Between January 2010 and May 2017 all orthotopic, first LTs (n=197) performed in a single center were retrospectively analyzed.
Results: LTs with an ICG-PDR <18%/min had a significantly higher one-month retransplantation rate (5%), compared to an ICG-PDR ≥18%/min (1%, logrank p=0.04). The positive predictive value of a K<18 was 5% (2/39), the negative predictive value was 99% (155/156).
Conclusions: In conclusion, K<18%/min is a significant risk-factor for one-month retransplantation. However, it has a low predictive value and is therefore not useful in clinical practice.

The efficacy of therapeutic anticoagulation in pancreas allograft thrombosis according the CPAT grading system

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Efficacy of anticoagulative treatment in pancreas allograft thrombosis has been extensively studied. However, conflicting outcomes of these studies, specifically for partial thrombosis, have not resulted in a universally applied anticoagulation protocol. This study was designed to separately evaluate the efficacy of anticoagulative treatment in the different grades of pancreas allograft thrombosis according the Cambridge Pancreas Allograft Thrombosis (CPAT) grading system. The CPAT grading system distinguishes four grades of thrombosis: no thrombosis (CPAT-0), peripheral thrombosis (CPAT-1), intermediate non-occlusive thrombosis (CPAT-2) and central occlusive thrombosis (CPAT-3). All 177 pancreas transplantations performed at our center between January 1st, 2008 and September 1st, 2018 were included. Overall 5-year patient survival in this cohort was 88.6%. Patient survival was not affected by administration of anticoagulation in any grade of thrombosis. The overall 5-year graft survival in this cohort was 86.3%. In patients with CPAT-0 (p=0.715) and CPAT-1 (p=0.267), administration of anticoagulative treatment did not contribute to significantly better graft survival. In contrast, in patients with CPAT-2, administration of anticoagulative treatment showed a significantly better graft survival as compared to patients that did not receive anticoagulative treatment. (p=0.015). Due to the small number of patients with CPAT-3, analysis of the effect of anticoagulation was not performed in this category.
Conclusion: Based on our results, implementation of the CPAT grading system into our clinical practice would be desirable. Followed by adjustment of the current anticoagulation protocol to administration of anticoagulation solely in patients with CPAT-2.

Normothermic machine perfusion is a feasible preservation technique and a promising strategy for donor kidneys in the Eurotransplant Senior Program (ESP)

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Background: Due to suboptimal quality of elderly donor kidneys transplanted in the Eurotransplant Senior Program (ESP), graft outcomes have shown to be inferior. Recently, normothermic machine perfusion (NMP) was identified as a preservation method to optimize marginal donor kidneys. Therefore, as first center in the Netherlands, we aimed to investigate the safety of implementing NMP in the ESP population to improve graft outcomes.
Methods: In 2018, ESP patients awaiting deceased donor kidney transplantation were prospectively asked to participate in a pilot study. Before implantation, the donor kidney was placed on 2 hours NMP at 37°C with a blood-based perfusate. Flow, intrarenal resistance and pressure during NMP were continuously measured. Biopsies, perfusate and urine samples were collected to assess markers of injury. Our primary outcome was to identify logistic challenges during NMP. As secondary outcomes, we assessed clinical outcomes such as the incidence of delayed graft function (DGF) or primary non function (PNF), 3 and 6 months eGFR, and biopsy proven acute rejection (BPAR) within 3 months. Clinical outcomes were compared to a historical cohort of ESP controls. Linear regression analysis was used to investigate differences in perfusion parameters during NMP between donor kidneys who developed DGF/PNF and donor kidneys with immediate function.
Results: 11 patients were included in the NMP group and 54 were used as historical controls. There were no logistic problems during NMP. Baseline characeristics were statistically similar. The incidence of DGF/PNF was lower in the NMP group, but this was not statistically different (NMP group: 36.4%, controls: 63%, p=0.10). BPAR within 3 months was similar. No significant difference was shown for 3 months eGFR (NMP: 31 (IQR 17), controls: 29 (IQR 18.3), p=0.50) and 6 months eGFR (NMP: 31 (IQR 14), controls: 30 (IQR 17.3), p=0.97). 1-year graft survival was 0.89 ±0.11 in the NMP group and 0.85 ±0.05 in the control group (log-rank test 0.62). Linear regression analysis showed a significantly higher increase in flow during NMP for kidneys with immediate function compared to DGF kidneys (No DGF: y=108.3 ± 1.18, DGF: y=106.6 ± 0.70, p=0.01).
Conclusions: Two hours of NMP is safe and feasible in the ESP. No statistical significant differences could be found for clinical outcomes in this small sample size. Flow during NMP could give an indication of the chance of immediate function in the recipient. Well-powered studies are needed to validate our results.

Detrimental consequences of early graft loss after kidney transplantation: conclusions from a nationwide evaluation

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Background: Early graft loss (EGL) is a feared outcome of kidney transplantation. Consequently, kidneys with an anticipated risk of EGL are declined for transplantation. While a permissive policy towards anticipated high-risk organs will result in unacceptable high incidences of EGL, a more reticent attitude will compromise the donor usage, and as such contribute to increasing organ shortages and longer waiting list times. In the most favorable scenario, with optimal use of available donor kidneys, the donor pool size is balanced by the risk of EGL, with a tradeoff dictated by the consequences of EGL. Therefore, we considered a systematic evaluation of the impact of EGL relevant.

Methods: This observational study included all deceased-donor kidney transplantations performed in The Netherlands between 1990 and 2018 (n=11,415). Combined organ procedures, procedures with grafts donated after uncontrolled circulatory death, and procedures in recipients younger than 12 years were excluded. The remaining 10,307 procedures were used for analysis. Multivariate regression analysis was used to identify factors associated with EGL. Cox proportional hazards analyses were performed to evaluate differences in patient and death censored graft survival. EGL is defined as graft loss within 90 days after transplantation.

Results: The incidence of EGL in primary transplantation was 8.2% (699/8,511). The main causes were graft rejection (30%), primary non-function (25%), and thrombosis/infarction (20%). EGL profoundly impacted short- and long-term patient survival (adjusted HR; 95% CI: 8.2; 5.1-13.2, resp. 1.7; 1.3-2.1). Of the EGL recipients who survived 90 days after transplantation (617/699) 71% (440/617) was relisted for re-transplantation, leading to an actual re-transplantation rate of 43%. Noticeably, re-transplantation was associated with a doubled incidence of EGL, but long-term graft survival was equal to the reference group (adjusted HR 1.1; 0.6-1.8).

Conclusions: In conclusion, this nationwide study shows that EGL is associated with significant detrimental consequences that include profound short-term and long-term mortality rates, a reduced chance of relisting and re-transplantation, and for those re-transplanted an increased risk of recurrent EGL. While the development of EGL, and the associated poor outcomes are generally attributed to the use of suboptimal kidney grafts and procedural aspects, the data in this study imply convergence of recipient-associated risk factors as an eliciting factor for EGL.

Limited survival benefit of living versus deceased donor kidney transplantation in elderly recipients

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Background: Increasing numbers of elderly (≥65 years) patients need a kidney transplant. Currently, there is a poignant shortage of deceased donor kidneys, thus putting a strong emphasis on living donation. As waiting time for a deceased donor kidney within the Eurotransplant Senior Program is declining, it is important to understand the strengths and limitations of the different transplantation modalities. This study compares the survival outcome between living donor kidneys (LDK) and deceased donor kidneys (DDK) in elderly recipients.
Methods: This is a single-centre retrospective cohort study of elderly renal transplant recipients transplanted between 2005 and 2017. Primary outcome measures are patient-, graft- and death censored graft survival at 1 and 5 years post-transplantation (post-tx). Multivariate Cox regression analysis was performed to correct for potential confounders such as recipient comorbidity and dialysis vintage. Secondary outcome measures include rejection in the first year and renal function at 1 year post-tx, assessed using the creatinine based CKD-EPI equation to determine eGFR.
Results: In total 369 elderly patients were transplanted, 113 (30.6%) received an LDK and 256 (69.4%) a DDK. 62.5% of recipients were male, median age was 68 years. There is no significant difference in patient survival between LDK and DDK at 1 year (96.3% vs. 92.9%, p=0.202) or at 5 years post-tx (70.2% vs. 65.4%, p=0.534). At 1 year post-tx, graft survival is significantly higher in the LDK group (95.4% vs. 84.1%, p=0.003). At 5 years post-tx the difference is still significant, but remains about 11% (71.0% vs. 59.9%, p=0.017). Death censored graft survival was significantly higher for the LDK group at 1 year (99.1% vs. 89.0%, p=0.001) and 5 years post-tx (97.6% vs. 84.4%, p=0.017). Multivariate cox regression analysis did not alter our findings. The eGFR at 1 year was significantly higher in the LDK group (58.9 vs. 49.6 ml/min, p<0.001). The incidence of treated rejection in the first year did not differ significantly (LDK 14.1% vs. DDK 8.5%, p=0.138).
Conclusions: We conclude that in elderly recipients the patient survival benefits of an LDK compared to a DDK are limited. The lower graft survival in the DDK group is caused mainly by increased death censored graft loss in the first year. Nevertheless, the DDK graft survival remains satisfactory for elderly patients. These findings may support elderly patients, potential living donors and care professionals in choosing the transplant modality.

The impact of donor organ extraction time on pancreas graft survival

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Background: Prolonged cold and warm ischemia are known to have a deleterious effect on pancreas graft survival. Recently published evidence suggests that donor organ extraction time, defined as time from the initial phase of organ cooling directly after cross clamping until organ recovery from the abdominal cavity, might impact early graft function after liver and kidney transplantation. Whether this period has an adverse effect on pancreas function is not known.
Methods: In this dual center retrospective study, the effect of donor pancreas extraction time on short- and long-term graft survival was evaluated. All recipients from pancreas transplants performed between 1996 and 2018 at the University Medical Center Groningen, the Netherlands, and the Medical University Innsbruck, Austria, were included provided the pancreas extraction time was available. Graft survival was analyzed in both univariate and multivariable analysis and Kaplan-Meier analysis.
Results: A total of 317 patients were included, of which 305 (96.2%) received a pancreas graft from a Donation after Brain Death (DBD) donor and 12 (3.8%) from a Donation after Circulatory Death (DCD) donor. Median extraction time (IQR) was 64 minutes (52-79). 1-, 5-, and 10-year death censored graft survival was 85.7%, 76.7% and 61.9% respectively. Donor pancreas extraction time did not influence graft- and patient survival at 3 months, 1, 5 and 10 years. In addition to pancreas extraction time, the following significant factors in univariate analysis were added to a multivariable analysis: donor age, donor sex, Pancreas Donor Risk Index (PDRI), transplant type, first or re-transplantation. Multivariable analysis showed that donor age, PDRI and transplant type had a significant independent effect on pancreas graft survival, but not pancreas extraction time.
Conclusions: Our data suggest that donor extraction time does not influence pancreas graft survival in this large multicenter analysis.

Double J or percutaneous single J-uretic stent after renal transplantation; differences in urologic complication

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Background: Intraoperative uretic stenting reduces the risk of urologic complications after renal transplantation. Our standard protocol consisted of placement of internal double J stents (JJ) during renal transplantation, but hereby monitoring diuresis post transplantation is difficult in patients who have renal rest function. For this reason we changed our standard protocol to placement of a percutaneous single J-uretic stents (PS) in patients with a living kidney transplantation and rest function. JJ stents were left in situ for 6 weeks and single J splints for 7 days. Later on we also reduced the duration of the JJ catheter from 6 to 2 weeks. In this study we compare the urologic complication between JJ en PS.
Methods: This retrospective study includes 66 recipients of living donors who were transplanted in 2017 and 2018. In forty-nine living recipients, with rest diuresis more than 500cc, a PS was placed, in seventeen recipients, with rest diuresis less than 500cc, a JJ was placed. Urologic complications were monitored for 3 months.
Initial Immunosuppression regimen consisted of tacrolimus, mycophenolate mofetil and steroids (10 days).
Results: In both groups the patient survival was 100%, graft survival was 96% in group 1 and 94% in group 2. Urologic complications were comparable in both groups; hydronephrosis was for group 1 and 2 respectively, 12% and 6 %, p=0.46 Leakage was resp. 4% and 6%, p=0,55. The need for ureterreimplantation was resp. 2% and 5,9%, p= 0.43. The percentage of urine tract infection was resp 39% and 41% p= 0.86 between the two groups.
Conclusions: There are no differences in postoperative urologic complications between JJ or PS in recipients of living donors.

Transplanting livers from Hepatitis C virus positive donors; is it worth the risk?

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Background: Before the introduction of Direct-Acting Antivirals (DAAs), only selected organs from Hepatitis C virus (HCV) positive donors were successfully transplanted into HCV positive recipients. Since HCV infection is now curable in a large percentage of cases (>95%) it may be possible to transplant organs from HCV positive donors to HCV negative recipients. In this study we aim to analyse current utilization of livers of HCV positive donors in the Eurotransplant (ET) region and its future potential.
Methods: All reported post-mortem organ donors with age ≥16 years in the ET region between January 2007 and December 2018 were included. Donors from outside the ET region were excluded. Segmental liver transplantations were excluded as well. First, donor demographics were evaluated for all reported donors by HCV status. Then, utilization and graft survival were analysed for both groups.
Results: A total 22,474 donors were reported in the ET region and 287 (1.3%) donors were tested positive for HCV antibodies (ab), with a range of 0.0-1.7% per country in the ET region. A total of 141 (49%) livers of the HCV ab positive donors were transplanted, 74/141 (53%) in HCV ab positive recipients. Graft failure occurred in 25/141 (18%) recipients directly or later after transplantation. In 5/141 (3.5%) it was due to recurrence of HCV. Of the 21,998 HCV ab negative donors 17,745 (81%) livers were transplanted, 2,245/17,745 (13%) in HCV ab positive recipients. In 2,585/17,745 (15%) recipients graft failure occurred directly or later after transplantation. Recurrence of HCV as cause of graft failure was in 77/17,745 (0.4%) of the recipients with graft failure.
Conclusions: Liver utilization is much higher in HCV ab negative donors as compared to HCV ab positive donors. However, graft failure overall and specifically due to HCV infection occurs in 18% and 3,5% respectively after liver transplantation of HCV ab positive donors. Therefore, the absolute risk is recipients of a HCV ab negative graft is only slightly higher. Although the number of HCV ab positive donors is not very high in the ET region, with the new DAAs there is an opportunity to improve utilization of HCV ab positive donors and outcome after liver transplantation. With the increasing waiting lists and relatively stable number of donors, transplant centers should consider all liver grafts of HCV positive donors for transplantation.

The transition of frailty state after kidney transplantation

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Background: In today's aging population, an increasing number of patients are becoming frail. Frailty results from the body's failure to return to homeostasis after stressful events, leading to adverse outcomes. To study the dynamics of frailty in kidney transplant recipients we aimed to determine whether transitions in frailty and its specific domains are affected by the kidney transplantation.
Methods: A total of 176 kidney transplant recipients, transplanted between 2015-2017, were prospectively included. The presence and severity of frailty was measured using the Groningen Frailty Indicator (GFI). Frailty was assessed preoperatively during admittance (index measurement) and during follow-up. Transitions in frailty state and the individual domains, were determined between the index and the follow-up measurement. Additionally, specific changes in the different domains of the GFI and contributing patient characteristics were analyzed.
Results: Mean age (SD) was 51.8 (14.1) years and 63% were male. Sixty percent of the patients were dialysis dependent prior to the transplantation and 83% received a kidney from a living donor. Thirty patients (17%) were considered frail (GFI > 4) at baseline. After a mean follow-up of 22.8 ± 8.3 months, 34 patients (19%) transitioned from a non-frail to a frail state, 125 patients (71%) remained the same and 17 patients (10%) transitioned from a frail to a non-frail state (GFI < 4). The individual frailty domains "limited cognition" (19%) and "limited psychosocial functioning" (28%) contributed most to a deterioration in frailty state.
Conclusions: Almost one fifth of kidney transplant recipients transitioned from a non-frail to a frail state after their transplantation. These results can be used to inform patients on the impact of kidney transplantation and manage expectations regarding physical and cognitive decline after surgery. More emphasis needs to be put on specific, preventative interventions which combat the decline of the individual frailty domains.

Uncensored immune profiling in kidney transplantation: towards individualized immunosuppressive treatment

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Background: The favorable effects of more powerful immunosuppressive drugs (ISD) on patient and graft survival is accompanied by side effects such as infections and cancer. Until now we are not able to determine the minimal intensity of immunosuppressive therapy that is required for an individual renal transplant recipient (RTR). The aim of this study is to identify RTR who are eligible to lower doses of ISD without the risk of infection.
Methods: We analyze 10 patients with recurrent non-melanoma skin cancer (NMSC) at least 10 years after transplantation hypothesized to have clinically 'weak/quiet' immune status versus 10 matched patients without NMCS who potentially have a 'strong/responsive' immune status. Furthermore we include 20 pretransplant end-stage renal disease patients and 10 age-matched healthy controls. 20 ml blood is drawn and samples are analyzed within hours after collection. Flow cytometry is performed on whole blood and isolated PBMC's using 6 standardized 10 color panels, resulting in over 200 different leukocyte subsets. Additionally, PBMC's are stimulated for 30 minutes with pathway specific stimuli to induce ex vivo phosphorylation of various intracellular pathways. The combined data of the leukocyte subsets and the dynamic profile determined by the phosphorylation changes are expected to yield discriminative personalized profiles. Using different unsupervised multivariate analyses we will determine whether the immune status of NMSC patients is different from those without NMSC and how this differs from pretransplant patients and HC.
Results: The preliminary results of this novel technique are promising. We already are able to discriminate the personalized profiles of patients long after transplantation versus pretransplant patients, and versus healthy controls. Individual profiles of the patients in the different subgroups are now analyzed. After inclusion and analysis are finished in February 2020 we will present the detailed data of all subgroups at the Boot-conference in March.
Conclusions: Our data suggest that a personalized immune signature can be identified by uncensored analysis of whole blood and PBMCs of renal transplant patients. This would help to avoid morbidity and mortality associated with over- and underimmunosuppression. Applying this method for the analysis of the immune system of RTR is a wholly new approach in the transplant field.

Potential protective effects of doxycycline on renal degradome during hypothermic machine perfusion and reperfusion

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Background: Donation after circulatory death donor kidneys (DCD) are used to enlarge the donor pool, however these kidneys are exposed to ischemia/reperfusion injury (IRI), making them more susceptible to chronic failure. In the Netherlands, hypothermic machine perfusion (HMP) is the standard way of preserving kidneys for clinical transplant. HMP allows you to add therapies to a functioning organ. Doxycycline shows to have protective effects during renal IRI. Therefore, our aim was to protect DCD kidneys from IRI using doxycycline during HMP and observe its effect on kidney function and the renal degradome.
Methods: Porcine kidneys (n=7) received 30min of warm ischemia, 24h of HMP with or without doxycycline, and 4h of *ex vivo* reperfusion. Renal cortex samples were obtained after HMP and after reperfusion. We performed a high-efficiency undecanal-based N termini enrichment workflow combined with nano-flow reversed phase chromatography-tandem mass spectrometry to identify the degradome. KEGG pathway analysis of proteins significantly up- or downregulated was performed using STRING 11 and the Merops protease database was used for matching proteolytic events to the most probable responsible protease.
Results: 717 peptides and 265 proteins were identified as the renal degradome. The addition of doxycycline during HMP led to significantly less protein degradation after HMP and after reperfusion compared to control. After 24h of HMP, 17 proteins were significantly more degraded and 3 proteins were less degraded in the control group compared to the group with added doxycycline. 4h of reperfusion led to 38 proteins that were significantly more degraded and 7 proteins that were less degraded in the control group compared to the doxycycline group. Degradation after reperfusion in the control group occurred mostly in metabolic pathways and more specifically in oxidative phosphorylation. These proteolytic events are most probably caused by a range of cathepsins, matrix metalloprotease 2 and Meprin α and β. No significant differences in renal function were observed during reperfusion.
Conclusions: Addition of doxycycline during HMP protects the kidney against protein degradation and disruption of metabolic processes during HMP and reperfusion. These identified degradation profiles could play an important role in provoking short- and long-term graft failure caused by IRI. Doxycycline could be a potential pharmacological intervention strategy to attenuate protein degradation during HMP of DCD kidneys.

Increased development of microthrombi and fibrin depositions in deceased donor kidney transplantation

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Background: Microthrombi and fibrin depositions in peritubular capillaries and glomeruli of the donor kidney may potentially lead to local perfusion disorders, and subsequently to deterioration of graft function. The primary aim of this study was to investigate how often, and when, these microthrombi and fibrin depositions occur. Second aim was to investigate whether different donor types and intraoperative heparinization of the recipient are associated with the development of microthrombi and fibrin depositions.
Methods: Two open-needle biopsies, at start anastomosis and after reperfusion, were obtained from 43 kidneys transplanted from 2005 to 2008. Immunohistochemical staining with antibodies for fibrin(ogen) was performed on paraffin-embedded sections. Microthrombi/mm^2 (MT/mm^2) were scored by a trained nephropathologist and fibrin deposition was categorized as none, low, moderate or high.
Results: An significant increase in MT/mm^2 (0.45 [0–1.21] vs. 0 [0–0.45]) and generalized fibrin deposition (100% vs. 20% moderate/high) was observed in postreperfusion biopsies compared to pre-anastomosis biopsies. The same was observed for deceased donor kidneys compared to living donor kidneys (0.09 [0–0.66] vs. 0.00 [0–0], p=0.02). Administration of heparin prior to reperfusion, significantly reduces the number of MT/mm^2 (0.49[0-0.69] vs. 0 [0-0], $p<0.01$).
Conclusions: Kidney transplantation is related with the development of microthrombi and a generalized deposition of fibrin in peritubular capillaries and glomeruli. Deceased donor kidneys are more prone to this development. There may be a role for prophylactic heparinization of the recipient to inhibit this process.

Generation of human monoclonal HLA-DR antibodies for verification of HLA-DR eplets

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Background: In renal transplantation, recipients can form *de novo* donor-specific antibodies (DSA) against the mismatched HLA antigens of the donor and especially DSA against HLA class II are formed. Recent studies have shown that the development of these *de novo* DSA correlates with the number of HLA-DR/DQ eplet mismatches between recipient and donor, but not every individual eplet mismatch will result in DSA response. HLA class II eplets are theoretically defined single or configurations of surface exposed polymorphic amino acids. Therefore, experimental verification of immunogenic eplets is required, but is currently lacking due to the limited number of available HLA class II monoclonal antibodies (mAbs). To this end, we aimed to develop recombinant human HLA-DR specific mAbs.
Methods: From peripheral blood mononculear cells of three pregnancy immunised individuals, single memory B cells positive for HLA-DR tetramers were sorted. After expansion, supernatants were screened for the presence of HLA antibodies. From the HLA antibody positive B cell clones, RNA was isolated to obtain the variable heavy and light chains for cloning into pcDNA3.3 expression vectors. Next, both vectors were co-transfected in Expi293 cells to produce recombinant human HLA mAbs, which were analysed with luminex single antigen beads (SAB).
Results: HLA-DRB1*07:01, -DRB1*01:01, and -DRB1*04:01 tetramers were used for cell sorting and an average of 5 (range 2-11) HLA positive clones were obtained from sorted memory B cells, which represented an average of 0.0002% of total B cells. From these clones, eight recombinant mAbs were generated with six different antibody reactivity patterns: DR7, DR7/DR9, DR7/DR12, DR1/DR4/DR15/DR51, DR1/DR9/DR10/DR51 and DR4/DR1303/DR8/DR11/DR15/DR16. By analysing the antibody reactivity patterns, single or configurations of amino acids uniquely shared by the reactive HLA alleles could be defined. This analysis led to antibody-verification of HLA-DR eplets, 78V, 70Q 73A, and 31F 32Y 37Y. In addition, these mAbs could bind their native HLA targets expressed on cells and led to complement dependent cytotoxicity.
Conclusions: In conclusion, recombinant human HLA-DR specific mAbs can be generated from single memory B cells, and antibody reactivity pattern analysis led to verification of HLA-DR eplets. Additionally, these mAbs can also be used for functional studies on the effect of HLA antibodies in transplantation.

Unbiased multiparameter analysis identifies increased immunosenescence of alloreactive CD8+ T cells in association with donor-specific hyporesponsiveness

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Background: The risk of T-cell mediated rejection (TCMR) progressively declines in the years after kidney transplantation (KT) in most recipients. This is reflected by a decreased proliferative response of recipient T cells to donor antigen presenting cells, a phenomenon called anti-donor-specific hypo-responsiveness (DSH). The onset of DSH is more rapid and pronounced in older recipients (55+), indicative of immunosenescence/exhaustion of T lymphocytes as a contributing factor.
Methods: To test this hypothesis, expression profiles of markers associated with immunosenescence were investigated within anti-donor-specific T cells of elderly stable kidney transplant recipients before and 3-5 years after KT . Anti-donor-specific T cells were identified as CD137 positive T cells upon stimulation with donor cells and further characterized by flow cytometry using a broad panel of known markers of immunosenescence/exhaustion. Traditional analysis of flow data by visual inspection of 2D scatterplots is biased and inefficient as the number of plots increases exponentially with the amount of markers used. This problem was circumvented through an unsupervised (and therefore unbiased) clustering and dimensionality reduction technique called Flow Self-Organizing Map (FlowSOM).
Results: All recipients demonstrated DSH 3-5 years after transplantation. Within the heterogeneous pool of CD137-expressing anti-donor specific T cells, clusters of CD4+ and CD8+ T-cells with a high fold-change of cell numbers between pre- and post-transplant time points were identified and confirmed by traditional flow cytometry analysis. Clusters of CD8+CD137+ T cells highly expressing exhaustion markers CD244 and TIGIT and immune checkpoint inhibitor, CD160, make up a larger proportion of CD8+CD137+ T lymphocytes post KT. In contrast, clusters of CD4+CD137+ T cells highly expressing TIGIT with or without exhaustion marker TIM3, decrease post Tx. One CD4+CD137+ T cell cluster which decreases post KT deviates from this trend, as it has no TIGIT expression but does express the immune checkpoint inhibitor PD1.
Conclusions: The results demonstrate the richness of data obtained by unbiased analysis of immunosenescence/exhaustion expression profiles as compared to classical 2D analysis. The results indicate that immunosenescence/exhaustion may be an important underlying mechanism causing DSH in the alloreactive CD8 T cells.

The small-molecule BCL6-inhibitor 79-6 suppresses follicular T helper cell differentiation and plasma blast formation

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Background: In kidney transplantation, antibody mediated rejection is a major cause of graft loss amongst patients. The currently prescribed immunosuppressive treatments insufficiently control this humoral B cell mediated immune response. This humoral response is not only B cell mediated, but is also dependent on follicular T helper cells. To prevent or inhibit this T cell dependent humoral alloresponse, we investigated whether targeting Bcl-6, the transcription factor mediating germinal center formation and the T – B reaction, inhibits this humoral response. For this reason, the effects of the small molecule Bcl-6 inhibitor 79-6 on T and B cell proliferation and differentiation were studied.
Methods: First, the effect on T cell proliferation by 79-6 was tested using a mixed lymphocyte reaction in the presence of different concentrations of 79-6.
Next, we determined whether 79-6 affected the generation of Tfh cells. Magnetic-sorted naïve peripheral CD4 helper T cells were stimulated with anti-CD3/28 along with the polarization cytokines IL-12 and IL-21.
To examine the direct effects of this agent on B cell differentiation, naïve B cells were stimulated with anti-IgM/anti-CD40 and IL-21 in the presence and absence of 79-6.
Results: In the mixed lymphocyte reaction we found a dose dependent effect of 79-6 on T cell proliferation. This includes the proliferation response of the specialized Bcl6+ T helper subset named follicular T cells (Tfh) that are fundamental in the B cell differentiation.
Differentiation of naïve T helper cells under cocktail-stimulated conditions resulted in a large population of "Tfh-like" cells with significantly reduced numbers in the presence of 76-9.
In the presence of the Bcl-6 inhibitor less expression of the B cell memory markers CD27 and CD38 was measured, as well as a decreased formation of plasma cells.
Conclusions: In summary, our studies show promising first results that targeting Bcl-6 transcription affects the functionality of activated T and B cells, thereby preventing the differentiation into B cell plasma blasts, the cell population secreting immunoglobulins.

Mesenchymal stromal cell treatment during ex vivo normothermic machine perfusion of donor kidneys - a porcine autotransplantation study

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Background: Donor kidneys of inferior quality are increasingly being accepted to decrease waiting time for a transplant. Normothermic machine perfusion (NMP) could provide superior organ preservation compared to other preservation methods. In addition, it offers the unique opportunity for active interventions to an isolated organ prior to transplantation. There is increasing evidence that mesenchymal stromal cells (MSCs) could have a positive effect on ischaemic injury. However, in most studies MSCs are administered to recipients after transplantation, which exposes the whole patient to circulating allogeneic cells. In this preclinical study, we aimed to investigate whether MSCs can also be administered ex vivo during pre-transplant NMP and whether this MSC treatment improved early graft function.
Methods: Female laboratory pigs were used in this series of auto-transplantation experiments. Four experimental groups were defined (n=7 per group) and kidneys were randomly assigned to each group. After 75 minutes of warm ischaemia kidneys were subjected to four different preservation strategies. In group 1 kidneys underwent oxygenated HMP for 14 hours (ox-HMP) and in group 2 oxygenated HMP for 14 hours was followed by NMP for 4 hours (NMP). Kidneys in group 3 were also subjected to oxygenated HMP for 14 hours and NMP for 4 hours but after 1 hour 10 million porcine adipose tissue derived MSCs were added to the circuit (NMP + pMSC). Group 4 followed the same protocol as group 3 but instead of porcine MSCs, 10 million human renal adipose tissue derived MSCs (NMP + hMSC) were added. Subsequently, all kidneys were autotransplanted and pigs were observed for 14 days. Creatinine levels were monitored and GFR measurement took place on day 14.
Results: Adding MSCs during pre-transplant renal NMP proved to be safe; no embolisms occurred and MSC treated kidneys did not show inferior posttransplant function. Posttransplant serum creatinine values in all groups were comparable, with slightly lower levels in the groups in which the kidneys were subjected to NMP in addition to HMP.
Conclusions: In this relatively short follow-up period, we did not see an effect of treatment with MSCs, but as viable MSCs remained detectable in the transplanted kidney at postoperative day 14, this allows for possible long-term effects which remain to be studied.

Anti-rejection therapy does not eliminate donor-reactive IFN-γ and IL-21 producing cells

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Background: IFN-γ and IL-21 have pro-inflammatory properties and support induction and expansion of aggressive cytotoxic T cells. IL-21 also regulates the differentiation of B cells into antibody producing plasma cells, and high numbers are associated with the occurrence of rejection. We investigated whether successful anti-rejection treatment eliminates circulating donor-reactive cytokine producing cells (pc).
Methods: PBMC samples of 85 stable kidney transplant recipients of whom 30 patients were successfully treated with rejection therapy [high-dose corticosteroids for 3 consecutive days followed by ATG treatment (n=7) at median 7 days after transplantation, range: 6-48] were analysed by IFN-γ and IL-21 Elispot after rejection treatment (1.22±0.91 years after transplantation). Patient's PBMC were stimulated with irradiated donor cells or third-party cells that were completely HLA mismatched.
Results: Significantly higher frequencies of donor-reactive IFN-γ and IL-21 pc were found in patients treated with rejection therapy compared to those without rejection [IFN-γ: median 24/3E5 PBMC (6-119) vs. 9/3E5 PBMC (3-27), p=0.01; IL-21: 27/3E5 PBMC (10-59) vs. 9/3E5 PBMC (4-32), p=0.004]. No difference was found between the patient groups after third-party stimulation. Remarkably, the number of donor-reactive IFN-γ and IL-21 pc in the rejection treated group was comparable with the third-party reactivity, while the number of donor-reactive cytokine pc in patients without rejection was significantly lower than the third-party reactivity [IFN-γ: 9/3E5 PBMC (3-27) vs. 33/3E5 PBMC (15-117), p<0.0001; IL-21: 9/3E5 PBMC (4-32) vs. 40/3E5 PBMC (19-88) p<0.0001].
Conclusions: High numbers of donor-reactive IFN-γ and IL-21 pc in patients subsequently and successfully treated with anti-rejection therapy appear to be insensitive to therapy. These patients should be more carefully monitored as they are at risk for rejection when their immunosuppressive adherence decreases.

Immunosuppression affects circulating follicular regulatory T cells in kidney transplant recipients

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Background: FoxP3$^+$ follicular regulatory T cells (Tfr) have been identified as the cell population controlling T follicular helper (Tfh) cells and B cells that are involved in effector immune responses against transplanted tissue.
Methods: To understand the biology of Tfr cells in kidney transplant patients receiving tacrolimus based immunosuppression, we measured circulating (c)Tfh and cTfr cells in peripheral blood at 5-7 years after transplantation by flow cytometry. Of this cohort 26% (58/227) had been treated for rejection of which 16% was diagnosed as T cell mediated rejection (TCMR), 7% as chronic (c)ABMR and 3% as mixed rejection. Median time after anti-rejection therapy was 4.9 years (range 0.4–7 years). Age and gender matched heathy individuals served as controls.
Results: While the absolute numbers of cTfh cells was comparable between kidney recipients and healthy controls, the numbers for cTfr cells were 46% lower in immunosuppressed recipients (median 8.8×10^6/L vs. 16.2×10^6/L, $p<0.001$). More importantly, the ratio of Tfr/Tfh was decreased, indicating a disruption of the balance between cTfh and cTfr cells. This shifted balance was observed for both non-rejectors and rejectors. Previous pulse steroid anti-rejection therapy led to 29% (median) fewer cTfr cells, IvIG to a 40% and alemtuzumab therapy to 85% ($p<0.01$ for all group vs non-rejectors). No association with tacrolimus trough levels was found. The Tfr/Tfh ratio was correlated with kidney function (eGFR: $r_s=0.13$, $p=0.04$).
Conclusions: Our work shows that anti-rejection therapy significantly affects the number of cTfr cells in kidney transplant recipients. The observed profound, long lasting effects by these agents might dysregulate cTfr functions.

Renal functional reserve predicts long-term kidney function in living donors

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Background: The healthy kidney has a remarkable capacity to increase its function by ~30% in response to an increased demand: the renal functional reserve (RFR). Although the RFR may add essential information to the glomerular filtration rate (GFR) in donor screening, its predictive value is unknown. Here we studied the clinical determinants of the RFR, defined as the single-kidney post-donation GFR increase, and assessed its capacity to predict long-term kidney function in living donors.
Methods: We used ^{125}I-iothalamate-based measured GFR (mGFR) data from 1028 living kidney donors who donated between 1984 and 2018. Five-year follow-up was available for 402 donors. The RFR was defined as the mGFR at three months after donation minus 50% of the pre-donation mGFR. Multivariable linear regression analysis was used to identify pre-donation determinants of the RFR and to study the association between RFR and five year post-donation mGFR. Finally, we assessed the predictive capacity of the RFR for five year post-donation mGFR using receiver operating characteristic analysis.
Results: Mean (SD) age before donation was 52 (11) yrs (52% female). Mean pre-donation mGFR was 114 (22) mL/min and mean mGFR at three months after donation was 72 (14) mL/min. The mean RFR was 15 (8) mL/min, with a range of -9 to 63 mL/min. Backward linear regression revealed that age (standardized β (β_{st})=-0.36), pre-donation mGFR (β_{st}=-0.11) and body surface area (BSA) (β_{st}=0.15) were independent determinants of the RFR (all P<0.001, model R^2=12%). The RFR was associated with mGFR five years after donation (β_{st}=0.25, P<0.001), independent of pre-donation mGFR, age and BSA (model R^2=0.76). Addition of the RFR to a prediction model of 5-year mGFR with pre-donation mGFR significantly increased the prediction accuracy (area-under-the-curve from 89% to 92%, P=0.01).
Conclusions: Our findings suggest that the kidney's capacity to increase its function upon increased demand predicts long-term kidney outcomes independently of pre-donation renal function and other potential confounders.

Posttraumatic growth in liver transplant recipients: result of a prospective cohort study

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Background: A significant number of liver transplant recipients report psychological problems after transplantation. On the other hand, they also report positive psychological changes, often referred to as post-traumatic growth (PTG). PTG is the positive psychological change witnessed as a result of the struggle with a highly challenging life event. Because little is known about PTG in liver transplant recipients, this study aimed to examine: 1) the extent to which PTG occurs, 2) the presence of distinct trajectories of PTG, and 3) demographic, clinical, and personal variables of influence on trajectories of PTG in liver transplant recipients.
Methods: A prospective cohort study among adult liver transplant recipients (n = 104) from three transplant centers in the Netherlands. Data regarding demographic, psychosocial, and personal variables were retrieved by self-report questionnaires before transplantation (T0) and at 3 (T1), 6 (T2), 12 (T3) and 24 (T4) months after transplantation. PTG was assessed by the Post Traumatic Growth Inventory (PTGI). Clinical data were retrieved by medical record review. Stratification was based on 0.5 SD of the difference in PTGI-score between T0 and T1. Kruskal-Wallis tests were used to compare groups.
Results: In the overall sample, the mean PTGI-score increased significantly from 43.0 (± 23.8) at T0 to 50.4 (±24.1) at T1, but did not change significantly afterwards (T2-T4). Based on the difference in score betweenT0-T1 three distinct trajectories of PTG were found: a group with an increase in PTGI-score (51.9%), a group with a stable PTGI-score (27.9%), and a group with a decrease in PTGI-scores (20.2%). Compared to transplant recipients within the trajectories of stable and increased PTGI-score, transplant recipients within the trajectory of decreased PTGI-score were found to be younger (p=.02), lived more often alone (p=.01), were longer hospitalized after the transplant (p=.01), showed higher anxiety (p=.04) and depression (p<.01) scores, a lower score on personal control (p=.03) and had a higher discrepancy between expected and observed quality of life score on all domains on T1 (p<.03).
Conclusions: A subset of transplant recipients experienced PTG after transplantation. Interventions aimed at regaining control may be helpful to enhance PTG in this group.

Validation of the Model for End-stage Liver Disease sodium score in the Eurotransplant region

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Background: The shortage of liver grafts results in the prioritization of the sickest patients on the waiting list for liver transplantation. Since 2006, the degree of disease severity in transplant candidates is estimated with the Model for End-stage Liver Disease (MELD) score. However, MELD does not account for the worse prognosis associated with hyponatremia. Since the prevalence of cirrhosis is on the rise, better prediction of mortality and improved allocation for liver transplantation are becoming increasingly important. This study researches the potential impact of using MELD-Na instead of MELD for the allocation of livers in the Eurotransplant region.
Methods: All candidates allocated through MELD with chronic liver disease on the Eurotransplant (ET) liver transplant waiting list between 2007-2018 were included. They were followed from first listing to delisting or until 90 days. The relation between MELD and Na values at listing and 90-day mortality was assessed through a multivariate Cox proportional hazard regression. A reclassification table was constructed of the relevant changes in MELD to MELD-Na score. This allowed an estimation of the lives saved if MELD-Na-based allocation would have been used.
Results: 5223 patients were included. After 90 days, 21.3% were transplanted, 24.2% were removed and 2.8% had died. Hyponatremia of <135, <130 and <125 mmol/L was found in respectively 28.5%, 8.8% and 2.6% of the listed patients. Between 140 to 125 mmol/L, the MELD-corrected risk of 90-day death increased by threefold (2.9; 95%CI 2.30-3.53; p<0.001). The hazard ratio for death was 1.16 (95%CI 1.15-1.17; p<0.001) per gained MELD point and 1.08 (95%CI 1.06-1.09; p<0.001) per 1-unit Na decrease. The MELD-Na had a c-index of 0.847 (SE 0.007, p<0.001). Of the deceased patients, 26.3% would have had a significantly higher chance of transplantation with MELD-Na, which equals to a 4.9% decrease in 90-day waiting list mortality.
Conclusions: The ET waiting list population has a relatively high prevalence of hyponatremia. For transplant candidates, a low Na increases the risk of 90-day mortality by threefold. If MELD-Na would have been used, 26.3% of the deceased patients would have had a significantly higher chance of transplantation. The 90-day waiting list mortality would have been lowered by 4.9%. Thus, MELD-Na-based allocation could reduce waiting list mortality for the ET region.

The effect of mannitol on kidney function after kidney transplantation: a systematic review and meta-analysis

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Background: The effect of mannitol usage during kidney donation and kidney transplantation is still unclear. Therefore, we performed a systematic review and meta-analysis to investigate difference in graft function between kidney grafts treated with and without mannitol.
Methods: A literature search was performed in five databases on the 6th of March 2019 and included seven eligible studies out of 3112 references. Relevant outcomes for meta-analysis were graft survival, acute tubular necrosis, delayed graft function, renal failure ,and serum creatinine. The quality of evidence was assessed using the Newcastle-Ottawa scale and Jadad score.
Results: Seven studies were identified, one study examining the effect of mannitol during kidney donation and six studies during kidney transplantation. Six studies were eligible for the meta-analysis. The risk of acute tubular necrosis, delayed graft function and renal failure was RR=1.22, 95% CI [0.84, 1.77], *P* = 0.31, RR=1.39, 95% CI [0.85, 2.28], *P* =0.19, RR=2.34, 95% CI [0.94, 5.85], *P* = 0.07 respectively. Graft survival showed a trend for Mannitol, but was not eligible for meta-analysis.
Conclusions: This systematic review and the meta-analysis do not provide evidence to use mannitol during kidney donation and kidney transplantation to significantly improve graft function.

Exploring health literacy and self-management after kidney transplantation: a prospective cohort study

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Background: Health literacy and self-management skills may influence how patients interpret and act on information about post-transplant self-care. This study aimed to investigate the influence of health literacy and self-management on complications, kidney function and graft failure after kidney transplantation.
Methods: We performed a prospective cohort study and included patients who received a kidney transplant between May 2012 –May 2013, and monitored them until December 2018. We measured health literacy and self-management before discharge and 6 and 12 months after transplantation. Health literacy was measured using the Newest Vital Sign and self-management using the Partner in Health scale. Subscales are aftercare & knowledge, coping, recognition and management of symptoms, healthy lifestyle. Complications were rejection, viral infections, and bacterial infections. Kidney function was measured by eGFR and graft survival with days until failure.
Results: We included 154 patients (73% response rate). Higher health literacy at baseline and at 12 months was related to more viral infections ($p=0.02$; $p<0.01$). No relationships were found between health literacy and kidney function and graft failure. Lower 'coping' at baseline was related to more bacterial infections ($p=0.02$). Higher 'after-care and knowledge' at 6 months ($p<0.01$), and 'recognition and management of symptoms' at 6 months were associated with lower graft failure ($p<0.01$).
Conclusions: Higher knowledge and management of symptoms were related to lower graft failure. Promoting these components of self-management may improve outcomes after kidney transplantation. There were few relationships found between health literacy and kidney transplant outcomes, which is contrary to previous studies. The support of self-management post-transplant is important, and is thus a key focus for nurses in the multidisciplinary team.

Participation of compatible kidney donor-recipient pairs in the Dutch Kidney Exchange Program (KEP): an exploration of the decision-making process

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Background: Participation of compatible pairs in KEP would increase the chances for the incompatible pairs. For compatible pairs too, it can offer advantages by e.g. finding a donor with a better HLA match. Which factors influence the decision of compatible pairs to participate in our voluntary (v)KEP? How do they experience the education about vKEP?
Methods: During June 2016-September 2017, all new recipients and donors who visit our outpatient clinic for the first time were informed orally and by means of a leaflet about vKEP. If during the next visit they were compatible, we discussed the willingness to participate in our vKEP and gave them a questionnaire.
Results: Of the 93 approached, 62 persons completed the questionnaire. 12 (6 pairs) intended to participate in vKEP and 50 did not. Among those who did not want to participate, common reasons were: 'My kidney fits well with my recipient' (32/50),and 'it doesn't feel good' (19/50). A longer waiting time (29/38) and that the donor would donate in another hospital (23/39) were seen as barriers. Among those who intended to participate in vKEP, the most important motivation was that it felt good (8/10), hope for a better kidney (7/10) and altruism (4/10). A longer waiting time (6/10) and that the donor would donate in another hospital (7/10) were seen as obstacles. In both groups, anonymity was not seen as a barrier (40/52), they were very satisfied with the verbal explanation (50/55) and the leaflet (45/53). There was little objection to being informed about vKEP (5/53). Ultimately 4 compatible pairs participated in our KEP which resulted in 11 transplants instead of 4.
Conclusions: The decision whether or not to participate as a compatible pair in our vKEP is based on emotional, logistical and medical factors. Donors and recipients were open to education about and consideration of this program. Insights into barriers and facilitators will be incorporated into our vKEP policy and processes.

Directed deceased donation in the Netherlands? An exploration

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Background: In the Netherlands, donors – or surviving relatives – have no control over the allocation of organs donated after death. The Dutch Organ Donation Act (WOD) states that the allocation of organs is the exclusive competence of a licensed Organ Center (see art. 24 WOD). In the Netherlands this license has been granted to the Dutch Transplantation Foundation (NTS).
In the case of a living donation, it's different. Art. 3:1 WOD states that the living donor grants permission for the removal of his organ for implantation *in a specific person*.
So, different rules apply to post-mortem and pre-mortem organ donations. Both situations have different assessment frameworks, with their own central values: 'donor autonomy' before death, 'equitable distribution of organs' after death.
Methods: In theory, the two options are clear. But reality is not limited to these two situations. Once in a while the NTS receives phone calls from potential donors who express their wish to donate after death to a specific person. Some of the requests concerned potential donors in an euthanasia process. Another case concerned a living donor, that passed away short before the transplant date. It also happened that relatives of an unregistered deceased potential donor, when asked for permission, indicated that one of them was on the waiting list, in need of an organ and. Up till now, it is believed that the Dutch Organ Donation Act leaves no room for directed deceased donation. Patients who wish to donate post-mortem to a specific person are told that there is no possibility to do so.
Until now, a request for directed deceased donation has not been granted in the Netherlands, with reference to legal arguments. It would not be allowed under the current Organ Donation Act, and it would not be consistent with our current, objective allocation system (based on the notion of a fair distribution of medical assistance and organs).
Results: Abroad, examples of directed deceased donation can be found. In the United Kingdom, the *Requested allocation of a deceased donor organ* directive entered into force in 2010. This "framework document provides policy advice about the circumstances in which a request for an allocation of a deceased donor organ to a close relative or friend could be considered in exceptional circumstances and when the needs of other patients should take precedence over that request for the allocation."#_ftn1 Conclusions: Considering the forementioned requests, the question should be answered whether the Dutch legal framework allows directed deceased donation in the Netherlands. If not, should it be changed? In that case, what legal measures are needed?

Steroid withdrawal is safe in pediatric kidney recipients

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Background: In the last decades, multiple developments in immunosuppressive therapy for pediatric kidney recipients were seen. Previous literature showed that steroid withdrawal has comparable outcome on graft function and survival as steroid-containing regimens. Less is known about side effects of these regimens. The aim of this study is to establish safety of steroid sparing protocols.
Methods: Data was collected among pediatric kidney transplant recipients during the first five years of follow-up. Use of immunosuppressive medication was documented, as well as infective parameters and other possible side effects of immunosuppressants. Occurrence of side effects was compared between patients remaining on steroids, patients remaining steroid free and those who switched during follow-up.
Results: After introduction of steroid sparing protocols a decline in prednisone use was seen (94% to 43%). Out of 100 recipients, 44 started a steroid-sparing regimen of which 22 remained on during whole follow-up. Reasons to switch medication were mainly gastro-intestinal complaints (23%) and EBV (23%) and BKV (17%) viremia.
Patients remaining on a steroid containing regimens had more UTIs ($p=0.012$) and worse growth velocity ($p=0.035$) than those on steroid sparing regimens. Other side effects did not differ between groups.
Conclusions: Steroid sparing immunosuppressive regimes are safe and effective in pediatric kidney recipients.

Active knowledge building and group learning is limited in online sources for patients on renal transplantation

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Background: Renal patients search the Internet thoroughly to improve their knowledge of renal transplantation. Yet, a gap remains between information provided and patients' understanding. Although digital learning has markedly increased in last decade, digital teaching strategies seem still insufficient applied to online resources. This study systematically evaluated the available teaching approaches for instruction, interaction, and assessment in online resources on renal transplantation.
Methods: The top 50 websites containing information on renal transplantation were retrieved by using the search engine "Google.nl". A data collection tool was composed and calibrated. From a total number of 1071 webpages on 24 different websites, 250 webpages were included based on compiled inclusion criteria. Websites were examined on organizational source, content topics, available teaching modes (instruction (e.g. text), interaction (e.g. discussion forum), assessment (e.g. open ended question)) and teaching approaches (receiving knowledge or active knowledge building, and individual or group learning) according to the Teaching Approach Framework of Arbaugh and Benbunan-Finch (2006).
Results: Most of included websites were hosted by a professional non-profit organization (n=20; 83.3%), such as hospitals. The information of each webpage was scored on five topics: cause of and treatment options for renal patients (n=105; 26.3%), renal transplant options and preparatory examination (n=88; 22%), operation and hospital stay (n=39; 9.8%), life after transplantation, including life style and medication (n=118; 29.5%) and contact with others (n=50; 12.5%). A total number of 1331 items dispersed over 16 different teaching modes were found, classified into instruction (n=1287; 96.7%), interaction (n=40; 3.0%) and assessment (n=4; 0.3%). Analysis of teaching approaches showed a frequent occurrence of receiving knowledge and individual learning (n=1285; 96.5%) compared to receiving knowledge and group learning (n=0), active knowledge building and individual learning (n=10; 0.8%) and active knowledge building and group learning (n=36; 2.7%).
Conclusions: Online resources on renal transplantation do not have a uniform teaching mode profile and active knowledge building, such as assessments, is hardly encountered. A more balanced availability of teaching modes and approaches is desirable to diminish the gap between information provided and patients' understanding of information on renal transplantation.

The management of aorto-iliac vascular disease in candidates for kidney transplantation: a worldwide survey among transplant surgeons

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Background: Aorto-iliac vascular disease (AIVD) is becoming more common among kidney transplant (KTx) candidates resulting in technical and ethical concerns due to accompanying cardiovascular disease. We performed a survey among KTx surgeons regarding the management of patients with AIVD.
Methods: A survey was constructed and spread among 939 transplant surgeons. The survey contained baseline questions and 2 vascular complex cases where respondents could decide their management based on patient details and a contrast-enhanced CT-scan video.
Results: 147 KTx surgeons replied. 71.4% worked in a hospital where <10 KTx/year are performed after a pre-transplant vascular intervention. High-volume centers (≥200 transplants/year) were more likely to consider KTx after such interventions ($p<0.001$). 96% agreed that an endovascular intervention would ideally take place prior to KTx. There was no consensus concerning the timing of an open vascular intervention; 67.8% answered preferably prior to KTx and 32.2% simultaneously. 37.8% of the respondents who answered 'preferably prior to KTx' pointed out that there are no guidelines about the length of time between an open vascular intervention and KTx. The most important concern when performing a KTx in patients with AIVD was technical problems (75.4%), followed by increased operative risk (17.5%) and ethical issues of transplanting a scarce kidney in a patient with lowered life expectancy (7.1%). According to our respondents, potential KTx recipients should have a median minimal life expectancy of 10 years for a living donor KTx (IQR 5-10), and 5 years (IQR: 5-8) for a deceased donor KTx. Respondents with vascular specialty training were more likely to consider an endovascular/open vascular treatment instead of rejecting the patient ($p=0.037$).
Conclusions: Major differences exist in the approach towards KTx candidates with AIVD. Referral to a higher volume center might increase the chance of receiving a transplant for a patient with AIVD. Also, consultation with a KTx surgeon with vascular specialty training might increase the chance of KTx. A consensus meeting is recommended to discuss a guideline on the management of AIVD and KTx.

Mental health of unspecified anonymous living kidney donors after donation

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Background: Anonymous living kidney donors donates to an unknown stranger. These donors undergo psychosocial assessment to minimize likelihood of psychological harm from donation. The aim of this retrospective interview study was to investigate post-donation psychological symptoms, well-being and psychiatric diagnoses.
Methods: All 147 unspecified anonymous kidney donors (2000-2016) in our center were eligible to participate. The structured interview MINI Screen was used to assess psychiatric diagnoses: on indication the M.I.N.I. plus was conducted. Questionnaires were used to assess psychological symptoms (Symptoms Checklist) and psychological well-being (Dutch Mental Health Continuum). We also conducted a semi-structured interview about expectations, anonymity, experiences and the support received.
Results: Of the 147 eligible, 11 had died: 114/136 participated (84% participation rate). Fifty-two were male, median age was 66.5 (25-94) years, and the follow-up time 76.5 (24-178) months. Participants scored higher on positive well-being than the general population. Psychological complaints were comparable to the general population. Regarding psychiatric diagnosis, 54/114 (47%) donors had an indication for a diagnosis for which the M.I.N.I. plus was conducted; a lifetime diagnosis was established among 36 (32%). Most common diagnosis were depression and post-traumatic stress disorder.
Conclusions: Willingness to participate in this study was very high. The rate of psychological symptoms at the time of the interview and life-time psychiatric diagnoses is comparable with prevalence in the general population. Whereas psychological well-being generally is higher than the general population. Qualitative interview data are currently being analyzed. Prospective studies are needed to assess symptoms and well-being on the long-term taking baseline levels into consideration in order to determine the burden and gains of unspecified donation.

Chronic diarrhea in renal transplant recipients: a metagenomic study of gut microbiota composition and functionality

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Background: Chronic diarrhea is a common problem in renal transplant recipients (RTR) and can lead to a lower quality of life. However, in many patients the underlying etiology is unknown and they silently carry this burden. RTR suffer from dysbiosis, a disruption of the gut microbiome, which is associated with the occurrence of diarrhea. Therefore, we aimed to objectively identify the occurrence of diarrhea and characterize the composition and the functionality of the gut microbiome of RTR with diarrhea.
Methods: Fecal microbiome data was generated using whole-genome metagenomic shotgun sequencing of 1000 fecal samples from the Transplantlines cohort study. Fecal samples were collected at different time points pre- and post-transplantation. Fecal dry matter analysis was used to objectively identify diarrhea. The occurrence of diarrhea was correlated to gut microbiota composition and functionality using MaAsLin.
Results: We included 177 healthy controls (50% female, age: 57.5 ± 10.8 years), 465 RTR (42% female, age: 56.23 ± 13.0 years) more than 1 year post-transplantation with a median time after transplantation of 8 years and an IQR of [3.0:13.0] and 86 RTR (46% female, age: 57.8 ± 11.2 years) with multiple fecal samples less than 1 year post-transplantation. In total 23% of RTR suffered from diarrhea and had a significantly lower diversity of the gut microbiome ($P<0.01$). We identified multiple different bacteria that were different in RTR with diarrhea (false-discovery rate (FDR) <0.1). Metabolic pathways were significantly different in RTR with diarrhea (FDR<0.1).
Conclusions: We combined gut microbiome composition with metabolic function, antibiotic resistance and bacterial growth rate analyses and concluded that the gut microbiome of RTR with diarrhea is different from RTR without diarrhea and healthy controls.

The effect of being overweight on surgical complications after living kidney donation

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Background: Obesity is considered a risk factor for peri- and postoperative complications. Little is known about this risk in overweight living kidney donors. The aim of this study is to assess the risk of surgical complications after living donor nephrectomy using different measures of body composition.
Methods: We included 776 living kidney donors who donated between 2008 and 2018 at the University Medical Centre Groningen. Pre-nephrectomy measures of body composition were body mass index (BMI), body surface area, waist circumference, weight and waist-hip ratio. Incidence and severity of peri- and postoperative complications were assessed using the Comprehensive Complication Index.
Results: Mean donor age was 53 ± 11 years, 382 (49%) were male and mean BMI at donor screening was 26.2 ± 3.41 kg/m^2. In total, 77 donors (10%) experienced peri- and postoperative complications following donor nephrectomy. Univariable linear regression analysis showed no pre-nephrectomy measure of body composition was associated with a higher risk of surgical complications. Female gender (std. beta=0.09, p=0.01), older age (std. beta=0.09, p=0.01) and longer duration of surgery (std. beta=0.11, p=0.005) were significantly associated with more surgical complications. Following multivariable linear regression analysis, corrected for gender and age, longer duration of surgery was significantly associated with surgical complications (std. beta=0.13, p=0.001).
Conclusions: This study shows that higher pre-nephrectomy BMI and other anthropometric measures of body composition are not significantly associated with peri- and postoperative complications following living donor nephrectomy. Only longer duration of surgery is significantly associated with more surgical complications in living kidney donors.

Metabolic acidosis is associated with increased risk for graft failure and premature death in stable renal transplant recipients

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Background: Metabolic acidosis is a risk factor of end-stage renal disease and death in patients with chronic kidney disease (CKD). Correction of metabolic acidosis has shown to help preserve kidney function and reduce mortality in CKD. It remains unclear, however, whether metabolic acidosis is associated with worse outcome in stable renal transplant recipients (RTR).
Methods: For this study we used data from the TransplantLines Food & Nutrition Cohort Study (NCT02811835), collected between 2008-2011. Venous bicarbonate (HCO_3^-) was assessed on a Radiometer 800 blood gas analyzer, and metabolic acidosis was defined as HCO_3^- <24 mmol/L. Cox regression analyses were used to analyze the associations of HCO_3^- levels and metabolic acidosis with graft failure and mortality. Additionally, separate analyses were performed in RTR to investigate the association of HCO_3^- in RTR without metabolic acidosis.
Results: We included 651 RTR (56% men, 53±13 years old, eGFR 52 ± 20 ml/min/1.73 m^2) at a median of 5 years after transplantation. Mean HCO_3^- was 24.6±3.1 mmol/L and 203 RTR had metabolic acidosis. During follow-up of 5.4 years, 77 RTR developed graft failure and 142 died. HCO_3^- was inversely associated with graft failure (HR 0.75; 95%CI 0.70-0.80) and death (HR 0.93; 95%CI 0.88-0.98). Adjustment for potential confounders including age, sex, eGFR, time after transplantation and proteinuria did not materially affect these results. RTR with metabolic acidosis had higher risk of graft failure (adjusted HR 2.41; 95%CI 1.42-4.09) and mortality (HR 1.71; 95%CI 1.18-2.47). We observed a similar inverse association of HCO_3^- in RTR without metabolic acidosis with graft failure (adjusted HR 0.75; 95%CI 0.56-0.99) but the association of HCO_3^- with mortality was not significant (adjusted HR 0.97; 95%CI 0.87-1.09).
Conclusions: Higher HCO_3^- levels are associated with lower risk of graft failure and mortality in RTR. Moreover, in RTR with HCO_{3-} within normal range, HCO_3^- levels were associated with lower risk of graft failure.

Robotic-assisted laparoscopic donornephrectomy: initial results and comparison with the hand-assisted laparoscopic technique

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Background: To evaluate morbidity and renal function of the donor and recipient during robotic-assisted laparoscopic donornephrectomy and comparison with the hand-assisted laparoscopic technique.
Methods: Retrospective study of our first 27 consecutive robotic-assited laparoscopic donornephrectomy procedures (RA). This was compared with an matched group of 27 hand-assisted laparoscopic procedures (HA). Matching was done according to donor aspects (age, gender, side and operating surgeon). The Da Vinci Xi robot was used and they were totally robotic procedures. 23 left-sided and 4 right sided robotic procedures. 10 of 27 robotic procedures had a complex vascular anatomy. The BMI range of the RA group was 19-32. Donor and recipient variables were analyzed.
Results: The mean operating time was 206 min for the RA group and 141 min for the HA group. The median warm ischemia time was 3 min for the RA group and 2 min for the HA group. The median bloodloss was 20 ml for the RA group and 50 ml for the HA group. These were statistically significant differences. The post-operative pain-score, post-opertaive hospital stay and complications for the donors were identical in both groups. There was no significant differences in renal function at 1 week (serum creatinine/eGFR in the RA group 181/42 vs HA group 180/39) and 1 month (serum creatinine/eGFR in the RA group 162/48 vs HA group 146/47) after transplantation.
Conclusions: Robotic-assisted laparoscopic donornephrectomy is an evolving technique which provide a highly detailed three-dimensional visualization of the operative field, 360 degree rotating (Endowrist) instruments and better ergonomics for the operating surgeon. Robotic-assisted laparoscopic donornephrectomy is safe for the donor and for the graft.

Prolonged organ extraction time negatively impacts kidney transplantation outcome

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Background: During a deceased donation procedure, organs are flushed with cold fluid before retrieval, to reduce metabolism and preserve organ quality. However, the intended 0-4°C are never reached and kidneys stay around 18°C and ischemic during the procurement surgery. A prolonged organ extraction time could therefore have a detrimental influence on transplantation outcome.
Methods: We analyzed data from 5426 multicenter transplant procedures from the Dutch Organ Transplantation Registry, performed between 01-2002 and 12-2016. Extraction time was defined as start of the cold aortic flush until end of nephrectomy. Extraction times shorter than 5 minutes or longer than 5 hours where excluded. We studied the association between extraction time, patient survival, graft survival and delayed graft function (DGF). Analysis was performed on those cases for which both extraction time and outcome were known, using multivariable Cox regression or binary logistic regression, where appropriate.
Results: Median kidney extraction time was 58 minutes. Extraction time was independently associated with graft loss (HR 1.025 [1.002-1.048]; P=0.036) and with delayed graft function (OR 1.040 [1.017-1.063]; P=0.001) for every 10 minutes increase, but not with patient survival (HR 1.001 [0.983-1.019]; P=0.922). An extraction time above 80 minutes was associated with a 23.7% higher risk of graft failure (4.6-46.3%; P=0.013) and those kidneys with an extraction time above 70 minutes had 22.0% higher odds of developing DGF (6.0-40.4%; P=0.005).
Conclusions: Prolonged extraction time significantly influences graft survival and DGF. New strategies may be required to achieve better organ preservation during kidney retrieval.

Preformed donor specific antibodies in CDC-XM negative living unrelated male to female spousal kidney transplantations are associated with an increased risk of acute antibody-mediated rejection

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Background: Shortage of deceased donor kidneys has led to increased numbers of living unrelated kidney, in particular spousal, donors. Female recipients of a spousal kidney have an increased risk for pre-immunization and acute antibody-mediated rejection (ABMR). The aim of this study is to assess the incidence of ABMR and preformed donor specific antibodies (pDSA) in living unrelated donors (LURD) and to identify risk factors for acute ABMR.
Methods: We identified all 349 ABO compatible, CDC-crossmatch negative, LURD transplants performed at our transplant center between 1997 and 2015. All for-cause biopsies were classified according to the BANFF 2017 classification. All patients with ABMR were retrospectively tested for the presence of pDSA with multiplex and single antigen tests. Risk factors for immunization were extracted from personal health records and questionnaires.
Results: The overall incidence of biopsy-proven acute rejection in the first 6 months was 20% (TCMR: 85%; ABMR: 15%); median time to onset of ABMR was 8 days (range 5-75 days). Outcome was poor in ABMR as compared with patients with TCMR or those w/o rejection (graft loss or eGFR <30ml/min at month-6: 36%, 12% and 2% respectively). Eight patients with ABMR were female (73%) and six of these (75%) were recipients of a spousal kidney. Of these spouses four had given birth to a child of their kidney donor and 2 received blood transfusions prior to transplantation. Retrospectively 80% of spousal recipients with ABMR had pDSA in single antigen test, of which 67% had a negative multiplex initially.
Conclusions: Female spousal kidney recipients have a relatively high risk of ABMR. Traditional methods for detecting pDSA are not sensitive enough to rule out pDSA. Multiplex and single antigen should be included in the standard work-up of potential female spousal kidney transplant recipients to prevent ABMR and guide the option of indirect (cross-over) donation.

The effect of different mean arterial pressures on renal function during ex vivo normothermic machine perfusion of porcine kidneys: towards optimal conditions

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Background: In transplantation settings, machine perfusion aims to reduce the detrimental consequences of IRI. Although machine perfusion is now widely implemented, there are still knowledge gaps around rather basic aspects of machine perfusion. Perfusion pressure is one of these aspects that have not been studied thoroughly, although clinicians rely on it heavily. The aim of this study is to evaluate the effect of different mean arterial pressures on renal function and morphology, during ex vivo normothermic machine perfusion.
Methods: Porcine kidneys, obtained from a local abattoir, were subjected to 35 min of warm ischemia. After a flush of cold 1L saline, kidneys were prepared and placed on oxygenated, pressure controlled (25mmHg), hypothermic machine perfusion for 3 h and transported to the laboratory. Subsequently, kidneys were perfused normothermically for 4 h with a leucocyte depleted, blood based solution. Kidneys were divided into three groups (n=6) with mean arterial pressures (MAPs) of either 55, 75 or 95 mmHg. Perfusate, urine and tissue samples were taken during and after machine perfusion to assess both renal function and morphology.
Results: No significant differences between groups were observed with regard to flow, intrarenal resistance, creatinine clearance or urine production. Moreover, oxygen consumption and oxygen-demanding processes such as fractional sodium excretion were not different between groups. In all groups a decreasing oxygen-consumption trend is seen over time. Total urine protein concentration, reflecting disrupted glomerular integrity, was not significantly different between groups either.
Conclusions: Despite different MAPs during normothermic machine perfusion, no differences in perfusion or functional parameters were observed, which indicate that during NMP vasoreactive processes are not present. The observed trend of decreasing oxygen consumption indicates mitochondrial malfunction, but needs further evaluation. Whether different MAPs also affect morphology will also be examined.

PROlonged normothermic machine PERfusion of human discarded donor kidneys: first results of the PROPER study

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Background: In order to utilize the regenerative potential of kidneys on normothermic machine perfusion (NMP), continuous perfusion beyond 1-hr is warranted. The aim of this study is to test safety and feasibility of a newly developed PROPER protocol of 6-hrs of prolonged NMP using discarded human donor kidneys.
Methods: Discarded deceased donor kidneys (n=15) were perfused for 6h. A pulsatile pressure of 75mmHg at 37°C using an open drainage system and oxygenated with 95%O2/5%CO2 was used. As a starting point, the clinically applied 1 hour protocol as previously published by Hosgood et al. was applied for prolonged perfusions in group 1 (n=5) kidneys. Based on the first results and early modifications, the PROPER protocol was developed. Group 2 (n=10) kidneys were perfused with this modified perfusate, including crucial adjustments such as washing the red blood cells (RBCs) and the addition of albumin. When urine was produced, this was recirculated. Renal flow, perfusate parameters, and histologic assessment were recorded.
Results: No statistically significant demographic differences were found between the groups. No significant change in flow was observed in group 1 after start of perfusion to t=6h (70±34 vs 60±28 ml/min/100gr, p=0.51), however, it increased significantly in group 2 (54±35 vs 114±37 ml/min/100gr, p=0.001). There was a trend of more urine production in group 2 (cumulative 399±371 and 130±160 ml, p=0.07). Compared to group 1, group 2 kidneys maintained a more stable and physiological pH and sodium levels at 6h. Potassium levels in group 1 at t=0 and t=6hrs remained high (11.8±2.4 vs 13.1±1.9 mmol/L, p=0.42), compared to group 2 (1.9±1.8 vs 5.8±1.6 mmol/L, p=0.001).
Conclusions: This study shows that prolonged end-ischemic NMP is feasible and potentiates assessment of the kidney. It also demonstrates that for prolonged NMP an adapted perfusate is required to maintain stable flow. Therefore, we strongly recommend the addition of albumin, urine-recirculation and washed RBCs for longer perfusions.

Magnetic resonance imaging to assess renal flow distribution during ex vivo normothermic machine perfusion - It takes time to obtain cortical perfusion

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Background: With increased use of renal grafts from suboptimal donors, the need for objective pre-transplant organ quality assessment has become more important than ever. Ex vivo normothermic machine perfusion (NMP) is a potentially promising method for evaluating kidney viability prior to transplantation. However, the exact physiological mechanisms that govern a kidney during NMP are unclear. Hence, it remains to be discovered which perfusion-based biomarkers are relevant for ex vivo organ evaluation and at which time point such assessment should be done. This study utilized functional magnetic resonance imaging (fMRI) to determine how regional flow distribution develops during NMP and indicates an appropriate window for on-pump viability assessment

Methods: Three viable porcine kidneys were retrieved from a slaughterhouse. NMP on a special MRI compatible setup was performed with a perfusate containing red blood cells, crystalloids and a colloid. Longitudinally, arterial spin labeling (ASL) sequences were performed. This technique is used to quantify blood perfusion without the use of an exogenous contrast agent. For each time point, we calculated the ratio of the average cortical and medullar signal intensity on the perfusion map (CM ratio). Absolute flow values for the whole kidney were externally measured with a flow sensor.

Results: During the first 30 minutes of NMP, cortical flow was extremely low compared to flow in the medulla, with an average CM ratio of 0.20. CM ratio gradually increased over time, with an average CM ratio of 0.42 after 60 minutes, 1.01 after 120 minutes and 1.14 after 180 minutes. It took approximately 2.5 hours before renal flow distribution reached a predominant cortical perfusion. Externally measured whole-kidney flow rates stabilized much earlier, after 60-90 minutes. At comparable whole-kidney flow rates within one experiment, completely different CM ratios were observed.

Conclusions: Externally measured flow values during renal NMP did not reliably correlate with cortico-medullar flow distribution. Perfusate flow distribution gradually shifted from mainly medullar to predominantly cortical during NMP. Only after approximately 2.5 hours, this pattern resembled a near-physiologic distribution. Since most functional units of the kidney are located in the cortex, ex vivo viability assessment should most likely be performed at time points past 2.5 hours from the start of NMP.

What is the clinical relevance of HLA-C antibodies detected by luminex single antigen bead assays?

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Background: HLA antibody detection using luminex single antigen beads (SAB) aids in defining acceptable and unacceptable HLA antigens for patients awaiting a transplant. While being highly sensitive and specific, not all HLA antibodies detected by SAB assay appear to be clinically relevant, possibly resulting from differences in the quality and quantity of HLA molecules on the beads compared to natively expressed HLA antigens. Considering the instability of the HLA molecules and low HLA-C expression on the cell surface, we investigated whether HLA-C antibodies with high MFI values in SAB assay bind to cells natively expressing the corresponding HLA-C antigen.
Methods: Eight serum samples containing HLA-C antibody specificities with MFI values >5000 as detected by SAB assay (One Lambda, USA) were included. Complement dependent cytotoxicity (CDC; n=28) and/or flow cytometric crossmatches (FC-XM; n=33) were performed using peripheral blood mononuclear cells (PBMC) from 38 healthy donors. Each serum sample was crossmatched with 1-8 different donor PBMC targeting only one HLA-C antigen in each crossmatch (XM).
Results: Three sera harboured only HLA-C antibodies while in 5 sera HLA-C antibodies were coinciding with HLA-A and HLA-B antibodies. All CDC-XM were negative in samples with isolated HLA-C antibodies (median MFI: 8520; range: 5624-13990). Only 3 (11%) CDC-XM were positive in samples with multi-loci class I antibodies. Overall, only 36% of FC-XM were positive and MFI values were higher (median: 19803; 8520-23612) for FC-XM positive specificities than for negative ones (median: 10659; 5624-22215). Subsequently, when we absorbed a serum sample positive in FC-XM for HLA-C*03:04 with cells bearing HLA-C*03:04, MFI value for C*03:04 decreased from 23612 to 8622. FC-XM became negative when absorbed serum was re-crossmatched against the C*03:04, indicating that C*03:04 antibody can be absorbed and can bind to intact C*03:04 on cells. In contrast, when we absorbed the same serum sample negative in FC-XM for HLA-C*01:02 with cells bearing HLA-C*01:02, there was only a slight decrease in MFI values from 11590 to 6900, suggesting that reactivity was due to denatured HLA-C molecule on the beads.
Conclusions: HLA-C antibodies may be binding epitopes on native and denatured HLA-C antigens coated on beads affecting MFI values. Results from SAB assays must be assessed in combination with cellular assays in order not to preclude a possible transplantation for a particular patient.

Why should we pursue abdominal normothermic regional perfusion in donation after circulatory death donors: a critical appraisal

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Background: Abdominal Normothermic Regional Perfusion (aNRP) for Donation after Circulatory Death (DCD) is an emerging organ preservation technique that may lead to increased donor organ utilisation due to better assessment of organ viability, the prospect of reduced ischaemic injury with improved outcomes, and possible decrease of unintentional surgical damage. The aim of this critical appraisal is to evaluate the added value of aNRP when compared to standard techniques before its possible implementation in The Netherlands.
Methods: A systematic literature review was conducted using the PRISMA guidelines and registered with PROSPORO (CRD42019125387). Relevant literature databases were searched. Primary outcomes were donor organ utilisation rate and patient- and graft survival after one year. Secondary outcomes included delayed graft function, primary non-function (PNF), serum creatinine, and estimated or measured glomerular filtration rate for kidneys. With regards to the liver, it included PNF, biliary complications including ischaemic cholangiopathy, and early allograft dysfunction. For pancreas, YIELD after islet isolation was included.
Results: From 1268 hits in the literature, finally a total of 20 articles was included. The results of this review show that aNRP is feasible and safe and all available studies show successful implementation of the technique in clinical practice. Function and outcomes after kidney and liver transplantation using aNRP are at least equivalent to non-aNRP DCD donors. A few studies demonstrated increased survival and lower complication rates. However, it should be noted that the available studies are characterized by considerable bias and heterogeneity as the current definitions and protocols regarding aNRP differ widely between centres and countries, e.g. the possibility of pre-mortem intervention, definition of functional warm ischaemia time and use of continuous versus end-ischaemic ex-situ machine perfusion.
Conclusions: aNRP appears to be an asset to clinical practice but more uniform reporting of definitions and outcome measures is needed for aNRP to refine conclusions on transplant outcomes and organ utilisation. A randomized controlled trial comparing aNRP with standard donation technique in DCD donors seems mandatory to show added value and cost effectiveness of the procedure and determine aNRP's place amongst modern preservation techniques.

Reparative effect of mesenchymal stromal cells on endothelial cells after ischemic and inflammatory injury

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Background: Renal endothelium is damaged by ischemia reperfusion injury during transplantation as a result ischemia-reperfusion injury. It has been shown that mesenchymal stromal cells (MSC) are able to repair injured renal tissue. However, the mechanisms behind these MSC effects are still poorly understood.
Therefore, our objective was to evaluate the role of MSC in repairing injured endothelium and to determine the specific interactions involved in this process. The role of physical interaction and cytokine secretion in the reparative action of MSC was studied as well as its molecular mechanisms.
Methods: Human umbilical vein endothelial cells (HUVEC) were submitted to hypoxic and inflammatory insult with TNF-a during culture. HUVEC became activated, which was proven by an increased expression of activation molecules such as CD54, CD62e and HLA-II. Consequently, an increase of 20% in the adherence of MSC to HUVEC was observed. Moreover, an increase of 20% on MSC migratory capacity towards injured HUVEC was observed, the same increase which was observed in their ability to transmigrate through HUVEC monolayers.
Results: MSC were added to culture either prior or after injuring the endothelial cells. Once MSC were in contact with HUVEC, the oxidative stress of HUVEC decreased as observed by a decrease in reactive oxygen species, their proliferative status improved and MSC restored the endothelial monolayer stability to levels close to those from healthy HUVEC.
To determine whether physical interaction or soluble factors released by MSC are fundamental for MSC regenerative capacity we performed experiments in a Boyden chamber system and we observed that both were required to achieve the full reparative effect of MSC. Moreover, we observed an increase in the expression of CD44 and CD29 adhesion molecules on MSC membrane as well as their ligands CD62e and CD106 on HUVEC membrane.
Conclusions: We conclude that MSC are able to prevent and repair the injury caused by both ischemic and inflammatory injury on HUVEC via a mechanism that requires both physical and paracrine interaction between MSC and HUVEC. We are currently studying possible effector proteins for cell-to-cell interaction of MSC and HUVEC as specific molecules involved in this reparative effect which will allow us to target them to further improve the regenerative effects of MSC therapy on injured endothelial cells.

Influence of pregnancy on eGFR slope 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 higher risk of gestational hypertension, preeclampsia and dysmaturity compared with the general population. Less is known about the effect of pregnancy on kidney transplant function. For counselling prior to pregnancy, it is important to know the effect of pregnancy on eGFR slope.
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, kidney function and pregnancy were collected from health records. Changes in eGFR slope before and after pregnancy were analysed using individual pre-conception eGFR and post pregnancy eGFR values in a multilevel analysis performed by GEE.
Results: For this eGFR slope analysis we could include 197 women, with 3228 eGFR measurements. 109 (55%) with one 78 (40%) with 2 and 10 (5%) with 3 pregnancies after KT. Mean preconceptional eGFR was 62 ml/min (±21) at the first, 55 ml/min (±26) at the second and 51 ml/min (±25) at the third pregnancy. Overall the eGFR slope between pregnancies was not significantly different than the slope before the first pregnancy (p = 0.31). Subanalysis of women who only had one pregnancy did show a significant decline in eGFR slope after pregnancy (p = 0.01) Preconceptional eGFR (p = 0.00) and birthweight (p = 0.01) are the first identified predictors for a faster decline in eGFR after first pregnancy.
Conclusions: In the overall analysis eGFR slope is not affected by pregnancy in KT women. Women with only one pregnancy showed a faster decline of eGFR after pregnancy. Worse fetal outcome expressed in birthweight and worse preconceptional eGFR are riskfactors for a faster decline of eGFR after pregnancy.

National implementation of the Kidney Team at Home educational intervention

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Background: Research has shown that home-based education for patients with end-stage renal disease results in better knowledge and communication skills on renal replacement options, and more living donor kidney transplantations compared to care-as-usual. However, these studies were conducted in one region in the Netherlands. The aims of this study were (1) to assess whether the effects can be replicated when the intervention is implemented nationally (thus demonstrating generalizability), and (2) to evaluate the implementation process.
Methods: In the period 2016-2018, 4 university hospitals and 4 regional hospitals in 4 regions of the Netherlands participated in the implementation project. Both pre-dialysis and dialysis patients and their social network were offered the intervention. The education was delivered by trained social workers, psychologists and nurses. Effect outcomes of the intervention were patients' and invitees' knowledge on renal replacement therapy, communication skills between the patients and the invitees of the intervention, and the choice of treatment of patients after the intervention. Feasibility (participation rate), fidelity (protocol adherence), and implementation costs (intervention costs) were assessed as part of the process evaluation.
Results: 812 patients with end-stage renal disease were approached for the intervention and 334 interventions were conducted. There was a significant increase in knowledge and communication skills among both patients and invitees. At the 2 year follow-up 59 participants had undergone a living donor kidney transplantation and another 53 patients were in a living donation trajectory. Participation rate per hospital varied between 32.9% and 100%. The average protocol adherence score was 4.69 out of 5. Intervention cost is estimated to lie between €2500 and €3000 per patient educated.
Conclusions: The results of the implementation project show that the intervention can be implemented nationwide in The Netherlands, while maintaining impact and quality. Variability among the hospitals in terms of feasibility and fidelity might be the result of regional differences, and the degree to which the intervention was embedded in the established nephrology care path. We recommend uptake of the Kidney Team at Home in standard-care and structural financing for this effective form of education.

The impact of cold ischaemia time on outcomes of living donor kidney transplantation: a systematic review and meta-analysis

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Background: Multiple studies have been carried out to investigate the effect of a longer cold ischaemia time (CIT) on the outcome of living donor kidney transplantation (LDKT). There is no unambiguous consensus as to whether it is safe to expose a living donor kidney to a longer CIT. Therefore, we performed a systematic review and meta-analysis to provide a comprehension of the available literature to date and to provide more evidence around the effects of different cold ischaemia times on delayed graft function, graft survival, patient survival and the incidence of rejection after LDKT.
Methods: Searches were performed in Embase, Medline Ovid, Cochrane CENTRAL, Web of Science and Google Scholar up to the 1st of March 2019. For this systematic review, all aspects of the Cochrane Handbook for Interventional Systematic Reviews were followed and it was written based on the PRISMA-statement. Articles comparing different CIT in LDKT describing delayed graft function, graft- and patient survival and acute rejection were considered for inclusion.
Results: Twelve-hundred articles were identified, of which two prospective cohort studies and five retrospective cohort studies were included, resulting in a total number of 164.179 patients. Meta-analyses using random effects models showed significantly lower incidence of delayed graft function (OR = 0.65, 95% CI, 0.45 to 0.75, P = 0.004), and significantly higher 1- and 5-year graft survival (respectively, OR = 0.79, 95% CI, 0.62 to 0.99, P = 0.04 and OR = 0.85, 95% CI, 0.76 to 0.96, P = 0.009), all three favouring a CIT of less than four hours. There was no difference in acute rejection and patient survival.
Conclusions: Based on our results, a shorter CIT (<4 hours) in LDKT is associated with significant lower incidence of delayed graft function and higher graft survival compared to a longer CIT (>4 hours). We recommend that the CIT in LDKT should be shorter than four hours and that further research is needed regarding potential consequences in living kidney sharing schemes (which usually have a longer CIT).

Reasons for disapproval of potential living kidney donors

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Background: During the last decades the number of living kidney donors (LKD) has increased considerably in our centre, partly due to the allowance of HLA mismatched LKD and because of more liberal selection criteria (older age, higher BMI and pre-existent hypertension). Previously we showed that the percentage of approval for donation decreased with increasing donor age. In the current study we investigated the role of gender and endogenous creatinine clearance (ECC) as cause for refusal.
Methods: After an initial informative visit potential LKD proceed with medical examinations. At both visits contraindications for donation can be found. The results of the screening are registered in our NOTR database. We retrospectively analysed the evaluation results in a cohort of LKD candidates who were registered between May 15th 1997 and May 24th 2019.
Reasons for refusal were categorized in four groups: 1) psychosocial reasons or the availability of another LKD candidate (e.g. with a better fitting blood type), 2) medical reasons (e.g. proteinuria, extreme overweight, hypertension, diabetes, kidney stones, malignancy), 3) surgical renal reasons (e.g. renal veins considered too short, renal cysts, multiple arteries or asymmetrical renal function) and 4) insufficient renal function (ECC considered to low).
Results: In this period 531 LKD candidates were not accepted for kidney donation, mean age was 55 years (range 20-80), 281 of them were women. Psychosocial reasons or another LKD candidate were the reason for refusal in 98 (19% of 531) (55 women, mean age 51 years). Medical reasons were the cause of refusal in 289 (54%) (142 women, mean age 55 years). Surgical renal reasons were the main cause of refusal in 102 (19%) (53 women, mean age 57 years). Insufficient renal function as only cause for refusal was registered in 42 (8%) (31 women, mean age 61 years). Mean ECC in this group was 76 ml/min (range 43-104). In the other three groups mean ECC was 116 to 119 ml/min (range 53-228).
Conclusions: In the medical and surgical group often several reasons for refusal were registered, e.g. multiple renal vessels with relatively low ECC or asymmetrical kidney function. Reasons for refusal were equally distributed between both sexes in the psychosocial, medical and surgical group. In the rather small group with insufficient renal function women were in the majority with a slightly higher age confirming the known lower ECC in women and gradual decline of kidney function with higher age.

Posttraumatic stress after lung transplantation

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Background: Little is known about the prevalence and correlates of Posttraumatic Stress Disorder (PTSD) after lung transplantation. We studied the prevalence, symptom occurrence and risk factors of PTSD in lung transplant recipients to plan future preventive measures.
Methods: A cross-sectional study among all lung transplant recipients transplanted between January 2014 and May 2018 (n = 105) at the University Medical Center Groningen was performed. Data regarding demographics were collected by self-report questionnaire and PTSD was scored by the Self-Rating Inventory for Posttraumatic Stress Disorder (SRIP). Clinical data were retrieved by medical record review.
Results: Of the 105 eligible recipients, 87 (82.9%) responded to the questionnaire. Clinical relevant symptoms of PTSD were found in 9.2% of the respondents. Of these 6.9% fulfilled the criteria of full PTSD and 2.3% met the criteria for partial PTSD. Symptoms regarding arousal such as hypervigilance, irritability and sleep disorders, were most frequently mentioned by recipients with PTSD. Younger age and longer time on mechanical ventilation significantly associated with the development of PTSD.
Conclusions: Almost 10% of lung transplant recipients developed PTSD. The identified risk factors allow transplant clinicians to identify recipients at risk for PTSD. Further research is needed to gain insight into additional risk factors as psychological co-morbidity, and which specific aspects of lung transplantation are experienced as traumatic.

Mate van arbeidsparticipatie na levertransplantatie en determinanten van invloed, een single centrum retrospectieve studie

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Achtergrond: Arbeidsparticipatie na een levertransplantatie heeft een positieve invloed op de lichamelijke- en geestelijke gezondheid van de patiënt. In een levertransplantatiecentrum is de mate van arbeidsparticipatie na transplantatie gemeten, alsook de factoren die van invloed zijn op het arbeids(re-)integratieproces.
Methode: Geïncludeerd zijn patiënten in de leeftijd van 18-65 jaar, getransplanteerd in het tijdvak 2006-2017, die poliklinische nazorg ontvangen in het transplantatiecentrum.
Een retrospectief cross-sectioneel onderzoek werd uitgevoerd met behulp van een vragenlijst. De data werden verzameld met een schriftelijke vragenlijst en klinische informatie uit het patiëntendossier. Uit de literatuur bekende determinanten voor werkhervatting (leeftijd, geslacht, opleidingsniveau, samenstelling huishouden, etiologie leverziekte, de ernst van de leverziekte, kwaliteit van leven (RAND-36) en werkend voor de transplantatie) werden vergeleken tussen werkende en niet-werkende patiënten. Determinanten zijn in een univariabele analyse en in een logistisch regressiemodel getoetst op significantie.
Resultaten: Het responspercentage was 48,9% (185/378). Van de respondenten was 50,8% na transplantatie aan het werk. Van de patiënten die niet werken na transplantatie geeft 21,1% aan arbeidsongeschikt te zijn en 9,2% heeft (bijna) de pensioengerechtigde leeftijd bereikt.
Significante determinanten van invloed op het hebben van werk na de transplantatie zijn: het hebben van werk vooraf ($p<0.001$), leeftijd ($p<0.001$), opleidingsniveau ($p<0.001$), etiologie leverziekte (p 0.002) en de fysieke gezondheid ($p<0.001$). In een multivariabel regressiemodel bleek het hebben van werk vooraf de enige voorspellende factor voor werk na de transplantatie te zijn.
Conclusie: In ons onderzoek vonden we dat de helft van de posttransplantatiepatiënten participeren in het arbeidsproces. Beinvloedbare determinanten verdienen meer aandacht in de praktijk. Interventies gericht op (behoud van) een betere fysieke gezondheid en behoud van werk is geadviseerd. Multidisciplinaire interventies voor transplantatiepatiënten zijn geadviseerd te richten op behoud van werk in de wachtlijstperiode pre-transplantatie en dienen door te lopen in het gehele transplantatietraject.

The association between pre-transplant SIPAT-score and transplant related outcomes in lung and liver transplant patients: a retrospective cohort study

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Background: Psychosocial assessment has become a standard part of the organ transplantation assessment process. The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT) is a tool to conduct a structured pre-transplant psychosocial assessment. So far, little is known about the relationship between the SIPAT-score and outcomes after transplantation. This study aimed to examine the association between pre-transplant SIPAT-score and clinical and psychosocial outcomes in Dutch lung and liver transplant recipients at one year after transplantation.
Methods: A retrospective cohort study was performed among adult lung (n=57) and liver (n=61) transplant patients who received an organ transplant in 2016 or 2017 within the University Medical Center Groningen. SIPAT-scores and clinical data were retrieved by medical record review. Psychosocial outcome data were retrieved from the TransplantLines Biobank & Cohort study database. Data were analyzed using Spearman's rho and Mann-Whitney U-test.
Results: The median SIPAT-score was 11 (range 1-70). The median SIPAT-scores differed significantly ($p = 0.002$) between the lung and liver transplant candidates, respectively 9 (1-42) and 15 (2-70). No significant correlations were found between the SIPAT-score and clinical data regarding duration of the post-transplant hospitalization ($p=.35$), survival ($p=.51$), graft survival ($p=.34$), rejection ($p=.45$), unplanned hospital readmissions ($p=.67$) and number of days re-hospitalized ($p=.28$). Transplant recipients who were rated as minimally acceptable to poor candidates (SIPAT-scores ≥ 21) showed a higher level of anxiety ($p=.02$) when compared to excellent to good candidates (SIPAT-score ≤ 20) at one year after transplantation. Regarding depression ($p=.21$), medication adherence ($p=.99$) and physical and mental quality of life ($p=.33$ and $p=.53$) no significant differences were found between these groups.
Conclusions: Except for level of anxiety, the SIPAT-score was not found to be of influence on clinical and psychosocial outcomes at one year post-transplant. Examination of the association of separate SIPAT domains and items with clinical and psychosocial outcomes is needed to gain more in-depth insights.

Plasma mitochondrial DNA levels and damage correlate with post-transplant renal allograft function

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Background: The definition of an organ's transplantability and prediction of early graft dysfunction is hindered by the lack of sensible biomarkers. Mitochondrial DNA (mtDNA) in plasma was identified as a propagator of tissue injury in trauma and sepsis, and as a marker predicting progression of acute kidney injury progression. Here we explore the potential of plasma mtDNA level and damage as a marker in organ evaluation in a cohort of living donor kidney transplantations, a post-hoc analysis of VAPOR1.
Methods: Plasma was obtained from 57 donor-recipients undergoing living kidney donation and transplantation at various timepoints. MtDNA levels were measured in donors preoperatively (pre-op) and in recipients pre-, intra- and post-operatively, with intraoperative samples taken from both the renal vein and systemic arterial circulation, using polymerase chain reaction for D-loop, ND1 and ND6. MtDNA damage was determined using ND/Dloop ratios, under the assumption that D-loop is less prone to DNA damage than ND1 and ND6. MtDNA levels and damage were associated with recipient's kidney function parameters and urinary kidney biomarkers KIM-1 and NAG.
Results: Pre-op mtDNA levels were higher in recipients than donors. Highest levels of mtDNA from the renal vein were highest directly upon reperfusion. Recipients showed increased mtDNA levels 9 days post-op compared to pre-op, those receiving a kidney from a related donor having higher mtDNA levels than those with unrelated donation. Recipient's mtDNA levels at 2 hours post-op correlated with creatinine at 6 and 24 months. MtDNA levels at 9 days correlated with KIM-1 at day 9, creatinine at 6 and 24 months and glomerular filtration rate at 6 months. Pre-op mtDNA damage was comparable between donors and recipients, while it increased in recipients 9 days post-op. Recipients with high mtDNA damage directly after reperfusion of the kidney, both from the renal vein and systemic circulation, had significantly higher levels of KIM-1 at 1 and 9 days, but lower creatinine at 6 and 24 months post-op compared to recipients with low mtDNA damage. Conversely, patients with the highest mtDNA damage at 9 days post-op showed lower KIM-1 and NAG.
Conclusions: Levels and damage of plasma mtDNA obtained early after kidney transplantation are associated with momentuous kidney damage markers and a long-term accelerated decline in renal function markers. Measurement of post-op mtDNA levels may aid to the identification of patients at risk for accelerated kidney dysfunction.

Low protein intake is associated with severe fatigue in stable outpatient renal transplant recipients

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Background: Severe fatigue is a frequent complaint in renal transplant recipients (RTR) that is often accompanied by functional impairment and poor quality of life. Low protein intake may lead to protein-energy malnutrition and thereby contribute to fatigue in RTR. We aimed to (1) compare the prevalence of severe fatigue between RTR and healthy controls, (2) investigate impact of severe fatigue on quality of life in RTR, and (3) investigate the association of protein intake with severe fatigue in RTR.
Methods: We included 601 stable RTR with a functioning graft >1 year and 237 kidney donors from the TransplantLines Study (NCT03272841). Fatigue was assessed using the Checklist Individual Strength (CIS) Questionnaire. A CIS-score >76 was considered to indicate fatigue. Quality of Life (QoL) was assessed with the RAND-36 Questionnaire. Patients were instructed to collect 24-hr urine according to a strict protocol and the Maroni formula was used to calculate protein intake from 24-hr urinary urea excretion. Chi-Square was used to test differences in prevalence of severe fatigue in RTR and donors. Linear regression analyses was used to test differences in QoL of RTR with and without severe fatigue. Logistic regression was used to analyze the association between protein intake and presence of severe fatigue.
Results: Thirty-three percent of RTR were severely fatigued compared to 6% of kidney donors (P<0.001). QoL was significantly lower in RTR with compared to RTR without severe fatigue (mean QoL-score 56 [45-71] *vs* 88 [80-92], P<0.001). Mean protein intake in RTR was 83 ± 22 grams per day; 1.0 ± 0.3 g per kg bodyweight/day. Protein intake was inversely associated with severe fatigue in RTR and remained inversely associated after adjustment for potential confounders including age, ssex, eGFR, BMI, hsCRP, anemia and TSAT (per 0.1 g protein/kg/bw: adjusted HR 0.88; 95%CI 0.80-0.96 and per 10g protein/d: adjusted HR 0.82; 95%CI 0.73-0.93).
Conclusions: Severe fatigue is highly prevalent in RTR and a determinant of poor quality of life. Low protein intake is associated with higher risk of severe fatigue in RTR, independent of potential confounders, including age, sex, eGFR, BMI, and anaemia

No clear influence of non-adherence on tacrolimus intra-patient variability in stable kidney transplant recipients

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Background: High intra-patient variability (IPV) in tacrolimus exposure has been associated with a higher risk of graft rejection and graft loss. Several factors may increase IPV of tacrolimus exposure. Recent literature states that medication non-adherence (MNA) has highest impact on IPV and is also the most modifiable risk factor. However, while the association between high IPV in tacrolimus exposure and reduced long-term graft results is established, the relation between tacrolimus IPV and MNA is not clearly established yet.
The objective of this study is to assess the correlation between tacrolimus IPV and MNA.
Methods: 64 Kidney(pancreas) transplant recipients from an ongoing single centre trial were enrolled in this study. MNA was assessed through daily electronic monitoring (EM) of tacrolimus intake, patient-reported questionnaire (Immunosuppressant Therapy Adherence Scale), physician rating by one nephrologist, tacrolimus time-in-therapeutic range (TTR venous trough concentrations (C_0); TTR dried blood spot (DBS) area-under-the-concentration-time-curve (AUC)) and a previously developed composite adherence score. Tacrolimus C_0-concentrations were collected from 5 sampling instances and DBS AUCs were collected from 3 sampling instances. IPV of dose-corrected C_0 and AUC was expressed with the coefficient of variation (CV= ((standard deviation/mean)*100). The correlation between tacrolimus IPV as a continuous variable and the separate MNA markers was assessed. Also, the separate MNA markers were compared in stratified tacrolimus IPV groups (cut-off 20%) based on previous literature.
Results: MNA rates were 7%, 31.1%, 28.1%, 40.6%, 61.7%, 68.9%, according to EM, self-report, physician rating, TTR C_0, TTR AUC and CAS, respectively. Mean tacrolimus IPV was 17.9% (Sd ±11.1%) and 20.2% (±12.6%), respectively for C_0-concentrations and AUCs. No correlation between continuous tacrolimus IPV and MNA was found (highest Pearson R^2 = 0.22 for tacrolimus AUC IPV versus TTR AUC). Patients with IPV <20% were significantly more adherent according to self-report (p=0.035) and TTR AUC (p=0.030).
Conclusions: A large variation in MNA prevalence was found after assessment with various diagnostic markers. No significant correlation between tacrolimus IPV and MNA was found. Only after stratification of tacrolimus IPV with a 20% cut-off, a significant difference in adherence was found with self-report and TTR AUC.

Walk & Talk, a program to stimulate an active lifestyle after kidney transplantation

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Background: In Amsterdam UMC, location VUmc, we focus on self-management of patients after kidney transplantation. We train patients in interpretation of lab results, blood pressure values and we discuss possible (lifestyle) interventions with them. Patients in this program experience irrefutable benefit of the training, possibly resulting in better therapy compliance. However, we frequently observe post-transplantation physical inactivity, weight gain and new-onset diabetes, compromising a healthy lifestyle. We also are aware of many patients seeking for peer-contact, to get advice or to share transplantation related experiences. We therefore designed the 'Walk & Talk program'.
Methods: The program: Every Sunday morning a group of (new) transplanted patients go out for a walk, accompanied by a trained patient guide (called: 'koploper') at a fixed location (for the current pilot: the 'Amsterdamse Bos'). 'Koplopers' are trained by members of the medical team. During the walk, patients are encouraged to share experiences and provide each other with 'tips and tricks'. Once a month, one of the members of the medical team (dietician, transplant coordinator or nephrologist) joins the walk to provide extra education and to stimulate an active lifestyle of the respective patients. The program is further supported by the 'Kidney Box', given to the patients shortly after transplantation. This box contains information about the program, healthy recipes, a bottle of water, sunscreen and a medication box. In parallel, a website and app are currently being developed to share practical information on the walks and the educational program. Since kidney transplantation patients are referred from several hospitals from across Noord-Holland, a second walking group will be initiated in Alkmaar at the beginning of 2020. We would like to share our experiences with other transplant clinics to accomplish a national Walk & Talk program, providing added value in post-transplant care.
Results: The Walk and Talk program started in september 2019 in Amsterdam UMC, location VUmc. Currently, we are finetuning the program in collaboration with enthousiastic transplant patients.
Conclusions: The first Walk & Talk program has started at the Amsterdam UMC, location VUmc, to support a healthy and more active lifestyle of patients after kidney transplantation. The program has the potential to be implemented around all Dutch transplant clinics, resulting in a national program with uniformity in training and support.

Impact of immunosuppressive drugs on endothelial barrier

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Background: Cardiovascular disease is still the major cause of death in renal transplant recipients. This group of patients has an extremely increased cardiovascular risk as compared to the general population with high prevalence of traditional and non-traditional risk factors. Both success and limitation of transplantation are primarily determined by the immunosuppressive medication. Apart from amplification of traditional risk factors, these drugs may also have a direct detrimental effect on endothelium. In this study we aim to investigate the effects of several immunosuppressive drugs on the endothelial barrier.
Methods: To analyze the effects of immunosuppressive drugs on the endothelial barrier function we used quantification of trans-endothelial electrical resistance using the Electrical Cell-substrate Impedance Sensing (ECIS) device. ECIS measurement was performed of human umbilical vein endothelial cells (HUVEC's) pre-incubated with several drugs with different concentrations (prednisolon, cyclosporin, tacrolimus and everolimus). Regeneration of integrity after artificial electrical wounding was also measured. A comparison was made with a control condition.
Results: With the ECIS measurements tacrolimus seems to induce a concentration dependent improved barrier function as compared to the control condition. After wounding the tests also suggest an improved regeneration. Everolimus, however, seems to induce endothelial barrier dysfunction with disturbed regeneration after wounding. Cyclosporin did not show any effects on endothelium. Prednisolon revealed conflicting data.
Conclusions: Our data suggests the possibility of opposite effects of tacrolimus and everolimus on endothelial barrier function, Data validation, however, is necessary.

High tacrolimus intra-patient variability is associated with elevated anti-donor reactivity after kidney transplantation

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Background: High numbers of donor-reactive, IFN-γ producing peripheral blood mononuclear cells (PBMCs) prior to transplantation have been associated with acute rejection. Additionally, a high tacrolimus (Tac) intra-patient variability (IPV) has previously been associated with higher rejection rates. Currently, knowledge about the effect of a high IPV on donor-reactive IFN-γ producing cells is unknown. In this present study, our aim is *i.* to validate whether donor-reactive, IFN-γ producing cells are associated with rejection and *ii.* to asses if their frequency is affected by Tac IPV after kidney transplantation.
Methods: PBMC samples from 78 kidney transplant patients were obtained at pre-transplantation, at 1 year and 5-7 years after transplantation. The frequency of IFN-γ producing PBMCs was determined by Elispot. Patient PBMCs were stimulated with irradiated donor or completely HLA mismatched third-party cells. Tac IPV was calculated between 6 to 12 months after transplantation of at least 3 pre-dose Tac concentrations corrected for the corresponding daily Tac dose.
Results: The number of donor-reactive, IFN-γ producing cells prior to transplantation was associated with rejection episodes after transplantation [median and interquartile range: no rejection 20/1x10^5 PBMC (7-48) vs rejection 42/1x10^5 PBMC (23-72), p=0.018], while third party reactivity was comparable between patients with and without rejections. Approximately 22% of patients had a high Tac IPV of 30% or more. Tac IPV was positively correlated with high numbers of donor-reactive IFN-γ producing cells 1 year after transplantation (r=0.30; p=0.02).
Conclusions: Patients with high variability in Tac pre-dose concentrations are at risk for high numbers of donor-reactive T cells at 1 year after transplantation. These patients should be carefully monitored to prevent rejection.

Nanoparticle release by Extended Criteria Donor kidneys during normothermic machine perfusion

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Background: Extended criteria donor (ECD) organs suffer from more injury due to more severe ischemia/reperfusion injuries and other donor morbidities compared to standard criteria donors. Therefore, new methods of organ preservation and assessment are needed. Machine perfusion (MP) has extensively been studied and allows for the *ex vivo* examination of kidneys through analysis of perfusion fluids. We postulate that analysis of kidney derived nanoparticles, including Extracellular Vesicles (EVs), in perfusion fluid during normothermic MP may allow for the assessment of kidney quality prior to transplantation.
Methods: ECD kidneys were perfused at 37 °C for 2h during which perfusate samples were taken at 30 min intervals. Samples were centrifuged at 16.000g for 10 min to discard cellular debris, diluted 10x in 0.22 µm filtered PBS and analysed by Nanoparticle Tracking Analysis (NTA) to determine nanoparticle size and concentration.
Results: Perfusates from three ECD kidneys (2 donors after cardiac death, 1 donor after brain death, comparable warm ischemia times of 15 minutes followed by 12 hours of cold ischemia, age 66/73/65, all male) were analysed. Although two size populations (120 & 170 nm) were observed in the perfusate after 2h of perfusion, the average particle size was found to remain unchanged (~155 ± 7.6 nm) during the entire perfusion procedure. An ~7.75-fold increase in cumulative nanoparticle concentration was observed over time: $9.03E^9$ particles/mL after 2h compared to $1.17E^9$ particles/mL after 0 min of perfusion. Particle excretion increased in a linear manner.
Conclusions: These results indicate that analysis of perfusion fluid by NTA may be utilized to assess renal quality prior to transplantation. The released nanoparticles are likely to contain kidney-derived EVs which may be indicative for renal quality. Nevertheless, whether this release of nanoparticles reflects kidney function requires further research.

Circulating cell-free nucleosomes as marker of graft integrity in kidney transplantation patients

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Introduction: There is an unmet need for non-invasive markers, specific for graft rejection and early identify graft injury, which eventually could overcome the need for a transplant biopsy. Here, we evaluated the potential of circulating cell free nucleosomes (ccfn) to serve as a marker for graft injury and rejection in serum samples from kidney transplantation recipients.
Material and methods: Forty kidney transplant recipients after de novo kidney transplantation were evaluated for ccfn. Per patient 4 fixed time points were studied: before transplantation, day 3-6, 1 month and 6 months after transplantation. In addition, serum collected at times of allograft rejection (n=13) were also analysed. The global amount of ccfn was measured with a Nu.Q™ Total Assay kit (VolitionRx), an ELISA-based assay with antibodies directed against nucleosomes.
Results: At 3-6 days after transplantation the concentration of ccfn was significantly higher than the values measured before transplantation [median and interquartile range: 4.9 ug/mL (4.4-5.3) vs. 4.2 ug/mL (3.1-4.7), $p<0.01$, respectively]. During rejection the values of ccfn were significantly higher than in patients without rejection (non-rejectors) at month 6 [4.6 ug/mL (3.7-5.4) vs. 3.7 ug/mL (2.2-4.2), $p<0.01$, respectively]. In patients without any clinical problems, the values did not change significantly between pre transplant, month 1 and month 6 after transplantation.
Conclusion: For the first time, we demonstrate that ccfn are significantly increased in the first period after transplantation and at times of rejection. This likely reflects tissue injury resulting from ischemia-reperfusion injury during transplantation and from alloreactivity. Ccfn could serve as non-invasive markers for the detection of graft injury and rejection, nevertheless the release of ccfn in other pathological conditions needs to be elucidated.

Phenotyping circulating endothelial cells as a marker for transplant kidney damage

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Background: The diagnosis of transplant rejection is mostly based on late and insensitive markers that do not reliably discriminate from other causes of kidney transplant injury. Early, specific and minimally-invasive biomarkers may improve rejection diagnosis. Endothelial cell (EC) layer damage is one of the reasons for functional deterioration or rejecting kidney transplants. Bioassays quantifying circulating EC numbers and its characteristics as a read-out parameter is an attractive method to monitor kidney transplant integrity.
Methods: We examined the association between the count and phenotypic characteristics of circulating EC from peripheral blood or kidney transplant recipients and clinical outcome, including allograft function (eGFR using creatinine). A cohort of 52 kidney recipients transplanted in 2019 was studied. Circulating EC were measured 1 day before transplantation and 3 and 7 days after transplantation. In addition, blood was sampled and analyzed whenever acute rejection was suspected during the first three months after transplantation. Flow cytometry assessed the number of circulating EC by staining for CD31, CD34, CD45, CD105, CD133, and CD146. This panel also included, the kidney injury molecule (KIM-1). Data analysis was performed using a non-linear generalization or principal component analysis (PCA), unsupervised clustering, and t-SNE visualization for unbiased selection of circulating EC.
Results: Paired analysis revealed that the number of circulating EC increased 2.6 [0.5-5] fold at the third day after transplantation, recovering to preoperative levels at day 7 post-transplant. Interestingly, patients who had a biopsy proven acute rejection and recorded a higher amount of circulating EC in comparison to the previous measured time-point, showed a significant (2-fold) increase in the MFI for the damage marker KIM-1 ($p < 0.05$).
Conclusions: Our results demonstrate a subset of kidney transplant recipients show an increase in circulating EC and KIM-1 expression at the time of rejection. The relevance of these findings will be examined in further studies.

Peripheral blood analysis by flow cytometry and gene expression profiling in long-term renal transplant recipients with squamous cell carcinoma

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Background: The development of squamous cell carcinoma (SCC) is a major problem in renal transplant recipients (RTRs). In these patients, the increased risk of malignancy is associated with the use of immunosuppressive agents, an increased frequency of regulatory T cells (Tregs), and cellular exhaustion. This study aimed to identify a signature in the peripheral blood that is associated with SCC development after transplantation and which could contribute to the risk assessment of SCC in RTRs.
Methods: We used flow cytometry and multiplex gene expression profiling to analyse the peripheral blood mononuclear cells of 30 matched long-term RTRs with or without SCC incidence within a follow up period of five years. Different populations of Tregs and exhausted CD8+ and CD4+ T cells were identified and correlated with SCC development.
Results: The frequency of CD70-expressing Tregs was higher in RTRs with SCC development compared with patients who did not develop SCC. There was no difference in the frequency of total Tregs between these groups. Additionally, there was no difference in the expression of the exhaustion markers PD-1, TIGIT, LAG3 and TIM-3 by CD8+ or CD4+ T cells between RTRs with and without SCC development.
Conclusions: In this study we demonstrated that the frequency of CD70-expressing Tregs in RTRs that developed SCC within the follow-up period of five years is increased compared with patients without SCC development. The potential of CD70 as a clinical marker for the identification of patients with a high risk of SCC warrants further investigation.

Donor blood composition is a risk factor for biliary injury in donation after circulatory death liver transplantation

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Background: Post-transplant cholangiopathy following ischemia-reperfusion injury severely inhibits widespread application of donation after circulatory death liver transplantation (DCD-LT). Platelets and red blood cells are known to influence ischemia-reperfusion injury. We hypothesized that the platelet count and hematocrit of the DCD donor would influence biliary injury during DCD-LT. To study all cellular blood components, we also analyzed the influence of the donor leukocyte count on biliary injury.
Methods: First, the influence of platelet and leukocyte counts and hematocrit on bile duct histology prior to and bile composition during (pre)clinical normothermic machine perfusion (NMP) was assessed. Secondly, in a nationwide retrospective study, all adult DCD-LT between 2010-2017 were included to assess the influence of platelet and leukocyte counts and hematocrit on the development of non-anastomotic biliary strictures (NAS). Multivariate Cox Proportional-Hazards regression analyses were used to assess the influence of platelet and leukocyte counts and hematocrit on NAS.
Results: Analysis of bile duct biopsies of 40 NMP procedures revealed a significant impact of donor platelets (OR 2.553, 95% CI 1.082-6.021, p = 0.029) and leukocytes (0.734 95% CI 0.581-0.927, p = 0.009) on bile duct injury. Donor platelets also influenced biliary bicarbonate and pH levels during NMP. In the retrospective study, a total of 235 DCD-LT were included. In a multivariate Cox regression analysis, donor platelets (HR 1.047 95% CI 1.007-1.089, p = 0.022) and hematocrit (HR 1.044 95% CI 1.005-1.083, p = 0.025) were identified as significant independent risk factors for the development of NAS after DCD-LT.
Conclusions: Donor platelets and leukocytes significantly influence histological bile duct injury. Platelets influenced bicarbonate secretion and bile pH during NMP. Additionally, platelet count and hematocrit are significant independent risk factors for the development of NAS after DCD-LT.

Model-based estimation of iohexol plasma clearance for renal function evaluation in the renal transplant setting

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Background: In certain clinical situations, creatinine clearance (CrCl)-based glomerular filtration rate (GFR) estimation lacks accuracy for renal function evaluation. Measured GFR by determination of the plasma clearance of the exogenous marker iohexol may then provide an alternative. The need for 5-10 samples up to 8h postdose has however hampered its widespread use in routine clinical care. We developed a population pharmacokinetic (PK) and limited sampling model (LSM) to enable pragmatic iohexol-based GFR estimation in the renal transplant setting.

Methods: Blood samples (n = 328) drawn at 5 min to 4 h after iohexol administration were available from 30 renal transplant donors and 19 recipients. A population pharmacometric model was constructed to describe iohexol PK. Model evaluation was performed using diagnostic plots, visual predictive checks and bootstrap analysis. The final model was applied to develop LSMs based on 1-4 samples drawn within 3h postdose to find a sampling scheme which ensured accurate GFR estimation and clinical feasibility. GFR estimations of each LSM (GFR_{lsm}) were compared to those of the full model (GFR_{full}) to evaluate LSM predictive performance. Predictive performance was assessed using the Pearson R^2, mean percentage prediction error (MPPE), root mean squared prediction error (RMSE) and the percentage of GFR_{lsm} within ±5% of the GFR_{full} (5%-discordance).

Results: Iohexol PK were best described by a 2-compartmental first order elimination model. Clearance (CL), intercompartmental clearance (Q) and distribution volumes of the central (Vc) and peripheral (Vp) compartments were 4.89 L/h (6% residual standard error; RSE), 7.26 L/h (25% RSE), 9.20 L (6% RSE) and 5.48 L (14% RSE). Interpatient variability of CL, Q, Vc and Vp was 34.4% (14% RSE), 86.2% (18% RSE), 35.2% (12% RSE) and 41.7% (44% RSE). Internal model evaluation indicated good performance. LSMs using three or more samples including an early and a late sample yielded the most accurate GFR estimations. The LSM with sampling at 5min, 1h, 2h and 3h showed the optimal combination of predictive performance (R^2: 0.997; MPPE: 0.36%; RMSE: 0.39%; 5%-discordance: 95.92%) and clinical feasibility.

Conclusions: Our population PK model and LSM provide a promising approach to enable pragmatic iohexol plasma clearance-based GFR estimation in the renal transplant setting. External validation of the model is however warranted before implementing this technique in routine clinical care.

HLA selected allogeneic mesenchymal stromal cell therapy in renal transplantation: the Neptune study, a phase I open-label single-center study

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Background: In renal transplantation, new strategies are needed to minimize the side effects of immunosuppressive drugs and to ensure long-term graft survival. Mesenchymal stromal cells (MSC) are an interesting candidate because of their anti-inflammatory, immune-regulatory and reparative properties and may therefore allow tapering of standard immunosuppression. So far, most clinical studies in renal transplantation have used autologous MSCs but to meet the need for acute treatment options, allogeneic MSCs are more suitable. However, allogeneic MSCs hold the risk to elicit an anti-donor immune response which might induce graft dysfunction, or sensitize patients for future transplants.
Methods: In this clinical phase I study 10 patients were included who received two doses of $1.5x10^6$ allogeneic MSCs infused 6 months after renal transplantation. At this point maintenance immunosuppression consisted of low dose calcineurin inhibitor (CNI) (trough levels of 1.5-3 ng/ml), everolimus and prednisone. In order to minimize the risk of an anti-donor immune response we selected allogeneic MSCs without repeated HLA mismatches with the allograft. The primary endpoint was safety, as measured by biopsy proven acute rejection (BPAR) and graft loss 12 months after transplantation. In addition, immune monitoring was performed before and after MSC infusion, including measurements of anti-HLA antibodies (DSA).
Results: No BPAR occurred and patient and graft survival was 100%. Mean tacrolimus trough level after MSCs was 3.04 ng/ml. Of importance, no de novo DSAs were formed against the MSCs or against the kidney graft. There were no major differences in T- and B-cell populations before and after infusion. Plasma cytokine analysis showed no significant changes directly after MSC infusion. CMV and BK viremia were comparable to numbers described in literature and no opportunistic infections occurred.
Conclusions: We demonstrate that selected allogeneic MSCs in combination with low dose CNI, 6 months after transplantation are safe. No dnDSA were formed and clinically there were no signs of rejection, graft loss and no decline in renal function. Immune monitoring in this study did not show specific T- and B-cell responses and no significant changes in cytokines, which demonstrates safety as no major immunological responses occurred. These results underline the potential immune modulatory effects of MSCs. Long term results of immune monitoring and clinical endpoints will be necessary to ensure safety in the long term.

Population pharmacokinetics of meltdose tacrolimus (Envarsus®) in stable adult liver transplant recipients

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Background: Meltdose tacrolimus (Envarsus®) is a new tacrolimus formulation marketed as a tacrolimus formulation with a more consistent exposure. Due to the narrow therapeutic window of tacrolimus, therapeutic drug monitoring is essential to achieve adequate exposure. The area under the concentration-time-curve over 24 hours (AUC) is the best link between concentration and effect. The aim of this study was to develop a population pharmacokinetic (PK) model of Envarsus® in adult liver transplant and construct a limited sampling strategy (LSS) in order to predict the AUC.
Methods: Stable adult liver transplant patients were converted from prolonged release tacrolimus (Advagraf®) to Envarsus® and AUC measurement (8 time points) was performed 2 weeks after conversion. Nonlinear-mixed-effects-modelling (NONMEM) and R statistics were used for the analyses.
Results: 55 patients were converted to Envarsus® with a median dose of 2mg once daily (range:0.75-6mg) of which 53 (total 748 concentrations) could be included for PK analysis. 35% was female and the median age was 57 years (range 21-70), median body weight was 81 kg (range 54-135).
Envarsus® absorption varied widely between and within patients in terms of Cmax and Tmax. The PK was best described by a two compartmental model based on. Absorption was best described by 1,6 transit compartments with mean transit time of 3,4h. The PK parameters along with their % interindividual variability (IIV) were as follows: clearance (CL): 3,27 L/h (34%); intercompartmental clearance (Q): 9,6 L/h, volume of distribution of compartment 1: 95 L (141%); volume of distribution of compartment 2: 500 L.
Two LSS of 4 time points (t=0,4,8,12 & 0,1,3,6) resulted in adequate AUC prediction with a median(range) bias of 1,5% (-9,2 – 12,5) and 0% (-7,6 - 13,4). The best 3-point LSS was t=0,4,8 with a median bias of 1,8% (-12,5 – 12,5). A correlation coefficient (Pearson, r^2) of 0,89 between trough concentrations and AUC was found.
Conclusions: The PK of Envarsus® in stable adult liver transplant patients was adequately described by a 2-compartmental model with transit compartments for absorption. The PK model was used to develop a 3-point LSS in order to predict the AUC with maximal 12,5% bias. A 4-point LSS (t=0,4,8,12 or 0,1,3,6), led to even lower bias. This LSS can be used in routine clinical care to adequately predict AUC in a patient-friendly way with reduced health-care costs.

Real-time visualization of cortical renal perfusion using laser speckle contrast imaging

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Background: Determining cortical renal perfusion might give surgeons insight in organ quality during transplantation. However, currently, there is no objective technique to measure renal cortical perfusion. Laser speckle contrast imaging (LSCI) is a fast, full-field, cheap and relatively simple imaging method that can give 2D-perfusion maps of large surfaces. In this study we developed a setup that is capable of visualizing the cortical renal perfusion in real-time with high spatial and temporal resolution on isolated perfused porcine kidneys.
Methods: Slaughterhouse retrieved porcine kidneys were obtained from a local abattoir. The experiments were conducted while the kidneys were on normothermic machine perfusion. The use of LSCI as a perfusion measuring tool was evaluated using flow altering experiments. The change in flow were caused by an increase in temperature, altering pump output, local ischemia as a result of a balloon catheter and by subsequently infusing 4 ml of 100% O_2, air and 100% N_2.
Results: A good agreement is found between the blood flow and LSCI with a change in temperature and pump output. Local ischemia appears directly after use of the balloon catheter with LSCI as can be seen in figure 1. The infusion of all gasses show a decrease in cortical renal perfusion of which the length seems to be determined by the N_2 content. When perfusion restores, LSCI can pick up on local individual high activity active units that initially show up as high perfusion areas (figure 2). The reduced cortical flow areas were not visible at any moment by human inspection which emphasizes the power of LSCI.
Conclusions: LSCI can identify the slightest of changes in cortical renal perfusion with extremely high temporal and spatial resolution in real-time, ahead of human inspection. More research is required to link cortical renal perfusion to organ viability.

Enhancing ex vivo perfusion of the liver by restoring positive pressure in the inferior caval vein

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Background: In the field of liver transplantation, organ shortage pushes physicians to use more marginal organs. Machine perfusion provides the opportunity to test or even improve the quality of these grafts. For ex-vivo organ therapy, e.g. with stem cells or drug components, the perfusion time needs to be extended. However, ill-perfused macroscopic spots appear in the liver parenchyma during long-term perfusion. Ex vivo perfusion controls the pressure in the portal vein and hepatic artery, however, the pressure in the inferior caval vein is not monitored or controlled. Therefore, we aim to investigate if inducing positive pressure in the inferior caval vein (IVC) – like positive end-expiratory pressure in the lung -can enhance ex vivo perfusion.
Methods: Normothermic machine perfusion (NMP), with an erythrocyte based perfusate, was performed in 2 human livers and 5 pig livers. The pressure in the hepatic artery and portal vein was set on 70 and 11 mmHg. The IVC was cannulated and the pressure was monitored. The pressure in the IVC was adjusted by clamping the IVC cannula. Flow was monitored within an IVC pressure range of 0-10 mmHg. Furthermore, we monitored the blood flow in the liver parenchyma with laser speckle technique in 3 conditions: no pressure intervention, pressure increase to 2 mmHg and 5 mmHg in the IVC.
Results: Without any intervention, the pressure in the IVC was between -6 and 0 mmHg. After inducing the pressure in the IVC, the flow in the portal vein remained stable until a pressure of 6 mmHg, above 6 mmHg the portal flow decreased. The flow in the hepatic artery was not altered by the pressure in the IVC.
Laser speckle imaging at the start of the perfusion showed a heterogeneously perfused liver, with almost no detectable blood flow in several places of the liver while there was increased flow in other spots in the liver. After increasing the IVC pressure to 2 mmHg, the parenchyma parts of the livers became 50 % (40 - 70%) more perfused, and after adjusting the pressure to 5 mmHg the flow was increased by 34 % (8 – 58%) in the parenchyma, compared to no pressure intervention.
Conclusions: In conclusion, adjusting the IVC pressure to a positive pressure of 2 mmHg induces optimal perfusion of the liver parenchyma and this strategy may be incorporated in ex-vivo organ perfusion.

Prognostic factors for graft function in peadiatric kidney transplant

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Background: Graft survival in paediatric kidney transplant recipients has increased in the last decades. Determining prognostic factors for graft function over time allows the identification of patients that are at risk for graft loss and the improvement of current care guidelines.
Methods: Data were collected among paediatric kidney transplant recipients in a single centre during the first five years of follow-up. Mixed model analysis was used to indicate possible prognostic factors for the loss of graft function.
Results: A total of 100 paediatric kidney transplant recipients were analysed. Prognostics factors that were found to negatively influence graft function are a higher donor age and higher recipient age, an urological cause for end-stage renal disease (ESRD), re-transplant and occurrence of BK virus (BKV) infection. Patients with a steroid-sparing regimen had better graft function over time than those who used steroids. The influence of both donor age and having an urological cause of ESRD became stronger with time. In this study, the prognostic factors that do not influence graft function over time are the number of HLA-DR mismatches, pre-transplant dialysis, intra-abdominal graft placement, ischemia time, presence of lower urinary tract dysfunction, occurrence of urinary tract infections and infections with cytomegalovirus and Epstein-Barr virus.
Conclusions: This study revealed a higher donor age and higher recipient age, an urological cause for ESRD, a re-transplant and the occurrence of BKV infection to be negative prognostic factors for graft function over time in the first five years after transplant. Steroid sparing regimens appeared to be safe.

Medication-related problems in liver transplant patients in the Netherlands: the role of the clinical pharmacist in the outpatient setting

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Background: After livertransplantation (LTx), adherence to immunosuppressive medication and avoidance of contra-indicated drugs is essential for long-term survival. Therefore, signalling and treatment of medication-related problems (MRPs) in LTx recipients opens opportunities to improve medication safety. This study aimed to investigate the prevalence and types of MRPs and interventions initiated by a clinical pharmacist (CP) in a cohort of stable LTx recipients in the outpatient setting.
Methods: This study was a prospective, observational study conducted between September–December 2018 in LTx recipients that visited the outpatient clinic for an annual extensive check-up. A 20-minutes face-to-face consultation with a CP was part of this check-up and consisted of medication reconciliation and a structured conversation about medication, adherence, adverse drug reactions (ADRs) and drug use. Potential interventions were discussed with the patient and hepatologist and initiated by the CP. The MRPs and interventions were registered by the CP and categorized into predefined categories. Analysis was performed using descriptive statistics.
Results: The CP consulted 64 LTx recipients with a median age of 59.5 years (IQR: 47-66) and a median of seven medications. Frequent comorbidities were chronic kidney disease (n=26), cardiovascular disease (n=26), and diabetes mellitus (n=19). In 57.8% of the patients, one or more discrepancies were found in the medication registered in the hospital and actually used by the patient. Most discrepancies (60.4%) were missing medications.
In total, 98 MRPs were identified in 53 patients, with a median of 2 MRPs per patient. Most frequent MRPs were: ADRs (22.4%), nonadherence (19.3%), unnecessary drugs (16.3%) and untreated indications (12.2%). Interventions most frequently proposed were: optimizations in dosage regimen (21.2%), medication compliance advises (16.8%) and stopping of medication (12.4%). Most interventions proposed by the CP (93.6%) were followed by both patients and hepatologists.
Conclusions: In this cohort, LTx recipients experience a median of 2 MRPs of which ADRs, nonadherence and unnecessary drugs are most frequently reported. An outpatient monitoring program of a CP for LTx recipients can signal MRPs and lead to interventions that are accepted by both patients as hepatologists and hence contribute to medication safety in LTx recipients.

Therapeutic window for ribavirin therapy in transplant recipients with chronic hepatitis E virus infection

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Background: The optimal dose, target concentration and duration of ribavirin (RBV) therapy in solid organ transplant (SOT) and hematopoietic stem cell transplant (HSCT) recipients with chronic hepatitis E virus (HEV) infection are unknown. The aim of this study was to investigate the association between RBV plasma concentrations and virologic response and anemia. Next, to define the therapeutic window for ribavirin in SOT and HSCT recipients with a chronic HEV infection.

Methods: In this retrospective, multicenter, cohort study, data of adult SOT and HSCT recipients with chronic HEV infection, who had been treated with RBV monotherapy between 2008 and 2018 were included. Data were collected in four European university hospitals. Receiver operating characteristic curve analyses were performed and the half-maximal effective concentration was calculated to determine a representative therapeutic window. Factors associated with a sustained virologic response (SVR) were investigated using multiple binary logistic regression analysis. A SVR was defined as an undetectable level of HEV RNA in serum at least 6 months after completion of ribavirin therapy. A clinically relevant response to ribavirin was defined as a decrease of the HEV RNA load after the initiation of ribavirin therapy with at least a factor 2. No response was defined as a rise in the HEV load.

Results: A total of 96 patients with 300 RBV plasma determinations (ribavirin concentration range 0.10–7.40 mg/L) were included. RBV monotherapy for a median of three months resulted in a SVR in 62.5% of the patients and 88.5% of the patients developed anemia. RBV plasma concentrations at steady-state were significantly higher in the response group compared to the non-response group: median 1.96 (IQR 1.81–2.70) versus 0.49 (IQR 0.45–0.73) mg/L, p=0.0004. RBV caused dose-dependent hemoglobin reduction with higher RBV plasma concentrations resulting in more hemoglobin reduction.

Conclusions: RBV monotherapy resulted in a SVR in 62.5% of the patients. RBV plasma concentrations at steady-state were significantly higher in the group with a virologic decline. The therapeutic window for RBV for treating a chronic HEV infection in SOT and HSCT recipients ranges between 1.8 and 3.0 mg/L.

Resting energy expenditure in cystic fibrosis patients decreases after lung transplantation, which improves validity of prediction equations for energy requirement

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Background: Resting energy expenditure (REE) is used to tailor dietary counselling in cystic fibrosis (CF) patients before and after lung transplantation (LTx). Cross-sectional studies suggest REE decreases after LTx. Follow-up data in patients are lacking. Therefore, we assessed REE in CF patients before and after LTx, and compared measured REE to predicted REE using Harris-Benedict (1919, 1984), Schofield and FAO/WHO/UNU prediction equations.
Methods: REE was measured in 14 CF patients (mean age 32, range 15 - 49 years) in fasted state using indirect calorimetry; once before and 4 times after LTx, with a 2-year follow-up. REE was expressed as kcal/day and kcal/kg fat-free mass (FFM)/day. Linear mixed models were used to analyze time differences.
Results: Before LTx, mean measured REE was 1787 kcal/day or 40 kcal/kg FFM, which was 122 – 124% of predicted REE, depending on the prediction equation. Twelve months after LTx, this had significantly decreased to 1620 kcal/day (P<.001) or 33 kcal/kg FFM (P<.001), which was 107 – 108% predicted (all P≤.001). A year after LTx, values stabilized and prediction was accurate (i.e. within 10% of measured REE) in about two thirds of patients. Body mass index (BMI), fat-free mass index (FFMI) and pulmonary function improved significantly after LTx (all below P=.012).
Conclusions: This longitudinal study indicates that measured REE in CF patients decreases by almost 10% after LTx. Prediction equations consistently underestimate energy needs, even after LTx. If measuring REE is no option, it seems prudent to expect energy demands to be at least 20% higher than predicted.

Survival prediction models in liver transplantation - comparisons between Cox models and machine learning techniques

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Background: Predicting survival of patients after liver transplantation is regarded as one of the most challenging areas in modern medicine. Hence, selecting the best prediction model is of great importance. Nowadays, there is a strong discussion in the medical field about machine learning (ML) and whether it has greater potential than Cox models when it comes to complex data. Criticism to ML is related to unsuitable performance measures and lack of interpretability which is important for the medical personnel to take decisions. Here, the potential of ML is investigated for large data of 62294 patients in USA with 97 prognostic factors (52 donor, 45 recipient characteristics) selected from over 600. It is also of particular interest the identification of potential risk factors for liver transplantation.
Methods: A comparison is performed between 3 different Cox models (Cox with all variables, Cox backward and Cox LASSO) and 3 machine learning techniques: a random survival forest (RSF) and 2 partial logistic artificial neural networks (PLANNs). Emphasis is given on the advantages and pitfalls of each method and on extracting interpretation from the ML techniques. The clinical endpoint is overall graft-survival (defined as the time between transplantation and the date of graft-failure or death).
Results: The most prognostic variables are re-transplantation (1st for the Cox models and the PLANN 1) and donor age (1st for RSF and PLANN 2). Other prognostic variables for all models are life support, HCV serology status, donor type, diabetes, race, and pre-treatment status. RSF shows slightly better predictive performance than the Cox models. In addition, neural networks show in general a good performance. However, instability is present due to the lack of a global measure for performance evaluation in survival setting.
Conclusions: It is shown that machine learning techniques can be a useful tool for both prediction and interpretation. Cox models have a straightforward interpretation but make the proportional hazards assumption. Machine learning techniques are very flexible since they do not make any assumptions about the underlying data. Nevertheless, they have limitations with respect to variable interpretation.

Minor negative effects of calcineurin inhibitor based immunosuppression on pregnancy outcomes after renal transplantation in the Netherlands

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Background: Pregnancies after renal transplantation have been more frequent over the past years, also in patients with a compromised renal function. Immunosuppression may influence pregnancy outcome. It is not yet clear whether replacing a calcineurin inhibitor (CNI) by azathioprine favourably influences pregnancy outcomes of mother or child. We therefore compared maternal and fetal outcomes of pregnancies after renal trans-plant using CNI-based or CNI-free immunosuppression.
Methods: We retrospectively analyzed pregnancy outcomes in women with a renal transplant in the Netherlands between 1986 and 2017 by checking their medical records. Patients were divided in two groups based on the use of a CNI during the first trimester of pregnancy. For statistical analyses we used one-sample T, Mann-Whitney-U and Chi-square tests.
Results: We identified 254 pregnancies in 177 renal transplant recipients: 129 with CNI during pregnancy (CNI+) and 125 without CNI (CNI-). Demographic statistics did not differ between the two groups except for higher BMI in CNI+ (25.3 vs 23.7, P=0.01) and year of renal transplant (median 2000 for CNI+ vs 1989 for CNI-, P<0.01). Preconceptionally, in the 1st and 2nd trimester of pregnancy creatinin levels were slightly, but not significantly higher in CNI+. In the 3rd trimester creatinin levels were significantly higher in CNI+ (127 vs 105, P<0.01). The percentual increase in creatinin from preconceptional to the 3rd trimester level was also higher in CNI+ (+3.1% vs -2.2%, P=0,05). In both CNI+ and CNI- groups, a postpartum 11-12% increase of creatinin from preconceptional level was observed, which was comparable in CNI+ and CNI- groups (p=0,92). Regarding fetal outcomes, in CNI+ more children were born with birth weight less then 2500 gr (27% vs 19%, p=0,07). Other obstetric and fetal outcomes were comparable in both groups.
Conclusions: Our data indicate that CNI do not negatively influence the course of renal function on the long term after pregnancy in renal transplant patients, but only temporarely cause a higher increase in serum creatinin levels towards the end of pregnancy. These results suggest that it is not necessary to replace CNI by azathioprine in renal transplant recipients to preserve renal function. However, the multidisciplinary team taking care of these high risk pregnancies needs to be aware of the lower birth weights observed in neonates born to women using a CNI. Our data do not allow to draw conclusions on possible long term effects of CNI on overall health outcome, renal function or hypertension in the children. This will be subject of future studies.

Prevalence and predictors of sensory polyneuropathic signs and symptoms in kidney transplant recipients

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Background: Sensory polyneuropathy is a common finding in kidney transplant recipients (KTR). Patients with end stage renal disease are at a high risk to develop uremic or diabetic polyneuropathy. Kidney transplantation frequently fails to improve polyneuropathic signs and symptoms post-transplantation. So far, little is known about the exact prevalence of post-transplantation sensory polyneuropathy. Therefore, our aim is to determine prevalence and possible predictors of sensory polyneuropathy in KTR.
Methods: We included KTR and healthy subjects, examined prior to kidney donation. The primary outcome was the result of the adapted modified Toronto Clinical Neuropathy Score (amTCNS), a scoring tool designed to quantify neurological complaints and to rate symptoms of sensory polyneuropathy. Information on relevant clinical parameters i.e. age, height, weight, systolic blood pressure, diastolic blood pressure, hemoglobin levels, eGFR, levels of parathyroid hormone, potassium, folic acid, vitamin B-12, advanced glycation end product levels, HbA1c, use of calcineurin inhibitors, time since transplantation, and information on dialysis was collected from all subjects. A chi-square test was used to compare prevalence of sensory polyneuropathy between KTR and healthy subjects. Cumulative odds ordinal logistic regression analyses were performed to assess the relationship between explanatory variables and sensory polyneuropathy.
Results: A total of 209 KTR (65.1% males) with a mean age of 54.9±13.4 years, and 122 healthy subjects (46.7% males) with a mean age of 55.9±11.2 years were included. Signs and symptoms of sensory polyneuropathy were present in 48 (23.0%) KTR and in 6 (4.9%) healthy subjects (P<0.001). Age (OR=1.04, 95% CI=1.00-1.09, P=0.04), weight (OR=1.03, 95% CI=1.01-1.07, P=0.02), hemoglobin (OR=0.57, 95% CI=0.33-0.97, P=0.04), time since transplantation (OR=1.01, 95% CI=1.00-1.01, P=0.01), preemptive transplantation (OR=0.30, 95% CI=0.12-0.80, P=0.02) and advanced glycation end products score (OR=2.18, 95% CI=1.12-4.25, P=0.02) were associated with the odds of sensory polyneuropathy in KTR.
Conclusions: Polyneuropathic signs and symptoms were more than four times more frequent in KTR than in healthy subjects. Next to age, weight, hemoglobin, and time since transplantation, dialysis before transplantation was shown to be associated with the later presence of sensory polyneuropathy in KTR. Interestingly, advanced glycation end products were predictors of sensory polyneuropathy in KTR, even after correction for the presence of diabetes.

Induction therapy determines graft and patient survival in ABO-incompatible kidney transplantation

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Background: Rituximab is the standard induction agent for ABO-incompatible (ABOi) kidney transplantation. Alternative regimens are basiliximab on top of rituximab and alemtuzumab. We compared graft and patient survival in ABOi transplant recipients according to three different induction regimens, with 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 till March 2019. Outcomes for ABOi, ABOc living and ABOc deceased donor transplantations were recorded. Using propensity scores, ABOi recipients were matched to ABOc living donor recipients and deceased donor recipients and in a 1:4 ratio. The propensity score model included transplant center, recipient age, number of transplantations, peak panel-reactive antibodies (PRA) and dialysis duration. For comparison, ABOi recipients were divided in three groups according to induction therapy: rituximab, rituximab/basiliximab and alemtuzumab. Propensity matched survival was analyzed both with the total ABOi cohort and after excluding the rituximab group.
Results: 11.706 Kidney transplantations were performed between March 2006 and March 2019, of which 302 ABOi procedures. If patients received a second ABOc kidney allograft in this period, only the first ABOc transplantation was included. 8579 individual ABOc recipients were identified. Induction therapies in ABOi recipients consisted of rituximab alone (43%), rituximab with basiliximab (20%), alemtuzumab (33%) or other (4%). After matching, baseline characteristics for the ABOi compared to the ABOc-living donor group were: recipient mean age 54 vs 55 years, donor mean age 55 vs 54 years, mean total HLA mismatches 3.5 vs 3.5, peakPRA 4% in both groups and retransplant 17% vs 5%. 66% of ABOi recipients were blood group O. ABOi recipients had a higher risk of death-censored graft failure compared to ABOc living donor recipients (HR=2.68, 95%CI 1.71-4.19). After excluding the rituximab group, both rituximab/ basiliximab and alemtuzumab treated recipients had similar graft and patient survival compared to their propensity matched ABOc controls (Cox regression data by induction therapy will be available by early 2020).
Conclusions: Both rituximab/basiliximab and alemtuzumab induction are superior to rituximab alone therapy for ABOi kidney transplantation. With these induction agents graft and patient survival after ABOi kidney transplantation are similar to ABOc controls.

Testosterone levels and the development of posttransplantation diabetes mellitus in male renal transplant recipients

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Background: Despite major improvements in outcomes, male renal transplant recipients (RTR) remain predisposed to numerous mortality risk factors, including low levels of testosterone and development of Posttransplantion Diabetes Mellitus (PTDM). These latter two risk factors have recently been linked in male mice models, uncovering that sufficient testosterone levels are required for adequate insulin secretion and bèta cell health. This raises the question whether a similar relationship can be observed in RTR. Hence, we hypothesized that low levels of testosterone are associated with the development of PTDM in male RTR.
Methods: We conducted a single-center prospective cohort study including adult male RTR with a function graft ≥ 1 year post-transplantation. Androgen levels were assessed by liquid chromatography tandem mass spectrometry. The development of PTDM was defined according to the American Diabetes Association's diagnostic criteria for diabetes. Cox proportional hazard regression analyses models were utilized to assess the association between testosterone and development of PTDM.
Results: We included 257 male RTR (age 51±14 years), with median [interquartile range] levels of testosterone of 12.0 [9.4–15.7] nmol/L. During 5.3 [3.7–5.8] years of follow-up, 32 RTR developed PTDM. In univariable Cox regression analyses, we found an inverse association between testosterone as continuous variable and the risk for development of PTDM (HR 0.45; 95%CI 0.31–0.66; *P*<0.001). In multivariable analyses, the association remained, independent of adjustment for age, eGFR, glucose levels, and HbA1c (HR 0.49; 95%CI0.29–0.83; *P*=0.008). In Cox regression analyses according to tertiles of the distribution of testosterone, we obtained similar results, with RTR in the lowest tertile, with testosterone levels of 8.4 [7.2–9.4] nmol/L, having an independently increased risk for the development of PTDM (HR 4.16; 95%CI 1.15–14.98; *P*=0.03), as compared to RTR in the highest tertile, with testosterone levels of 17.3 [15.7–20.7] nmol/L.
Conclusions: Our results demonstrate that low post-transplantation testosterone levels in males are independently associated with an increased risk for development of PTDM. This finding offers new insights to strategies to prevent late development of PTDM in male RTR.