NEDERLANDSE **TRANSPLANTATIE** VERENIGING

Bootcongres 2022

Wetenschappelijke voorjaarsvergadering

Nederlandse Transplantatie Vereniging

15 en 16 juni 2022

Hooglandse Kerk te Leiden

georganiseerd in samenwerking met

Leids Universitair Medisch Centrum

LUMC

Inhoudsopgave

Algemene informatie

Schematisch overzicht programma woensdag 12

Schematisch overzicht programma donderdag 14

Welkom op het Bootcongres in Leiden, European City of Science 2022!

Na twee jaar is het eindelijk weer mogelijk fysiek bij elkaar te komen, van elkaar te leren en ervaringen uit te wisselen. De zorg rond orgaandonatie en transplantatie heeft, net als de rest van de gezondheidszorg in Nederland, de afgelopen periode vanwege Covid-19 onder grote druk gestaan. Dankzij de inzet van een zeer diverse groep van zorgprofessionals blijft het mogelijk om, ook in moeilijke tijden, optimale zorg te leveren voor onze zeer kwetsbare patiënten.

Het is geen toeval dat voor het woord 'divers' is gekozen om onze zorgprofessionals te beschrijven: juist onze verscheidenheid maakt dat wij creatiever en vernieuwender zijn, en beter in staat problemen op te lossen. Bovendien is het belangrijk dat naast diversiteit ook inclusiviteit wordt nagestreefd opdat de handen aan bed van onze patiënt ook daadwerkelijk een weerspiegeling zijn van onze maatschappij en dat iedereen in onze samenleving gelijke toegang heeft tot (transplantatie)zorg. Voor het lokaal organiserend comité is dit voldoende reden om 'Diversiteit en inclusiviteit' tot centraal thema van het Bootcongres 2022 te benoemen.

Het congres zal worden geopend met een voordracht over 'Kijken in de (genees)kunst' waar het belang van observeren op een interactieve manier wordt toegelicht. Tijdens de tweede plenaire sessie 'Diversiteit en inclusiviteit' zal vervolgens onder andere worden besproken hoe de manier van kijken naar elkaar in belangrijke mate bepaalt hoe wij als maatschappij en in de zorg omgaan met diversiteit en inclusiviteit. Op een creatieve manier zal in deze sessie vervolgens de verbinding tussen diversiteit en het immuun systeem worden gevonden. De parallelsessie van de Young Professionals in Transplantation zal ook in het teken staan van diversiteit.

Op de tweede congresdag zal ruimschoots aandacht worden geschonken aan inspirerende innovaties in ons veld. Tijdens de plenaire sessies 'From bench to bioscience park' en 'Artificial Intelligence in de zorg' hoort u uit de eerste hand hoe ideeën hun weg vinden naar de kliniek en wat daar zoal bij komt kijken. Verder zullen de nieuwste ontwikkelingen rond datagedreven zorg en Dashboards in een parallelsessie aan bod komen.

Natuurlijk zijn transplantaties niet mogelijk zonder orgaandonoren en hun nabestaanden. Speciale aandacht zal dit jaar aan donatie bij euthanasie worden gegeven middels een gesprek met een donorfamilie. Ook zal in het kader van Leiden European City of Science 2022 de avond voor het Bootcongres een publiek donatie symposium plaatsvinden. Het congres volgt verder een vertrouwd format: naast de genoemde plenaire en parallelle sessies, gemodereerde postersessies, en prijsuitreikingen is er ruim voldoende mogelijkheden voor sociale interactie. Het diner en feest met live band van een van onze plenaire sprekers zal ongetwijfeld een hoogtepunt zijn!

Wij wensen u veel plezier tijdens het Bootcongres 2022!

Ian Alwayn,

voorzitter lokale organisatiecommissie LUMC

Organisatiecommissie Bootcongres 2022
Vanuit het Leids Universitair Medisch Centrum:

Ian Alwayn, voorzitter
Cees van Kooten
Dave Roelen
Tamara Voskuil
Aiko de Vries

Met ondersteuning van de abstract beoordelaars:

André Baranski
Karin Beer
Jeannet Bisschop-van Leijden
Paul van der Boog
Hanneke Bouwsma
Minneke Coenraad
Ruth Dam
Jason Doppenberg
Jeroen Dubbeld
Teun van Gelder
Sebastiaan Heidt
Danny van der Helm
Bart van Hoek
Marion van der Hoeven
Martin Hoogduijn
Volkert Huurman
Jeroen de Jonge
Gonca Karahan
Jesper Kers
David Lam
Jan Lindeman
Coline Meijers
Wieneke Michels
Dirk Jan Moes
Jeroen Nieuwenhuizen
Mijntje Nijboer
Esther Nijgh
Bastian Ruijter
Sandro Schaapherder
Siebe Spijker
Maaike Swijnenbrug-Konijn
Ellen van Tiggelhoven
Maarten Tushuizen
Janneke Vervelde
Christa Vlieger
Dorottya de Vries
Caroline Vrijenhoek

Bestuursleden Nederlandse Transplantatie Vereniging:

Niels van der Kaaij, voorzitter
Arnold van der Meer, penningmeester
Dorottya de Vries, secretaris
Coby Annema
Sarwa Darwish Murad
Sebastiaan Heidt
Jan-Stephan Sanders

Secretariaat NTV te Haarlem

Jeanine van Aalst
Lucy van den Eeckhout
Charissa van Geenen
Marie José van Gijtenbeek
Sarah Smit
Marja Weber
Stella Zweerts

Accreditatie is aangevraagd bij de volgende verenigingen:

Nederlandse Vereniging voor Heelkunde

Nederlandse Vereniging voor Immunologie

Nederlandse Internisten Vereniging

Nederlandse Vereniging voor Kindergeneeskunde

Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose

Nederlandse Vereniging van Maag-Darm-Leverartsen

Nederlandse Vereniging voor Thoraxchirurgie

Nederlandse Vereniging voor Urologie

V&VN, kwaliteitsregister algemeen

V&VN, kwaliteitsregister, deskundigheidsgebied Dialyse

V&VN, verpleegkundig specialisten register

Nederlandse Associatie van Physician Assistants

Hoofdlocatie:

Hooglandse Kerk
Nieuwstraat 20
2312 KH Leiden
www.hooglandsekerk.nl
WiFi: hooglandsekerk-guest
Wachtwoord: Visitor@HK

In de Hooglandse Kerk vindt de ontvangst, alle plenaire sessies en de catering plaats. Het Weeshuis ligt op korte loopafstand van de Hooglandse Kerk.

Locatie subsessies:

Weeshuis
Hooglandse Kerkgracht
2312 HV Leiden
WiFi: Utopa_Weeshuis_ Gasten
Wachtwoord: Gast@Weeshuis

Bereikbaarheid met openbaar vervoer

De Hooglandse Kerk is per openbaar vervoer uitstekend bereikbaar. Bij station Leiden staan bussen die vlak voor de Hooglandse Kerk stoppen (lijn 4 richting station De Vink, lijn 45 richting Den Haag Centraal, lijn 400 richting Zoetermeer, halte 'Breestraat' of lijn 6 richting Leiderdorp Leyhof, halte 'Hogewoerd')

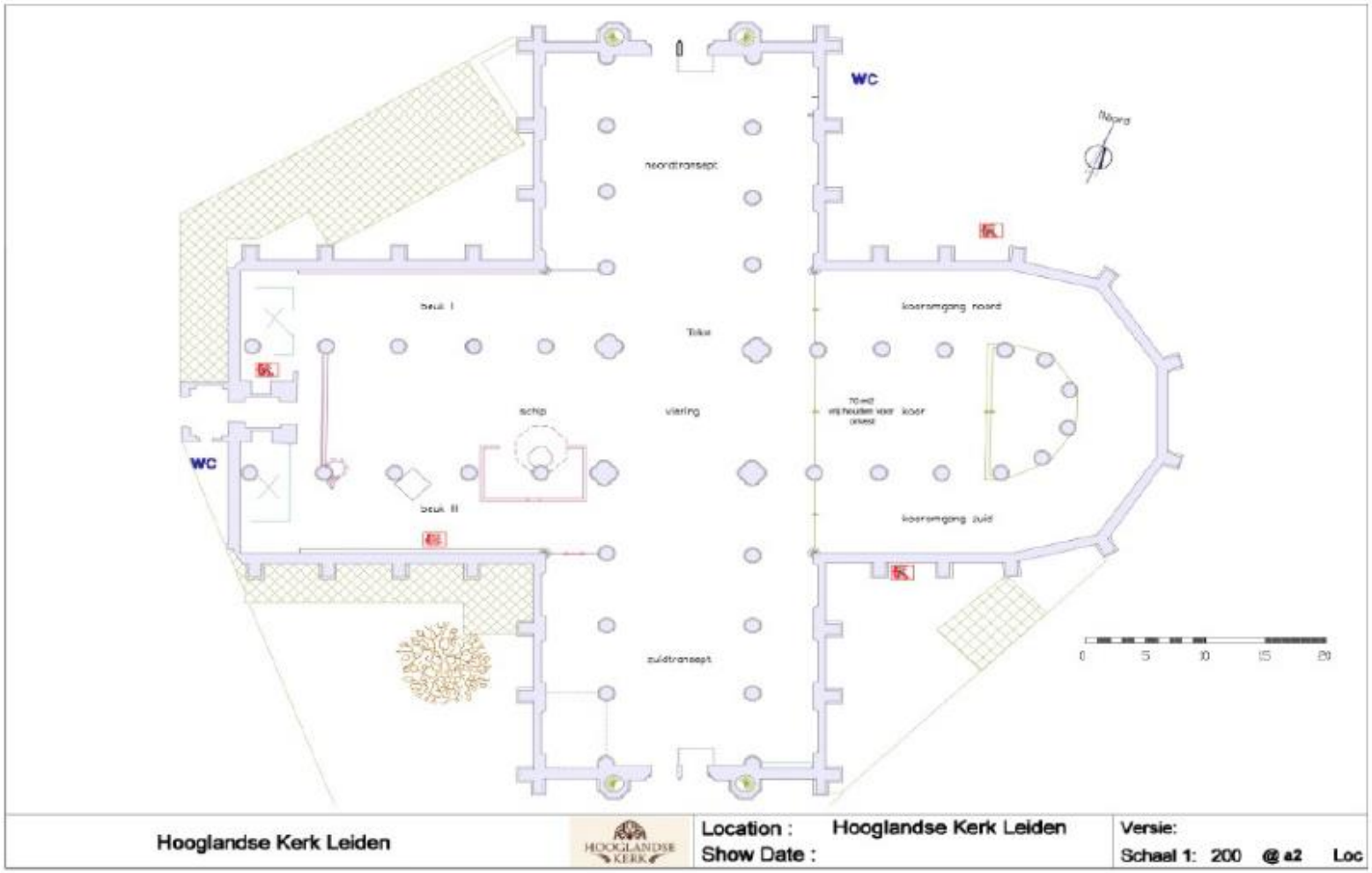
Bereikbaarheid met de auto

Indien u met een navigatiesysteem de kerk wilt bereiken, voert u dan 'Nieuwstraat 20, Leiden' in als adres. Met ingang van 13 juni mogen bezoekers niet langer parkeren in straten van de Leidse binnenstad - https://nos.nl/r/264544

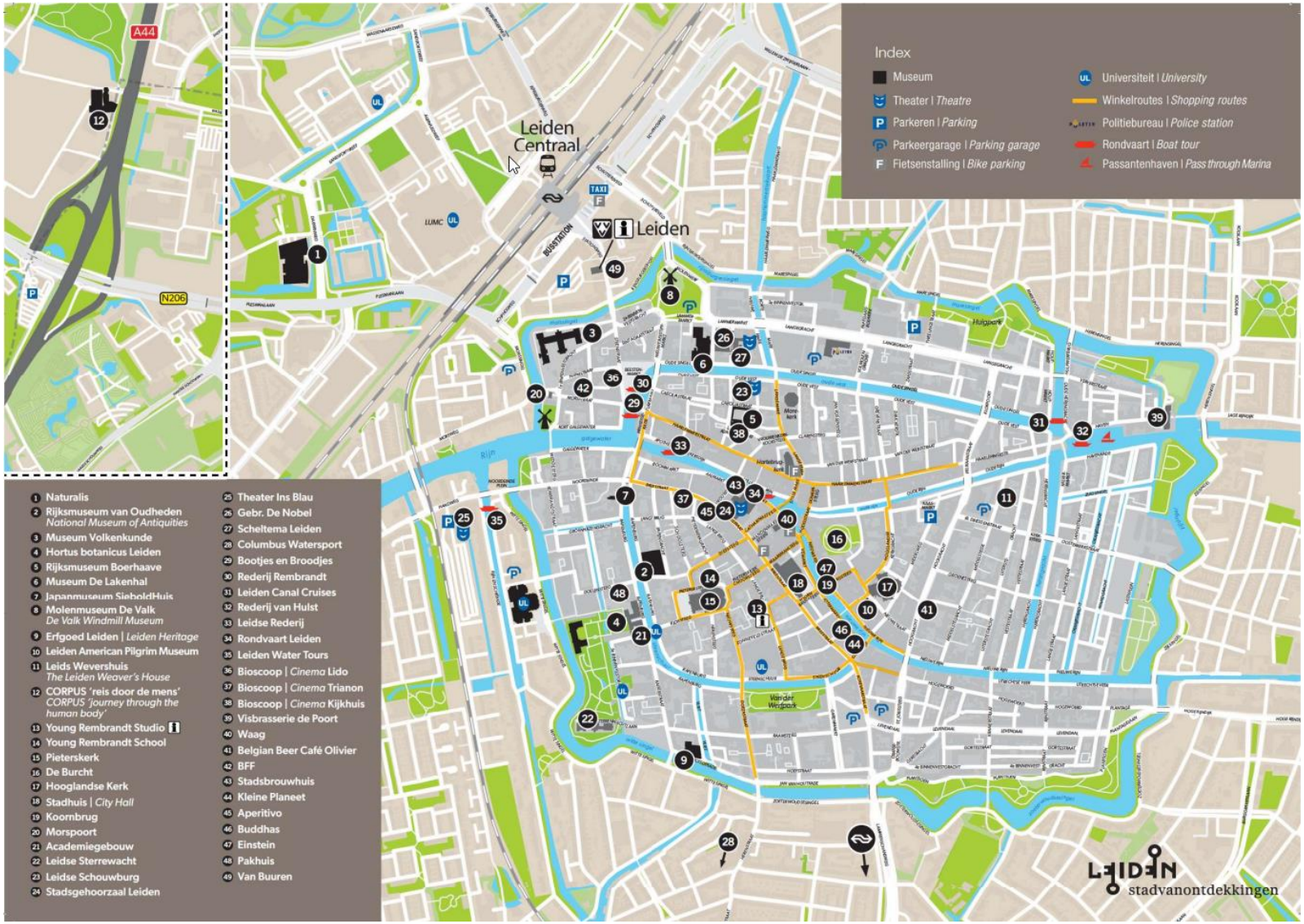
Parkeermogelijkheden

De dichtstbijzijnde parkeergarage is parkeergarage 'Breestraat'. Vanaf de parkeergarage kunt u lopend naar de Hooglandse Kerk. Een dagkaart kost € 16,00. Het uurtarief op straat is € 3,50.

Plattegrond Hooglandse kerk



Stadsplan Leiden Centrum (17 Hooglandse Kerk, 27 Scheltema)



Inleveren presentaties

Wij verzoeken sprekers zo spoedig mogelijk na aankomst de presentatie in te leveren in de daartoe aangewezen ruimte in de Hooglandse Kerk

Ophangen posters

De posters graag ophangen op de aangewezen plaatsen in het Noordtransept van de kerk. 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.

Tijdstip en locatie van de maaltijden

Woensdag

Lunch	13.00 – 14.00 uur in de Hooglandse Kerk
Diner Scheltema Leiden*	19.30 – 00.30 uur

Donderdag

Lunch	12.30 – 13.30 uur in de Hooglandse Kerk

**Adres van de avondlocatie:*

Marktsteeg 1

Vergaderingen voorafgaand aan Bootcongres

Dinsdag 14 juni 2022

Locatie: Fletcher Hotel direct naast Leiden CS
Adres: Bargelaan 180, 2333 CW Leiden

10.00 – 12.00 uur	LORUT commissie	Zaal Oude Meesters
13.00 – 17.00 uur	Nascholing uitname	Zaal Oude Meesters
13.00 – 14.30 uur	ODC-Nefrologenoverleg	Zaal Godfried Schalcken
15.00 – 17.00 uur	LONT commissie	Zaal Godfried Schalcken
17.00 – 18.00 uur	LWTV vergadering	

Het diner op dinsdag waarvoor kon worden ingeschreven vindt plaats in het restaurant van Fletcher hotel. Let op: ook voor dit diner moet tevoren worden ingeschreven. Aanmelden op de dag zelf is niet meer mogelijk.

Woensdag 15 juni 2022
Schematisch overzicht programma

Woensdagochtend	Hooglandse Kerk
09.00 – 09.30	Ontvangst met koffie
09.30 – 11.00	**Plenaire sessie I** *voorzitters: Ian Alwayn / Niels van der Kaaij*
09.30	Opening congres door *Ian Alwayn, voorzitter LOC* en introductie programma
09.35	Kijken in de (genees)kunst: is evidence-based leren observeren mogelijk? *Sprekers in deze sessie:* *Prof. dr. Frank Willem Jansen, hoogleraar gynaecologie, LUMC* *Dr. Marianne Crijns, dermatoloog Huid- en Melanoomcentrum, Antoni van Leeuwenhoek ziekenhuis, Amsterdam*
10.20	**Prijsuitreikingen** Chiesiprijs 2022 – Beste Idee in Transplantatie Astellas Transplantatie Researchprijs 2022, gevolgd door presentatie 2021 Novartis Transplantation Awards 2022 Presentatie NTV prijs Innovatie in transplantatie onderwijs 2021: *V.A. Lantinga, Student-onderzoeker/ Transplant technician, UMC Groningen*
11.00 – 11.30	Koffiepauze
11.30 – 13.00	**Plenaire sessie II** *voorzitters: Aiko de Vries / Azam Nurmohamed* Thema: Diversiteit en inclusiviteit
11.30	*Prof. dr. Martine de Vries, hoogleraar Normatieve aspecten van de geneeskunde, LUMC*: (Impliciet) bias in de zorg en het geneeskundeonderwijs. Je gaat het pas zien als je het door hebt.
12.00	*Prof. dr. Judi Mesman, hoogleraar Interdisciplinaire studie van maatschappelijke uitdagingen, Universiteit Leiden*: Vooroordelen - een menselijke eigenschap als oorzaak van onrecht
12.30	*Dr. Sebastiaan Heidt, hoofd Eurotransplant Referentielaboratorium:* Het Acceptabele Mismatch Programma voor hoog-geïmmuniseerde patiënten
13.00 – 14.00	Lunch met gemodereerde postersessies

Woensdag 15 juni 2022
Schematisch overzicht programma

Woensdagmiddag	Hooglandse Kerk	Grote Zaal (Weeshuis)	Blauwe Vogelzaal (Weeshuis)
14.00 – 15.30	**Parallelle sessie III**: klinische abstracts *Voorzitter: Hanneke Bouwsma en Stefan Berger*	**Parallelle sessie IV**: basale abstracts *Voorzitters: Gonca Karahan en Arnold van der Meer*	**Parallelle sessie V**: Young Professionals *Voorzitters: Femke Vrieling-Prince en Fenna van der Heijden*
15.30 – 16.00	Koffiepauze		
16.00 – 17.30	**Parallelle sessie VI**: klinische abstracts *Voorzitters: André Baranski en Jeroen de Jonge*	**Parallelle sessie VII**: basale abstracts *Voorzitters: Dorottya de Vries en Martin Hoogduijn*	**Parallelle sessie VIII**: ODC Donatie *Voorzitters: Marion van der Hoeven en Jolanda Winnemuller*
17.40 – 18.00	Ledenvergadering NTV, Hooglandse Kerk		
19.30 – 00.30	Diner Scheltema		
00.30	Einde programma		

Donderdag 16 juni 2022
Schematisch overzicht programma

Donderdagochtend	**Hooglandse Kerk**		
08.30 – 09.00	Ontvangst en registratie		
09.00 – 10.30 09.00 09.30 10.00	**Plenaire sessie III** *Voorzitters: Cees van Kooten / Marlies Reinders* Thema: From bench to bioscience park *Prof. dr. Frank Staal, hoogleraar Moleculaire stamcelbiologie, LUMC*: Beenmergtransplantatie 2.0: autologe gentherapie *Dr. Siebe Spijker, nefroloog, LUMC*: Van kweek naar kliniek; toepassing van stamcellen in orgaantransplantatie *Dr. Eric van der Veer, CSO & Founder, Hybridize Therapeutics, Leiden*: Een nieuwe, RNA-gebaseerde antivirale methode om vermenigvuldiging van het BK virus te remmen in niertransplantatie patiënten		
10.30 – 11.00	Koffiepauze		
	Hooglandse Kerk	**Grote Zaal (Weeshuis)**	**Blauwe Vogelzaal (Weeshuis)**
11.00 – 12.30	**Parallelle sessie IX**: klinische abstracts *Voorzitters: Minneke Coenraad en Sarwa Darwish Murad*	**Parallelle sessie X**: basale abstracts *Voorzitters: Marten Engelse en Cyril Moers*	**Parallelle sessie XI**: Verpleegkundig *Voorzitters: Koen van Duin en Coby Annema*
12.30 – 13.30	Lunch met gemodereerde postersessies		

Donderdag 16 juni 2022
Schematisch overzicht programma

Donderdagmiddag	Hooglandse Kerk	Grote Zaal (Weeshuis)	Blauwe Vogelzaal (Weeshuis)
13.30 – 15.00	**Parallelle sessie XII:** Klinische/basale abstracts *Voorzitters: Teun van Gelder en Aiko de Vries*	**Parallelle sessie XIII**: Klinische abstracts *Voorzitters: David Lam en Remco van Dijk*	**Parallelle sessie XIV**: Datagedreven zorg in transplantatie *Voorzitters: Paul van de Boog en Martijn van den Hoogen*
15.00 – 15.30	Koffiepauze		
	Hooglandse Kerk		
15.30	**Plenaire sessie IV** *Voorzitters: Dave Roelen en Niels van der Kaaij* Thema: Artificial Intelligence in de zorg Artificial Intelligence in de zorg: van krantenkop naar klinische praktijk *Prof. dr. ir. Boudewijn Lelieveldt, hoogleraar Biomedische beeldvorming, LUMC*		
16.00	**Prijsuitreikingen** Uitreiking LWTV Innovatie-Kwaliteitsprijs 2022, gevolgd door voordracht prijswinnaar 2021 Uitreiking Jon J. van Roodprijs 2022, gevolgd door voordracht Uitreiking Wetenschapsprijs 2022, gevolgd door voordracht Dr. M.M.A. Verstegen, prijswinnaar 2021		
16.45	Sluiting congres		

Woensdag 15 juni 2022

Plenaire sessie I – Openingssessie **Hooglandse Kerk**

09.00 Ontvangst met koffie

Voorzitters: *Prof. dr. Ian Alwayn, hoogleraar transplantatiechirurgie, voorzitter organisatiecomité LUMC*
Dr. Niels van der Kaaij, cardiothoracaal chirurg, voorzitter NTV, UMC Utrecht

09.30 Opening congres door voorzitter LOC en introductie programma

09.35 Kijken in de (genees)kunst: is evidence-based leren observeren mogelijk?
Prof. dr. Frank Willem Jansen, hoogleraar gynaecologie, LUMC
Dr. Marianne Crijns, dermatoloog Huid- & Melanoomcentrum, Antoni van Leeuwenhoek ziekenhuis, Amsterdam

10.20 **Prijsuitreikingen 2022**

Pitches Chiesi prijs 2022 – Beste Idee in Transplantatie

Astellas Transplantatie Researchprijs 2022

Voordracht winnaar Astellas prijs 2021
Preventing bioincompability in organ perfusion, with a focus on the oxygenator
Prof. dr. H.G.D. Leuvenink, onderzoeker, UMC Groningen

Novartis Transplantation Awards 2022
Uitgereikt door Dr. Arjan van Zuilen, internist-nefroloog UMCU en voorzitter Novartis Transplant Advisory Board

Presentatie NTV prijs voor Innovatie in transplantatie onderwijs 2021
V.A. Lantinga, Student-onderzoeker / Transplant technician, UMC Groningen

11.00 Koffie- / theepauze

Plenaire sessie II **Hooglandse Kerk**

Thema: Diversiteit en inclusiviteit

Voorzitters: *Dr. Aiko de Vries, internist-nefroloog, LUMC, Leiden*
Dr. Azam Nurmohamed, internist-nefroloog, Amsterdam UMC

11.30 (Impliciet) bias in de zorg en het geneeskundeonderwijs. Je gaat het pas zien als je het door hebt.
Prof. dr. Martine de Vries, hoogleraar Normatieve aspecten van de geneeskunde, LUMC

12.00 Vooroordelen - een menselijke eigenschap als oorzaak van onrecht
Prof. dr. Judi Mesman, hoogleraar Interdisciplinaire studie van maatschappelijke uitdagingen, Universiteit Leiden

12.30 Het Acceptabele Mismatch Programma voor hoog-geïmmuniseerde patiënten
Dr. Sebastiaan Heidt, hoofd Eurotransplant Referentielaboratorium, Leiden

Woensdag 15 juni 2022

13.00 Lunch en gemodereerde postersessies

Postersessie 1 – Basale abstracts **Noordtransept Hooglandse kerk**

Tijd: 13.15 uur

Moderatoren: *Dr. Sandro Schaapherder, chirurg, LUMC*
Dr. Danny van der Helm, datamanager, Transplantatie Centrum, LUMC, Leiden

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

1. Erythropoietin, renin and vitamin D release from human donor kidneys during normothermic machine perfusion: predictors of post-transplantation outcome? (p. 41)
Z. Du[1], H. Lin[2], S. Bouari[3], E. Rijkse[3], A.H.J. Danser[4], R.C. Minnee[3], M.J. Hoogduijn[1], [1]Dept. of Internal Medicine, Erasmus MC Transplant Institute, University Medical Center Rotterdam, Rotterdam, [2]Dept. of Internal Medicine, Vascular Medicine and Pharmacology, University Medical Center Rotterdam, Rotterdam, [3]Dept. of Surgery, division of HPB & Transplant Surgery, Erasmus MC Transplant Institute, University Medical Center Rotterdam, Rotterdam, [4]Dept. of Internal Medicine, Vascular Medicine and Pharmacology, University Medical Center Rotterdam, Rotterdam, The Netherlands.

2. Normothermic machine perfusion of diseased explanted livers of patients undergoing liver transplantation as novel preclinical model to study hepatic pharmacokinetic processes (p. 42)
L.J. Stevens[1], J. Dubbeld[1], J.B. Doppenberg[2], B. van Hoek[3], W.H.J. Vaes[4], C.A.J. Knibbe[5], E. van de Steeg[4], I.P.J. Alwayn[1], [1]Dept. of Surgery, Leiden University Medical Centre (LUMC), Leiden, [2]Heelkunde, Leiden University Medical Centre (LUMC), Leiden, [3]MDL, Leiden University Medical Centre (LUMC), Leiden,[4]Metabolic Health Research, TNO, Leiden, [5]Division of Systems Biomedicine and Pharmacology, Leiden Academic Centre for Drug Research (LACDR), Leiden, The Netherlands

3. Single-cell sequence analyses of circulating T follicular helper cells during antibody-mediated rejection (p. 43)
E.T.M. Peereboom[1], K. Geneugelijk[1], K. Boer[2], C.C. Baan[2], E. Spierings[1], [1]Center for Translationa Immunology, UMC Utrecht, Utrecht, [2]Dept. of Internal Medicine, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands

4. Extracellular Vesicles released during Normothermic Machine Perfusion are Associated with Human Donor Kidney Characteristics (p. 44)
W.W.W. Woud[1], A.S.A. Arykbaeva[2], I.P.J.A. Alwayn[2], A.M. Merino[1], C.C. Baan[1], R.C.M. Minnee[3], M.J.H. Hoogduijn[1], K.B. Boer[1], [1]Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, [2]Dept. of Surgery, Leiden University Medical Center, Leiden, [3]Dept. of Surgery, Erasmus MC Transplant Institute, Rotterdam, The Netherlands

5. Accumulation of individual cyto-/chemokines in perfusate during human ex vivo lung perfusion differs significantly per donor (p. 45)
T. Kardol-Hoefnagel[1], S. Braithwaite[2], H.G. Otten[1], N.P. van der Kaaij[3], [1]Center for Translational Immunology, UMC Utrecht, Utrecht, [2]Dept. of Anesthesiology, UMC Utrecht, Utrecht, [3]Dept. of Cardiothoracic Surgery, UMC Utrecht, Utrecht, The Netherlands

6. Validation of the preclinical models for renal ischemia reperfusion injury. A systematic review (p. 46)
L.J.S. Lerink[1], M.J.C. de Kok[1], J.F. Mulvey[2], A.F.M. Schaapherder[1], I.P.J. Alwayn[1], R.J. Ploeg[2], J.A. Bakker[3], J.H.N. Lindeman[1], [1]Surgery, LUMC, Leiden, The Netherlands. [2]Nuffield Dept. of surgical sciences, University of Oxford, Oxford, UK. [3]Laboratory genetic metabolic diseases, AMC, Amsterdam, The Netherlands.

Postersessie 2 – Klinische abstracts **Noordtransept Hooglandse kerk**

Tijd: 13.30 uur

Moderatoren: *Prof. dr. Bart van Hoek, hoogleraar maag-, darm- en leverziekten, LUMC, Leiden*
Drs. Jeroen Nieuwenhuizen, chirurg, LUMC, Leiden

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

7. Early exposure to tacrolimus is associated with BK-viremia in kidney transplant recipients (p. 47)
S. Meziyerh[1], A.L. van Rijn[2], D. van der Helm[3], P. van der Boog[4], T. van Gelder[5], A.C.M. Kroes[6], J.W. de Fijter[1], D.J.A.R. Moes[5], J.I. Rotmans[1], M.C.W. Feltkamp[6], A.P.J. De Vries[1], [1]Interne Geneeskunde-Nefrologie, LUMC, Leiden, [2]Medische microbiologie, LUMC, Leiden, [3]LUMC Transplantatie Centrum, LUMC, Leiden, [4]Interne Geneeskunde, LUMC, Leiden, [5]Klinische farmacologie en toxicologie, LUMC, Leiden, [6]Medische Microbiologie, LUMC, Leiden, Nederland.

8. Tacrolimus 4-hour monitoring in liver transplant patients is non-inferior to trough monitoring: the randomized controlled FK04 trial (p. 48)
B.N. Ruijter[1], M.E. Tushuizen[1], D.J.A.R. Moes[2], B.M. de Klerk[1], B. van Hoek[1], [1]Gastroenterologie en Hepatologie, LUMC, Leiden, [2]Farmacologie en Toxicologie, LUMC, Leiden, Nederland.

9. Intracellular Tacrolimus Concentration in CD3 T Lymphocytes and CD14 Monocytes and Association with Kidney Transplant Rejection (p. 49)
S.U. Udomkarnjananun[1], M.I.F. Francke[1], M.M.D. Marijnissen-Dieterich[1], D.V.D. van De Velde[2], J.G.H.P.V. Verhoeven[1], K.B. Boer[1], M.C.C.G. Clahsen-van Groningen[3], B.C.M.W. De Winter[2], C.C.B. Baan[1], D.A.H. Hesselink[1], [1]Internal medicine, Erasmus MC, Rotterdam, [2]Pharmacy, Erasmus MC, Rotterdam, [3]Pathology, Erasmus MC, Rotterdam, The Netherlands

10. Effect of Epstein Barr Virus infection on pharmacokinetics of tacrolimus; report of a single center study (p. 50)
H.P.J. van der Doef[1], D. Touw[5], A. Hosseini[2], R. Scheenstra[3], C.C. Van Leer[4], [1]Division of Pediatric Gastroenterology and Hepatology, Dept. of Pediatr, UMCG, Groningen, [2]Dept. of Clinical Pharmacy and Pharmacology, UMCG, Groningen, [3]Division of Pediatric Gastroenterology and Hepatology, Dept. of Pediatr, UMCG, Groningen, [4]Dept. of Medical Microbiology (Clinical Virology), UMCG, Groningen, [5]Dept. of Clinical Pharmacy and Pharmacology, UMCG, Groningen, The Netherlands.

11. The Effect of FK-binding Protein 12 and P-glycoprotein on the Intracellular Tacrolimus Concentration in CD3 T Lymphocytes and CD14 Monocytes (p. 51)
S.U. Udomkarnjananun[1], M.I.F. Francke[1], M.M.D. Marijnissen-Dieterich[1], D.V.D. van De Velde[2], J.G.H.P.V. Verhoeven[1], K.B. Boer[1], M.C.C.G. Clahsen-van Groningen[3], B.C.M.W. De Winter[2], C.C.B. Baan[1], D.A.H. Hesselink[1], [1]Internal medicine, Erasmus MC, Rotterdam, [2]Pharmacy, Erasmus MC, Rotterdam, [3]Pathology, Erasmus MC, Rotterdam, The Netherlands.

12. Ferric carboxymaltose and SARS-CoV-2 vaccination-induced immunogenicity in iron-deficient kidney transplant recipients: the EFFECT-KTx randomized, placebo-controlled clinical trial (p. 52)
J.S.J. Vinke[1], D. Altulea[1], M.F. Eisenga[1], R.L. Jagersma[1], D. van Baarle[2], M. van der Heiden[2], M. Steenhuis[3], T. Rispens[3], W.H. Abdulahad[2], J.S.F. Sanders[1], M.H. de Borst[1], [1]Nefrologie, Universitair Medisch Centrum Groningen, Groningen, [2]Immunologie, Universitair Medisch Centrum Groningen, Groningen, [3]Immunopathologie, Sanquin Research, Amsterdam, Nederland.

Postersessie 3 – Donatie abstracts — Noordtransept Hooglandse Kerk

Tijd: 13.45 uur

Moderator: *Dr. Mijntje Nijboer, chirurg, LUMC*
Ellen Kramer, Orgaan Donatie Coördinator, LUMC

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

13. A comparison between combined liver kidney transplants to liver transplants alone: the Dutch experience (p. 53)
S. Bouari[1], I.P. van Kluijve[1], J. van de Wetering[2], V. de Meijer[3], R. Pol[3], S. Berger[4], W.G. Polak[1], A. van den Berg[5], A.P.J. de Vries[6], B. van Hoek[7], I. Alwayn[8], R. Porte[3], H.J. Metselaar[9], J.N.M. IJzermans[1], R.C. Minnee[1], [1]Heelkunde, Erasmus MC, Rotterdam, [2]Interne geneeskunde, Erasmus MC, Rotterdam, [3]Heelkunde, UMCG, Groningen, [4]Interne geneeskunde, UMCG, Groningen, [5]Maag-, darm-, en leverziekten, UMCG, Groningen, [6]Interne geneeskunde, LUMC, Leiden, [7]Maag-, darm-, en leverziekten, LUMC, Leiden, [8]Heelkunde, LUMC, Leiden, [9]Maag-, darm-, en leverziekten, Erasmus MC, Rotterdam, Nederland.

14. Living kidney donation in Blacks and possible barriers (p. 54)
D. Berkhout[2], L. Pengel[3], J.G. Daams[1], F.J. Bemelman[4], [1]Nephrology, Amsterdam University Medical Centers, Amsterdam, Netherlands. [2]Internal medicine/nephrology, UVA/AMC, Amsterdam, The Netherlands. [3]Centre for Evidence in Transplantation Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, UK, [4]Nephrology, Amsterdam University Medical Centers, Amsterdam, The Netherlands.

15. Experiences of the first cohort of unspecified living kidney donors in [name of Dutch transplantation centre] – indicators for improvement of care? (p. 55)
M. Pronk[1], W. Zuidema[2], W. Weimar[2], J. Van de Wetering[3], S. Ismail[2], E. Massey[2], [1] University Medical Center Rotterdam Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, [2]University Medical Center Rotterdam Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, [3]University Medical Center Rotterdam Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, The Netherlands.

16. Illness perceptions and medication nonadherence to immunosuppressants after successful kidney transplantation: a cross-sectional study (p. 56)
Y. Wang[1], D.M.J. Veltkamp[2], P.J.M. Van der Boog[2], M.H. Hemmelder[3], F.W. Friedo Dekker[4], A.P.J. de Vries[2], Y. Meuleman[1], [1]Clinical Epidemiology, Leiden University Medical Center, Leiden, [2]Dept. of Internal Medicine, Division of Nephrology, Leiden University Medical Center, Leiden, [3]Dept. of Internal Medicine, Division of Nephrology, Maastricht University Medical Center, Maastricht, [4]Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands

17. The influence of the donation procedure on the mental health of unspecified kidney donors (p. 57)
M. Pronk[1], W. Zuidema[2], W. Weimar[2], J. Van de Wetering[3], S. Ismail[2], E. Massey[2], [1] University Medical Center Rotterdam Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, [2]University Medical Center Rotterdam Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, [3]University Medical Center Rotterdam Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, The Netherlands

Parallel sessie III – Klinische abstracts — Hooglandse kerk

Voorzitter: *Drs. Hanneke Bouwsma, internist-nefroloog, LUMC, Leiden*
Prof. dr. Stefan Berger, internist-nefroloog, UMC Groningen

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

14.00 Heart donation and transplantation of circulatory death donors: The Dutch experience (p. 58)
N.P. van der Kaaij[1], O.C. Manintveld[2], Y.J.H.J. Taverne[3], M.J.J. Sperber[4], K. Damman[5], L.W. van Laake[6], M.E. Erasmus[7], [1]Cardiothoracale Chirurgie, UMC Utrecht, Utrecht, [2]Cardiologie en transplantatie instituut, Erasmus MC, Rotterdam, [3]CTC en Transplantatie instituut, Erasmus MC, Rotterdam, [4]CTC en Transplantatie instituut, UMC Utrecht, Utrecht, [5]Cardiologie, UMC Groningen, Groningen, [6]Cardiologie, UMC Utrecht, Utrecht, [7]Cardiothoracale Chirurgie, UMC Groningen, Groningen, Nederland.

14.10 Short- and long-term maternal and pregnancy outcomes after orthotopic liver transplantation in the Netherlands (p. 59)
J.R. Meinderts[1], H.J. Metselaar[2], B. Van Hoek[3], C.M. Den Hoed[2], D. Rijntjes[4], M. Groenewout[5], J.R. Prins[5], H. Groen[6], S.P. Berger[1], A.P. Van den Berg[7], M.F.C. De Jong[1], [1]Dept. of Nephrology, University Medical Center Groningen, Groningen, [2]Dept. of Gastroenterology and Hepatology, Erasmus MC Transplant Institute, University Medical Center Rotterdam, Rotterdam, [3]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [4]Dept. of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [5]Dept. of Obstetrics and Gynaecology, University Medical Center Groningen, Groningen, [6]Dept. of Epidemiology, University Medical Center Groningen, Groningen, [7]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands.

14.20 Long term outcomes of pancreas-after-kidney and islet-after-kidney transplantation (p. 60)

M.F. Nijhoff[1], V.A.L. Huurman[2], J. Dubbeld[2], D. Roelen[3], M.A. Engelse[1], A.P.J. de Vries[1], A.J. Rabelink[1], P.J.M. van der Boog[1], E.J.P. de Koning[1], [1]Internal Medicine, LUMC, Leiden, [2]Surgery, LUMC, Leiden, [3]Immunology, LUMC, Leiden, The Netherlands.

14.30 Recent outcomes of liver transplantation for Budd Chiari Syndrome – Analysis of the European Liver Transplant Registry (ELTR) and affiliated centres - For the European Liver and Intestine Transplant Association (ELITA) (p. 61-62)

E.J. Dongelmans[1], W. Polak[2], R. Adam[3], V. Karam[3], S. Yilmaz[4], C. Kelly[5], J. Pirenne[6], K. Acarli[7], M. Allison[8], A. Hakeem[9], O. Rummo[10], M. Killic[11], A. Nordin[12], L. Fischer[13], A. Parente[14], D. Mirza[14], W. Bennet[15], Y. Tokat[16], F. Faitot[17], P. Muiesan[18], S. Nadalin[19], G. Berlakovich[20], D. Patch[21], F. Berrevoet[22], M. Ribnikar[23], T. Gerster[24], E. Savier[25], S. Gruttadauria[26], B. Ericzon[27], A. Valdivieso[28], V. Cuervas-Mons[29], B. Perez Saborido[30], R. Croner[31], L. De Carlis[32], G. Magini[33], L. Razvan[34], S. Schneeberger[35], H. Blokzijl[36], C. Duvoux[37], S. Darwish Murad[38], [1]Dept. of Gastroenterology and Hepatology, Erasmus Transplant Institute, Erasmus MC, Rotterdam, The Netherlands, [2]Dept. of Surgery, Erasmus Transplant Institute, Erasmus MC, Rotterdam, The Netherlands, [3]Dept. of Hepato-Biliary Surgery, Cancer and Transplantation unit, Hôpital Paul Brousse, Villejuif, France, [4]Dept. of Surgery, Liver Transplant Institute, Turgut Özal Medical Center, Malatay, Turkey, [5]Institute of Liver Studies, King's College Hospital, London, UK, [6]Dept. of Abdominal Transplant Surgery, Universitaire Ziekenhuizen Leuven, Leuven, Belgium, [7]Dept. of Liver and Biliary Tract Surgery, Memorial Hospital, Istanbul, Turkey, [8]Liver Unit, Cambridge University Hospitals NHS Foundation Trust, Cambridge NIHR Biomedical R, Cambridge, UK, [9]Dept. of HPB Surgery and Liver Transplantation, Leeds Teaching Hospitals NHS Trust, Leeds, UK, [10]Dept. of Transplantation, Minsk Scientific and practical centre for surgery, transplantology and hepatology, Minsk, Belarus, [11]Dept. of Surgery, Kent Hosp., Izmir, Turkey, [12]Transplantation and Liver Surgery Unit, Helsinki University Hospital, Helsinki, Finland, [13]Dept. of Surgery, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany, [14]Liver Unit, Queen Elizabeth Hospital, Birmingham, UK, [15]Dept. of Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden, [16]Dept. of General Surgery, International Liver Center and Acibadem Health Care Hospitals, Instanbul, Turkey, [17]Dept. of HPB Surgery and Transplantation, C.H.R.U. de Strasbourg, Strasbourg, France, [18]General and Liver Transplant Surgery Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [19]Dept. of General, Visceral and Transplant Surgery, Universitätsklinik Tübingen, Tübingen, Germany, [20]Dept. of Transplantation Surgery, Medical University of Vienna, Wien, Austria, [21]Dept. of Hepatology and Liver Transplantation, Royal Free Hospital, London, UK,[22]Dept. of General and HPB Surgery and Liver Transplantation, University Hospital Gent, Ghent, Belgium, [23]Dept. of Gastroenterology, University Medical Centre Lubljana, Lubljana, Slovenia, [24]Dept. of Gastroenterology and Hepatology, C.H.U. de Grenoble, Grenoble, France, [25]Dept. of Digestive Surgery and Liver Transplantation, Pitie Salpetriere university hospital, Sorbonne University, Paris, France, [26]Dept. for the Treatment and Study of Abdominal Diseases & Abdominal Transpl, IRCCS-ISMETT, UPMC, Palermo, Italy, [27]Dept. of Transplantation Surgery, Karolinska University Hospital, Huddinge, Sweden, [28]Dept. of HBP Surgery and Liver Transplantation, Cruces University ospital, Bilbao, Spain, [29]Dept. of Medicine, Hospital Universitario Puerta de Hierro, Madrid, Spain, [30]Dept. of General and Digestive Surgery, Hospital Universitario "Rio Hortega", Valladolid, Spain, [31]Dept. of Surgery, Medizinische Klinik iv Universitaetsklinken, Magdeburg, Germany, [32]Dept. of General Surgery and Transplantation, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [33]Dept. of Surgery, Hôpital Universitaire de Genève, Geneve, Swiss, [34]Dept. of Surgery, University of Medicine "Carol Davila", Bucharest, Romenia [35]Dept. of Visceral, Transplant and Thoracic Surgery, University Hospital, Innsburck, Austria, [36]Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands. [37]Dept. of Medical Liver Transplant

Unit and Liver, Hôpital Henri Mondor, Creteil, France, [38]Dept. of Gastroenterology and Hepatology, Erasmus Transplant Institute, Erasmus MC, Rotterdam, The Netherlands.

14.40 Machine perfusion or cold storage in deceased-donor kidney transplantation - a 10 year follow up analysis (p. 63)
R. Schutter[1], C. Moers[2], H.G.D. Leuvenink[2], J. Pirenne[3], A. Paul[4], R.J. Ploeg[5], [1]Surgery, University Medical Centre Groningen, Groningen, The Netherlands, [2]Surgery, University Medical Center Groningen, Groningen, The Netherlands, [3]Surgery, University Hospital Leuven, Leuven, Belgium, [4]Surgery, University Hospital Essen, Essen, Germany, [5]Transplant Biology, University of Oxford, Oxford, UK.

14.50 Randomized controlled trial of dual hypothermic oxygenated machine perfusion in donation after circulatory death liver transplantation (p. 64)
R. van Rijn[1], I.J. Schurink[2], Y. de Vries[3], A.P. van den Berg[4], M. Cortes Cerisuelo[5], S. Darwish Murad[6], R.J. de Haas[7], N. Heaton[5], B. van Hoek[8], J.I. Erdmann[9], V.A.L. Huurman[9], I. Jochmans[10], O.B. van Leeuwen[3], V.E. de Meijer[3], D. Monbaliu[10], W.G. Polak[2], J.J.G. Slangen[7], R.I. Troisi[11], A. Vanlander[11], J. de Jonge[2], R.J. Porte[3], [1]Dept of Surgery, University Medical Centre Groningen, Groningen, The Netherlands, [2]Dept. of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands, [3]Dept. of Surgery, University Medical Center Groningen, Groningen, The Netherlands, [4]Dept. of Gastro-Enterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands [5]Institute of Liver Studies, Kings College Hospital NHS Foundation Trust, London, UK, [6]Dept. of Gastro-Enterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands [7]Radiology, University Medical Center Groningen, Groningen, The Netherlands [8]Dept. of Gastro-Enterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands [9]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands, [10]Dept. of Abdominal Transplantation Surgery and Coordination, University Hospitals Leuven, Leuven, Belgium, [11]Dept. of Transplant Surgery, Ghent University Hospital, Ghent, Belgium

15.00 Real-life tacrolimus targets are associated with biopsy-proven acute rejection after the first year post-transplantation in kidney transplant recipients (p. 65)
S. Meziyerh[1], T. Van Gelder[2], D. Van der Helm[3], P. van der Boog[4], J.W.de Fijter[1], D.J.A.R. Moes[2], A.P.J. de Vries[1], [1]Interne Geneeskunde - Nefrologie, LUMC, Leiden, [2]Klinische farmacologie en toxicologie, LUMC, Leiden, [3]LUMC Transplantatie Centrum, LUMC, Leiden, [4]Interne Geneeskunde, LUMC, Leiden, Nederland.

15.10 Randomized trial of ciclosporin with two hours post-dose monitoring versus tacrolimus with trough level monitoring in first liver transplantation; the DELTA study (p. 66)
B.N. Ruijter[1], A. Inderson[1], A.P. van den Berg[2], H. Metselaar[3], J. Dubbeld[4], M.E. Tushuizen[1], R. Porte[5], W. Polak[6], D. van der Helm[1], M. van Reeven[6], M. Rodriquez-Girondo[7], B. van Hoek[1], [1]Gastroenterologie en Hepatologie, LUMC, Leiden, [2]Gastroenterologie en Hepatologie, UMCG, Groningen, [3]Gastroenterologie en Hepatologie, Erasmus MC, Rotterdam, [4]Heelkunde, LUMC, Leiden, [5]Heelkunde, UMCG, Groningen, [6]Heelkunde, Erasmus MC, Rotterdam, [7]Medische Statistiek, LUMC, Leiden, Nederland.

15.30 Koffie- / theepauze

Parallel sessie IV – Basale abstracts **Grote Zaal (Weeshuis)**

Voorzitters: *Dr. Gonca Karahan, onderzoeker, LUMC*
Dr. Arnold van der Meer, medisch immunoloog, Radboudumc, Nijmegen

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

14.00 T-cell epitopes shared between immunizing and donor HLA associate with kidney allograft failure (p. 67)
E.T.M. Peereboom[1], B.M. Matern[1], T. Tomosugi[2], T. Kobayashi[3], A.D. van Zuilen[4], K. Geneugelijk[1], E. Spierings[1], [1]Center for Translational Immunology, UMC Utrecht, Utrecht, The Netherlands. [2]Dept. of Kidney Diseases and Transplant Immunology, Aichi Medical University School of Medicine, Nagakute, Japan. [3]Dept. of Renal Transplant Surgery, Aichi Medical University School of Medicine, Nagakute, Japan. [4]Dept. of Nephrology, UMC Utrecht, Utrecht, The Netherlands.

14.10 T-cell cytokine profiles after mRNA-1273 COVID-19 vaccination in kidney patients (p. 68)
Y. den Hartog[1], S.R.K. Malahe[1], M. Dieterich[1], D. Geers[2], M.M.L. Kho[1], R.D. De Vries[2], M.E.J. Reinders[1], C.C. Baan[1], [1]Internal Medicine, Nephrology and Transplantation, Erasmus MC, Rotterdam, [2]Viroscience, Erasmus MC, Rotterdam, The Netherlands.

14.20 Donor-specific hyporesponsiveness following kidney transplantation is explained by progressive loss of donor-reactive polyfunctional CD4+ effector memory T cells and could guide lowering of immune suppressive medication (p. 69)
A.C.J. van der List[1], N.H.R. Litens[1], M. Klepper[1], F. Prevoo[1], M.G.H. Betjes[2], [1]Interne Geneeskunde, Erasmus MC, Rotterdam, [2]Inwendige Geneeskunde, Erasmus MC, Rotterdam, Nederland.

14.30 Trained immunity determines long-term kidney allograft survival (p. 70)
W.I. Jonkman, M.M.E. Jacobs, N. Rother, C. Yanginlar, J.van der Vlag, R. Duivenvoorden, Nephrology, Radboudumc, Nijmegen, The Netherlands.

14.40 Effects of Natural Killer cell alloreactivity on allograft failure in kidney transplantation (p. 71)
B. Duygu[1], M. Groeneweg[1], B. Winkens[2], H.G. Otten[3], C.E.M. Voorter[1], L.. Wieten[1], [1]Transplantation Immunology, MUMC+, Maastricht, [2]Methodology and Statistics, MUMC+, Maastricht, [3]Laboratory of Translational Immunology, University Medical Centre Utrecht, Utrecht, The Netherlands. On behalf of the PROCARE 2.0 consortium

14.50 HLA-DQ-specific recombinant human monoclonal antibodies allow for in-depth analysis of HLA-DQ eplets (p. 72)
C.S.M. Kramer[1], S. Bezstarosti[1], M.E.I. Franke-van Dijk[1], M. Vergunst[1], K.H. Bakker[1], M. Uyar-Mercankaya[1], R. Buchli[2], D.L. Roelen[1], J.W. De Fijter[3], F.H.J. Claas[1], S. Heidt[1], [1]Immunology, Leiden University Medical Center, Leiden, The Netherlands, [2]Pure Protein, Pure Protein LLC, Oklahoma City, UK, [3]Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands.

15.00 Novel Avenue of Allograft Monitoring: Direct Measurement of Donor-Specific Extracellular Vesicles in Human Plasma (p. 73)
W.W.W. Woud, A. Merino, D.A. Hesselink, M.J. Hoogduijn, C.C. Baan, K. Boer, Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, The Netherlands.

15.10 T cell mediated immune rejection of kidney organoids transplanted in a humanized mouse model (p. 74)
L.H. Gaykema[1], R.Y. van Nieuwland[1], E. Lievers[1], C.W. van den Berg[1], A. Zaldumbide[2], A.J. Rabelink[1], [1]Nephrology, LUMC, Leiden, [2]Cell and Chemical Biology, LUMC, Leiden, The Netherlands.

15.30 Koffie- / theepauze

Parallel sessie V – Young Professionals **Blauwe Vogelzaal (Weeshuis)**

Voorzitters: *Dr. Femke Vrieling-Prince, kindernefroloog, Erasmus MC, Rotterdam*
Drs. Fenna van der Heijden, arts-onderzoeker transplantatiechirurgie, Erasmus MC, Rotterdam

Interactieve sessie over diversiteit en inclusiviteit.

14.00 Naar inclusieve geneeskunde
Prof. dr. Hanneke Takkenberg, hoogleraar klinische besliskunde bij cardiothoracale interventies, Erasmus MC en hoogleraar onderwijsmanagement bij Rotterdam School of Management (RSM)

15.30 Koffie- / theepauze

Parallel sessie VI – Klinische abstracts **Hooglandse kerk**

Voorzitters: *Prof. dr. André Baranski, hoogleraar Heelkunde, LUMC, Leiden*
Dr. Jeroen de Jonge, chirurg, Erasmus MC, Rotterdam

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

16.00 High humoral response in relation to immunosuppressive blood levels in liver transplant recipients after SARS-CoV-2 vaccination: an observational, cohort study (p. 75)
M.B. Mulder[1], A.A. van der Eijk[2], C.H. Geurts van Kessel[2], N.S. Erler[3], B.C.M. de Winter[1], W. Polak[4], H.J. Metselaar[5], C.M. den Hoed[6], [1]Ziekenhuisapotheek, Erasmus MC, Rotterdam, [2]Afdeling Virologie, Erasmus MC, Rotterdam, [3]Afdeling Statistiek, Erasmus MC, Rotterdam, [4]Afdeling Chirurgie, Erasmus MC, Rotterdam, [5]Afdeling Gastroenterologie en Hepatologie, Erasmus MC, Rotterdam, [6]Afdeling Gastroenterologie en Hepatologie, Erasmus MC, Rotterdam, Nederland.

16.10 Longevity of antibody and T cell responses after COVID-19 vaccination in patients with chronic kidney disease, on dialysis, or living with a kidney transplant (p. 76)
J.S.F. Sanders[1], F.J. Bemelman[2], A.L. Messchendorp[1], R. van Binnendijk[3], C.H. Geurts van Kessel[4], R.D. de Vries[4], R.T. Gansevoort[1], L.B. Hilbrands[5], M.E.J. Reinders[6], [1]Nefrologie, UMCG, Groningen, [2]Nefrologie, AUMC, Amsterdam, [3]RIVM, [4]Erasmus MC, Rotterdam, [5]Nefrologie, Radboud UMC, Nijmegen, [6]Nefrologie, Erasmus MC, Rotterdam, Nederland.

16.20 Stronger antibody response after vaccination with mRNA-1273 as compared to BNT162b2 and AZD1222 in patients with chronic kidney disease, dialysis patients, and kidney transplant recipients - results from the prospective RECOVAC Antibody Study (p. 77)
P. Bouwmans[1], A.L. Messchendorp[2], C. Imhof[2], J.S. Sanders[2], L. Hilbrands[3], M.E. Reinders[4], P. Vart[5], F.J. Bemelman[6], A.C. Abrahams[7], M.A. Van den Dorpel[8], M.A. Ten Dam[9], A.P.J. de Vries[10], T. Rispens[11], M. Steenhuis[11], R.T. Gansevoort[2], M.H. Hemmelder[12], [1]FHML, Maastricht Universiteit, Maastricht, [2]Nefrologie, UMCG, Groningen, [3]Nefrologie, Radboudumc, Nijmegen, [4]Nefrologie, Erasmus MC, Rotterdam, [5]Clinical Pharmacy and Pharmacology, UMCG, Groningen, [6]Nefrologie, Amsterdam UMC, Amsterdam, [7]Nefrologie, UMC Utrecht, Utrecht, [8]Nefrologie, Maasstad Ziekenhuis, Rotterdam, [9]Nefrologie, Canisius Wilhelmina Ziekenhuis, Nijmegen, [10]Nefrologie, LUMC, Leiden, [11]Immunopathologie, Sanquin Research, Amsterdam, [12]Nefrologie, MUMC+, Maastricht, Nederland.

16.30 SARS-CoV-2 vaccination response in tacrolimus treated kidney transplant recipients with and without mycophenolate mofetil: follow-up of a randomized controlled trial (p. 78)
Z. Al Fatly[1], M.G.H. Betjes[1], A.L. Messchendorp[2], J.S.F. Sanders[3], M.E.J. Reinders[1], M.M.L. Kho[1], A.E. de Weerd[1], [1]Nefrologie en niertransplantatie, Erasmus MC, Rotterdam, [2]Interne geneeskunde, UMCG, Groningen, [3]Nefrologie, UMCG, Groningen, Nederland.

16.40 Mucosal antibody responses following SARS-CoV-2 infection and vaccination in kidney patients and healthy controls (p. 79)
V.J.C.H. Koomen[1], J. Fröberg[2], R. Philipsen[1], W. Mattheussens[1], E. Simonetti[2], M.I. de Jonge[2], R.G. van der Molen[2], M.C. Baas[1], L.B. Hilbrands[1], D.A. Diavatopoulos[2], [1]Nierziekten, Radboudumc, Nijmegen, [2]Laboratoriumgeneeskunde/ Medische immunologie, Radboudumc, Nijmegen, Nederland.

16.50 Influence of COVID-19 vaccination on the presence and level of HLA antibodies in patients with chronic kidney disease, on dialysis, or living with a kidney transplant (p. 80)
L.B. Bungener[1], A. Hamad[1], B.G. Hepkema[1], A.L. Messchendorp[2], C. Imhof[2], J.S.F. Sanders[2], RECOVAC collaborators[3], [1]Laboratoriumgeneeskunde, UMCG, Groningen, [2]Interne Geneeskunde, UMCG, Groningen, [3]Interne Geneeskunde, UMCG, Radboudumc,, Erasmus MC, AUMC, Groningen, Nederland.

17.00 Humoral response to SARS-CoV-2 infection among liver transplant recipients (p. 81)
C. Beccheti[1], A.G.C. Broekhoven[2], G. Dahlqvist[3], M. Fraga[4], M.F. Zambelli[5], O. Ciccarelli[6], A. Saouli[7], A. Trizzino[5], V. Banz[1], J. Dufour[1], A.H.E. Roukens[8], M.C.W. Feltkamp[9], M.J. Coenraad[2], [1]University Clinic for Visceral Surgery and Medicine, Inselspital, University Hospital Bern, Bern, Swiss. [2]MDL, Leiden University Medical Center, Leiden, The Netherlands. [3]Hepatogastroenterology Unit, Cliniques Universitaires Saint-Luc, Brussel, Belgium. [4]Division of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois, Lausanne, Swiss. [5]Dept. of Surgery, General Surgery and Abdominal Transplant Unit, "Papa Giovanni XXIII" Hospital, Bergamo, Italy. [6]7Dept. of Abdominal Surgery and Transplantation, Cliniques Universitaires Saint-Luc, Brussel, Belgium. [7]5Division of Gastroenterology and Hepatology & Transplantation Center, Centre Hospitalier Universitaire Vaudois, Lausanne, Swiss. [8]Dept. of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands. [9]Dept. of Medical Microbiology, Leiden University Medical Center, Leiden, The Netherlands.

17.10 COVID-19 vaccination induces a poor IL-21 memory T-cell response in kidney transplant recipients (p. 82)
S.R.K. Malahe[1], Y. Den Hartog[1], R. de Kuiper[1], D. Reijerkerk[1], D. Geers[2], C.H. Geurts van Kessel[2], M.M.L. Kho[1], R.D. De Vries[2], M.E.J. Reinders[1], C.C. Baan[1], [1]Interne Geneeskunde, Nefrologie en Transplantatie, Erasmus MC, Rotterdam, [2]Viroscience, Erasmus MC, Rotterdam, Nederland.

17.20 SARS-CoV-2 spike-specific IFNγ T-cell response after COVID-19 vaccination in Patients With Chronic Kidney Disease, on Dialysis, or Living With a Kidney Transplant (p. 83)
C. Imhof[1], A.L. Messchendorp[1], M. Van Der Heiden[2], R.T. Gansevoort[1], J.S.F. Sanders[1], D. Van Baarle[2], [1]Nefrologie, UMCG, Groningen, [2]Medische Microbiologie, UMCG, Groningen, Nederland.

17.40 **Ledenvergadering NTV**

19.30 Diner Scheltema

Parallel sessie VII – Basale abstracts **Grote Zaal (Weeshuis)**

Voorzitters: *Dr. Dorottya K. de Vries, chirurg, LUMC, Leiden*
Dr. Martin Hoogduijn, universitair hoofddocent, Erasmus MC, Rotterdam

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

16.00 Kidney graft immunogenicity on normothermic machine perfusion (p. 84)
A.S. Arykbaeva[1], L.W.D. Knijff[2], S.H. Hendriks[3], J. Vos[1], S. Heidt[3], C. Van Kooten[2], I.P.J. Alwayn[1], D.K. De Vries[1], [1]Heelkunde, Leids Universitair Medisch Centrum, Leiden, [2]Nierziekten, Leids Universitair Medisch Centrum, Leiden, [3]Immunologie, Leids Universitair Medisch Centrum, Leiden, Nederland.

16.10 Functional differences between in vivo and ex vivo renal tissue oxygenation assessed with magnetic resonance imaging (p. 85)
T.L. Hamelink[1], B. Ogurlu[1], C.C. Pamplona[1], H. Qi[2], S.S. Bennedsgaard[2], J.H. Potze[3], M. Eijken[2], H.G.D. Leuvenink[1], E.S.S. Hansen[4], C. Laustsen[5], A.K. Keller[6], S. Ringgaard[4], R.J.H. Borra[3], C. Moers[1], [1]Dept. of Surgery - Organ Donation & Transplantation, UMCG, Groningen, The Netherlands. [2]Dept. of Renal Medicine, Aarhus University Hospital, Aarhus, Denemarken. [3]Dept. of Radiology, UMCG, Groningen, The Netherlands. [4]Dept. of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark. [5]Dept. of Clinical Medicine, UMCG, Groningen, The Netherlands. [6]Dept. of Urology, Aarhus University Hospital, Aarhus, Denmark.

16.20 A droplet digital PCR-based indel quantification method for the detection of circulating donor-derived cell-free DNA as biomarker for acute kidney transplant rejection (p. 86)
J.G.H.P. Verhoeven[1], K. Boer[2], A.M.A. Peters[2], M.C. Clahsen- van Groningen[3], J.I. Roodnat[2], J. Van de Wetering[2], D. Nieboer[4], D.A. Bost[5], C.C. Baan[2], D.A. Hesselink[2], [1]Interne Geneeskunde, Nefrologie en Transplantatiegeneeskunde, Erasmus MC, Rotterdam, [2]Interne Geneeskunde, Nefrologie en Transplantatiegeneeskunde, Erasmus MC, Rotterdam, [3]Pathologie, Erasmus MC, Rotterdam, [4]Public Health, Erasmus MC, Rotterdam, [5]JETA Molecular, Utrecht, Nederland.

16.30 Galunisertib suppresses fibrosis in an ex vivo renal transplantation model (p. 87)
L.L. van Leeuwen[1], H.G.D. Leuvenink[1], P. Olinga[2], M.J.R. Ruigrok[2], [1]Dept. of Surgery, University Medical Center Groningen, Groningen, [2]Dept. of Pharmaceutical Technology and Biopharmacy, University of Groningen, Groningen, The Netherlands.

16.40 A novel immunosuppressive compound (79-6) that targets BCL6 prevents the humoral alloresponse (p. 88)
R. Kraaijeveld, D.A. Hesselink, C.C. Baan, Dept. of Internal Medicine, transplantation and nephrology, Erasmus MC, Rotterdam, The Netherlands.

16.50 The Anti-Inflammatory Effect of Perfusate from Prolonged Normothermic Machine Perfused Discarded Human Donor Kidneys on Monocyte derived Dendritic Cells (p. 89)
L.W.D. Knijff[1], A.S. Arykbaeva[2], D.K. de Vries[2], I.P.J. Alwayn[2], R.J. Ploeg[3], C. van Kooten[1], [1]Nefrologie, Leiden Universitair Medisch Centrum, Leiden, Nederland. [2]Heelkunde, Leiden Universitair Medisch Centrum, Leiden, Nederland. [3]Chirurgische wetenschappen, Universiteit van Oxford, Oxford, VK.

17.00 Is urine the new blood? - Similarity of venous and urine pO2 values could lead to a new non-invasive clinical evaluation tool of renal oxygen consumption (p. 90)
C. Pamplona[1], T.L. Hamelink[2], L. Lantinga[2], B. Ogurlu[1], H. Qi[3], S.S. Bennedsgaard[4], J.H. Potze[5], M. Eijken[3], H.G.D. Leuvenink[1], E.S.S. Hansen ESS[6], C. Laustsen[6], A. Keller[4], S. Ringgaard[6], R.J.H. Borra[5], C. Moers[1], [1]Surgery, University Medical Center Groningen, Groningen, The Netherlands. [2]Surgery Dept., University Medical Center Groningen, Groningen, The Netherlands. [3]Renal Medicine, Aarhus University Hospital, Aarhus, Denmark. [4]Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark. [5]Radiology, University Medical Center Groningen, Groningen, The Netherlands. [6]Urology, Aarhus University Hospital, Aarhus, Denmark.

17.10 Changes in expression of bile-acid dependent transporters and cholesterol metabolism during hepatic normothermic machine perfusion (p. 91)
L.J. Stevens[1], N. Tramper[2], M.P. Caspers[3], L. Verschuren[3], J. Dubbeld[1], J.B. Doppenberg[4], B. van Hoek[5], W.H.J. Vaes[2], C.A.J. Knibbe[6], E. van de Steeg[2], I.P.J. Alwayn[1], [1]Dept. of Surgery, Leiden University Medical Centre, Leiden, [2]Metabolic Health Research, TNO, Leiden, [3]Systems Biology, TNO, Leiden, [4]Dept. of Surgery, Leiden University Medical Centre, Leiden [5]Gastroenterology and Hepatology, Leiden University Medical Centre, Leiden, [6]Div. of Systems Biomedicine and Pharmacology, Leiden Academic Centre for Drug Research (LACDR), Leiden, The Netherlands.

17.40 Ledenvergadering NTV

19.30 Diner Scheltema

Parallel sessie VIII – ODC Donatie **Blauwe Vogelzaal (Weeshuis)**

Voorzitters: *Marion van der Hoeven, Orgaan Donatie Coördinator, LUMC*
Jolanda Winnemuller, Orgaan Donatie Coördinator, Radboud UMC

Voordrachten in het Nederlands, 5 minuten presentatie en 2 minuten discussie.

16.00 Belevingsonderzoek bij nabestaanden van donoren (p. 92)
S.C. Jobse[1], A. van Willigen[2], N.E. Jansen[3], B. Schaefer[3], [1]Beleid & Orgaancentrum, Nederlandse Transplantatie Stichting, Leiden, [2]Donorvoorlichting, communicatie en onderwijs, Nederlandse Transplantatie Stichting, Leiden, [3]Beleid- en orgaancentrum, Nederlandse Transplantatie Stichting, Leiden, Nederland.

16.07 The Dutch National Focal Point for Organ Trafficking (p. 93) - presentatie vervalt
M. Timmermann[1], M. van der Steen[2], W. de Weijze[2], B. Schaefer[3], [1]Communicatie, Nederlandse Transplantatie Stichting, Leiden, [2]Project NFP, Nederlandse Transplantatie Stichting, Leiden, [3]Directie, Nederlandse Transplantatie Stichting, Leiden, Nederland.

16.14 Radiological screening methods in deceased organ donation: an overview of guidelines worldwide (p. 94)
K.A. Chotkan[1], J.W. Mensink[1], R.A. Pol[2], N.P. Van der Kaaij[3], W.N. Nijboer[1], L.F.M. Beenen[4], B. Schaefer[5], I.P.J. Alwayn[1], A.E. Braat[1], [1]Dept. of Surgery, Division of Transplantation, LUMC, Leiden, [2]Dept. of Surgery, Division of Transplantation, UMCG, Groningen, [3]Dept. of Cardiothoracic Surgery, UMCU, Utrecht, [4]Dept. of Radiology, Amterdam UMC, Amsterdam, [5]Policy & Education, Dutch Transplantation Foundation, Leiden, The Netherlands.

Woensdag 15 juni 2022

16.21 Preliminary results evaluation Quality Standard Donation – Dutch new donor law (p. 95)
B. Schaefer[1], B.J.J.M. Haase-Kromwijk[2], [1]Beleids & Orgaancentrum, NTS, Leiden, [2]NTS, NTS, Leiden, Nederland.

16.28 The effect of contrast-enhanced Computed Tomography in deceased kidney donors on transplantation outcomes (p. 96)
K.A. Chotkan[1], L.B. Hilbrands[2], B. Schaefer[3], C. Konijn[4], R.A. Pol[5], A.E. Braat[1], [1]Dept. of Surgery, Division of Transplantation, LUMC, Leiden, [2]Nephrology, Radboud UMC, Nijmegen, [3]Policy & Education, Dutch Transplantation Foundation, Leiden, [4]Data management, Dutch Transplantation Foundation, Leiden, [5]Dept. of Surgery, Division of Transplantation, UMCG, Groningen, The Netherlands.

16.34 Orgaandonatie na euthanasie: Het verhaal van Petra
N. Moret, Erasmus MC Rotterdam, fam. Kapitein

17.40 Ledenvergadering NTV

19.30 Diner Scheltema

Plenaire Sessie III **Hooglandse Kerk**

Thema: From bench to bioscience park

Voorzitters: *Prof. dr. Cees van Kooten, hoogleraar Experimentele nefrologie, LUMC, Leiden*
Prof. dr. Marlies Reinders, hoogleraar Inwendige geneeskunde, niertransplantatie, Erasmus MC, Rotterdam

09.00 Beenmergtransplantatie 2.0: autologe gentherapie
Prof. dr. Frank Staal, moleculair bioloog LUMC, Leiden

09.30 Van kweek naar kliniek; toepassing van stamcellen in orgaantransplantatie
Dr. Siebe Spijker, internist-nefroloog LUMC, Leiden

10.00 Een nieuwe, RNA-gebaseerde antivirale methode om vermenigvuldiging van het BK virus te remmen in niertransplantatie patiënten
Dr. Eric van der Veer, CSO & Founder, Hybridize Therapeutics, Leiden

10.30 Koffie- / theepauze

Parallel sessie IX – Klinische abstracts **Hooglandse Kerk**

Voorzitters: *Dr. Minneke Coenraad, MDL-arts, LUMC*
Dr. Sarwa Darwish Murad, MDL-arts, Erasmus MC, Rotterdam

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

11.00 Successful kidney transplantation in patients with hyperoxaluria: 7 years experience (p. 97)
J.I. Roodnat[1], M.M.L. Kho[1], A.M.E. de Mik-van Egmond[2], W.J. Visser[2], H.J.A.N. Kimenai[3], J. van de Wetering[1], D. Severs[1], M.E.J. Reinders[1], [1]Nefrologie en Transplantatie, Erasmus MC Transplant Institute, Rotterdam, [2]Dietetiek, Erasmus MC Transplant Institute, Rotterdam, [3]Heelkunde, Erasmus MC Transplant Institute., Rotterdam, The Netherlands.

11.10 Reducing cold ischemia time by donor liver 'back-table' preparation under continuous oxygenated machine perfusion of the portal vein (p. 98)
V.A. Lantinga[1], C.I. Buis[2], R.J. Porte[2], V.E. de Meijer[2], O.B. van Leeuwen[2], [1]Chirurgie, Universitair Medisch Centrum Groningen, Groningen, [2]Hepato-Pancreato-Biliaire (HPB) chirurgie, Universitair Medisch Centrum Groningen, Groningen, Nederland.

11.20 Chronic active antibody-mediated rejection is the major cause of kidney graft failure long after transplantation: results of a cohort of recipients with a very long-time follow-up after transplantation (p. 99)
M.G.H. Betjes[1], D.L. Roelen[2], M. van Agteren[3], J. Kal-van Gestel[3], [1]Nephrol;ogy and Transplantation, Erasmus MC, Rotterdam, [2]Dept. of Immunology, Leiden University MC, Leiden, [3]Nephrology and Transplantation, Erasmus MC, Rotterdam, The Netherlands.

11.30 Systematic review and meta-analysis of TTV load as marker of infection and rejection in solid organ transplantation (p. 100)
A.L. van Rijn[1], R. Roos[2], J.I. Rotmans[3], M.C.W. Feltkamp[1], [1]Medical Microbiology, Leiden University Medical Center, Leiden, [2]Internal Medicine, Haga Hospital, Den Haag, [3]Internal Medicine, division Nephrology, Leiden University Medical Center, Leiden, The Netherlands.

11.40 Tacrolimus high metabolizers in a cohort of kidney transplants in Amsterdam Retrospective cohort study (p. 101)
N.A. Manson[1], M. Vergouwe[2], L. Vogt[2], F.J. Bemelman[3], [1]Nephrology, Amsterdam University Medical Centers, Amsterdam, [2]Nephrology, Amsterdam University Medical Centers, Amsterdam, [3]Nephrology, Amsterdam University Medical Centers, Amsterdam, The Netherlands.

11.50 Impact of endoscopic ultrasound in unresectable perihilar cholangiocarcinoma patients in liver transplantation work-up (p. 102)
D.M. de Jong[1], C.M. den Hoed[2], F.E.J.A. Willemsen[3], M.J. Bruno[1], B. Groot Koerkamp[4], J. de Jonge[5], V.A.L. Huurman[6], J.E. van Hooft[7], F. Hoogwater[8], F. van der Heide[9], A. Inderson[7], F.G.I. van Vilsteren[9], L.M.J.W. van Driel[1], [1]Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [2]Gastroenterology and Hepatology & Erasmus MC Transplant Institute, Erasmus University Medical Center, Rotterdam, [3]Radiology and Nucleair Medicine, Erasmus University Medical Center, Rotterdam, [4]Surgery, Erasmus University Medical Center, Rotterdam, [5]Surgery & Erasmus MC Transplant Institute, Erasmus University Medical Center, Rotterdam, [6]Surgery, Leiden University Medical Center, Leiden, [7]Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [8]Surgery, Groningen University Medical Center, Groningen, [9]Gastroenterology and Hepatology, Groningen University Medical Center, Groningen, The Netherlands.

12.00 Development and validation of a prediction model for nonseroconversion after SARS-CoV-2 vaccination in kidney transplant recipients (p. 103)
S.C. Frölke[1], P. Bouwmans[2], A.L. Messchendorp[3], F.J. Bemelman[4], M.H. Hemmelder[5], R.T. Gansevoort[3], L..B. Hilbrands[6], M.E.J. Reinders[7], J.S.F. Sanders[3], H. Peters-Sengers[4], [1]Interne geneeskunde, nefrologie , Amsterdam UMC, locatie AMC, Amsterdam, [2]Interne geneeskunde, nefrologie, Maastricht UMC+, Maastricht, [3]Interne geneeskunde, nefrologie, Universitair Medisch Centrum Groningen, Groningen, [4]Interne geneeskunde, nefrologie, Amsterdam UMC locatie AMC, Amsterdam, [5]Interne geneeskunde, nefrologie, Maastricht UMC+, Maastricht, [6]Interne geneeskunde, nefrologie, Radboud Universiteit, Nijmegen, [7]Interne geneeskunde, nefrologie, Erasmus MC, Rotterdam, Nederland, RECOVAC Collaborators.

12.10 Poor Sleep Quality, Fatigue, Social Participation and Health-Related Quality of Life in Kidney Transplant Recipients (p. 104)
D. Kremer[1], T.J. Knobbe[1], A.W. Gomes-Neto[1], M.F. Eisenga[1], M. van Londen[1], R.M. Douwes[2], J.H. Annema[3], U. Bültmann[3], I.P. Kema[4], G. Navis[1], S.P. Berger[1], S.J.L. Bakker[1], [1]Nefrologie, UMCG, Groningen, [2]MDL, UMCG, Groningen, [3]Gezondheidswetenschappen, UMCG, Groningen, [4]Medische en analytische chemie, UMCG, Groningen, Nederland.

12.30 Lunch met gemodereerde postersessies

Parallel sessie X – Basale abstracts **Grote Zaal (Weeshuis)**

Voorzitters: *Dr. Marten Engelse, hoofd Laboratorium Regeneratieve geneeskunde en eilandjes van Langerhans transplantatie, LUMC*
Dr. C. Moers, chirurg, UMC Groningen

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

11.00 Functional recellularized patient derived endothelium; a human vascular graft approach (p. 105)
H. Tejeda Mora[1], J. Willemse[2], Y. den Hartog[1], I. Schurink[2], M.M.A. Verstegen[2], J. de Jonge[2], R.C. Minnee[2], M.W.F. van den Hogen[3], C.C. Baan[1], L.J.W. van der Laan[2], M.J. Hoogduijn[1], [1]Erasmus MC Transplant Institute, Dept. of Internal Medicine, Erasmus Medical Center, Rotterdam, [2]Erasmus MC Transplant Institute, Dept. of Surgery, Erasmus Medical Center, Rotterdam, [3]Erasmus MC Transplant Institute, Erasmus Medical Center, Rotterdam, The Netherlands.

11.10 Improved nephron maturation and stromal composition upon vascularization of kidney organoids (p. 106)
M. Koning[1], S. Dumas[2], C. Avramut[3], R. Koning[3], E. Meta[2], E. Lievers[1], L. Wiersma[1], J. Mulder[4], S. Spijker[1], T. Jaffredo[5], B. van den Berg[1], P. Carmeliet[2], T. Rabelink[1], [1]Dept. of Internal Medicine - Nephrology, Leiden University Medical Center, Leiden, [2]Dept. of Oncology, Laboratory of Angiogenesis and Vascular Metabolism, KU Leuven, Leuven, Belgium. [3]Dept. of Cell and Chemical Biology, Leiden University Medical Center, Leiden, The Netherlands. [4]Dept. of Pediatrics, Leiden University Medical Center, Leiden, The Netherlands. [5]Developmental Biology Laboratory, Sorbonne Universite, Paris, France.

11.20 Creating a kidney-vasculature interaction model using a novel organ-on-chip system (p. 107)
A. Bas-Cristóbal Menéndez[1], Z. Du[2], H. Lin[2], H. Tejeda[2], T. van den Bosch[3], N. Gaio[4], A. Othman[4], A. Merino[2], M. Hoogduijn[2], [1]Internal medicine / Pediatrics, Erasmus MC, Rotterdam, [2]Internal medicine, Erasmus MC, Rotterdam, [3]Pathology, Erasmus MC, Rotterdam, [4]Company, Bi/Ond systems, Delft, The Netherlands.

11.30 Large-scale engineering and cryopreservation of hiPSC-derived nephron sheets (p. 108)
L.E. Wiersma[1], M.C. Avramut[2], E. Lievers[3], T.J. Rabelink[3], C.W. van den Berg[3], [1]Dept. of Internal Medicine - Nephrology, Leiden University Medical Center, Leiden, [2]Dept. of Cell and Chemical Biology - Electron Microscopy, LUMC, Leiden, [3]Dept. of Internal Medicine - Nephrology, LUMC, Leiden, The Netherlands.

11.40 Bile duct on a chip: engineering a microfluidic platform for studying biliary epithelium in a dish (p. 109)
J. Willemse[1], M.N.S. de Graaf[2], G.S. van Tienderen[1], L.J.W. van der Laan[1], V. Orlova[2], M.M.A. Verstegen[1], J. de Jonge[1], [1]Dept. of Surgery, Erasmus MC Transplant Institute, Rotterdam, [2]Dept. of Anatomy and Embryology, Leiden University Medical Center, Leiden, The Netherlands.

11.50 Single-cell RNA sequencing of human pancreatic islets reveals a role of pancreatic duct cells as mediator of the inflammation during the early stage of T1D (p. 110)
A.M.G. Amadeo[1], N.G. Nathalie[2], F.L. Floris [2], A.Z. Arnaud[3], E.D.K. de Eelco[1], F.C. Françoise[1], [1]Dept. of Internal Medicine, LUMC, Leiden, [2]Hubrecht Institute, Hubrecht Institute, Utrecht, [3]Cell & Chemical Biology, LUMC, Leiden, The Netherlands.

12.00 A novel approach for the generation of substantial numbers of intrarenal T cells from kidney biopsies allows for in-depth characterization at the single cell level (p. 111)
N.H.R. Litjens, F. Prevoo, M. Klepper, M.G.H. Betjes, Internal Medicine, Division of Nephrology and Transplantation, Erasmus MC, Transplant Institute, Rotterdam, The Netherlands.

12.10 Towards a GMP-compliant protocol for the differentiation of human pluripotent stem cells to Beta-like cells for the treatment of type 1 diabetes (p. 112)
B.R. Rajaei, B.B. Brinkhof, A.M.G. Muñoz García, E.D.K. de Koning, F.C. Carlotti, Nephrology, Leiden University Medical Center, Leiden, The Netherlands.

12.30 Lunch met gemodereerde postersessies

Parallel sessie XI – Verpleegkundig **Blauwe Vogelzaal (Weeshuis)**

Voorzitters: *Koen van Duin, physician assistant, LUMC*
Dr. Coby Annema, senior onderzoeker, UMCG, Groningen

11.00 Prehabilitation of Candidates for Renal transplantation; the PreCareTx project (p. 113)
A.J. Haanstra[1], C. Annema[1], S.J.L. Bakker[2], A.V. Ranchor[3], S.P. Berger[2], E.J. Finnema[1], [1]Gezondheidswetenschappen, sectie verpleegwetenschap, Universitair Medisch Centrum Groningen, Groningen, [2]Nefrologie, Universitair Medisch Centrum Groningen, Groningen, [3]Gezondheidswetenschappen, sectie Gezondheidspsychologie, Universitair Medisch Centrum Groningen, Groningen, Nederland.

11.10 Nierteam aan Huis, online netwerkvoorlichting ten tijde van COVID-19 (p. 115)
S.P.F. Hopman, M. Lobeek, Nierziekten, Radboudumc, Nijmegen, Nederland.

11.20 Ervaringen van nierdonoren in de periode vanaf ontslag uit het ziekenhuis tot 3 maanden na donatie: een exploratief kwalitatief onderzoek (p. 116)
S.R.C. Das, P.T.R. Ulrichts, E.M. van Duijnhoven, Interne geneeskunde/nefrologie, MUMC+, Maastricht, Nederland.

11.30 Bacteriële infecties na levertransplantatie.
R. Muiselaar, Transplantatie Centrum, LUMC, Leiden

11.45 Een ontvanger van een varkensniertransplantatie op de afdeling: hoe bereiden we ons hier op voor?
I.P.J. Alwayn, Transplantatie Centrum, LUMC, Leiden

Donderdag 16 juni 2022

12.30 Lunch met gemodereerde postersessies

Postersessie 4 – Basale abstracts **Noordtransept Hooglandse Kerk**

Tijd: 12.45 uur

Moderatoren: *Dr. Jason Doppenberg, hoofd OPR, LUMC*
Dr. Volkert Huurman, chirurg, LUMC

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

18. Hemofiltration improves the diluted whole blood perfusate of the isolated slaughterhouse porcine heart perfusion model (p. 117)
S.E. Kaffka genaamd Dengler[1], M. Mishra[1], M.T. Vervoorn[1], S. van Tuijl[2], P.A. Doevendans[3], N.P. van der Kaaij[1], [1]Cardiothoracale chirurgie, UMC Utrecht, Utrecht, [2]R&D, LifeTec Group, Eindhoven, [3]Cardiologie, UMC Utrecht, Utrecht, Nederland.

19. H2S-enriched flush-out in DBD and non-DBD porcine kidneys (p. 118)
H. Maassen[1], L.H. Venema[2], M.G. Weiss[3], T.M. Huijink[2], H.S. Hofker[2], A.K. Keller[4], T.E. Mollnes[5], M. Eijken[3], S.E. Pischke[5], B. Jespersen[3], H. van Goor[6], H.G.D. Leuvenink[2], [1]Pathology and medical biology, Surgery, UMCG, Groningen, The Netherlands. [2]Surgery, UMCG, Groningen, The Netherlands. [3]Nephrology, Aarhus university hospital, Aarhus, Denmark. [4]Urology, Aarhus university hospital, Aarhus, Denmark. [5]Immunology, Oslo university hospital, Oslo, Norway. [6]Pathology and medical biology, UMCG, Groningen, The Netherlands.

20. The effect of different nutrients on mitochondrial function during long term incubation of precision-cut kidney slices (p. 119)
L.A. van Furth[1], D. Efraimoglou[1], L.H. Venema[1], A. Gerding[2], B.M. Bakker[3], R.W.F. De Bruin[4], H.G.D. Leuvenink[1], [1]Surgery - organ donation and transplantation, UMCG, Groningen, [2]Laboratory Medicine, UMCG, Groningen, [3]Pediatrics, UMCG, Groningen, [4]Surgery, Erasmus MC, Rotterdam, The Netherlands.

21. Hypothermic machine perfusion improves survival of the isolated slaughterhouse porcine heart (p. 120)
S.E. Kaffka genaamd Dengler[1], M. Mishra[1], S. van Tuijl[2], P.A. Doevendans[3], N.P. van der Kaaij[1], [1]Cardiothoracale chirurgie, UMC Utrecht, Utrecht, [2]R&D, LifeTec Group, Eindhoven, [3]Cardiologie, UMC Utrecht, Utrecht, Nederland.

22. Alteration of oxygenation during renal normothermic machine perfusion: hyperoxia versus normoxia (p. 121)
V.A. Lantinga, T.L. Hamelink, B. Ogurlu, I.M.van Tricht, J.G.van Leengoed, H.G.D. Leuvenink, C. Moers, Chirurgie, Universitair Medisch Centrum Groningen, Groningen, Nederland.

23. Mitochondrial damage and kidney function in DCD porcine kidneys using different flush out solutions (p. 122)
T.M. Huijink[1], H. Maassen[2], W.T. Heeman[1], K.D.W. Hendriks[3], N. Grashuis[1], S.P. Berger[4], H. Van Goor[5], H.G.D. Leuvenink[1], [1]Chirurgie, Universitair Medisch Centrum Groningen, Groningen, [2]Chirurgie en Pathologie, Universitair Medisch Centrum Groningen, Groningen, [3]Intensive Care, Universitair Medisch Centrum Groningen, Groningen, [4]Nefrologie, Universitair

Medisch Centrum Groningen, Groningen, [5]Pathologie, Universitair Medisch Centrum Groningen, Groningen, Nederland.

24. *Furosemide* but not desmopressin can induce changes in renal function during normothermic machine perfusion that could potentially serve as relevant add-on parameters for pre-transplant viability assessment (p. 123)
B. Ogurlu, T.L. Hamelink, V.A. Lantinga, H.G.D. Leuvenink, M.B.F. Pool, C. Moers, Surgery – Organ Donation and Transplantation, University Medical Center Groningen, Groningen, Nederland.

Postersessie 5 – Klinische abstracts **Noordtransept Hooglandse Kerk**

Tijd: 12.30 – 13.30

Moderatoren: *Dr. Maarten Tushuizen, MDL-arts, LUMC*
Drs. Jacob de Bakker, chirurg, LUMC

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

25. Subtle association between TTV-load and tacrolimus exposure in kidney transplant recipients (p. 124)
A.L. van Rijn[1], S. Meziyerh[2], D. van der Helm[2], T. van Gelder[3], A.C.M. Kroes[1], J.W. de Fijter[2], D.J.A.R. Moes[3], A.P.J. de Vries[2], J.I. Rotmans[2], M.C.W. Feltkamp[1], [1]Medical Microbiology, Leiden University Medical Center, Leiden, [2]Internal Medicine, division Nephrology, Leiden University Medical Center, Leiden, [3]Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, The Netherlands.

26. Histological heterogeneity in a kidney transplant: does one biopsy represent the whole kidney? (p. 125)
S. Truijen[1], A.D. van Zuilen [2], S.N. Knoppert[3], T.Q. Nguyen[3], B.J. Petri[1], [1]Vaatchirurgie, UMC Utrecht, Utrecht, [2]Nefrologie, UMC Utrecht, Utrecht, [3]Pathologie, UMC Utrecht, Utrecht, Nederland.

27. Population pharmacokinetics of subcutaneous alemtuzumab in kidney transplantation (p. 126)
T.C. Zwart[1], S. Bezstarosti[2], F.R. Achini[3], M.E.J. Reinders[4], M.W. Schilham[3], S. Heidt[2], H.J. Guchelaar[1], J.W. de Fijter[4], D.J.A.R. Moes[1], [1]Klinische Farmacie en Toxicologie, LUMC, Leiden, [2]Immunologie, LUMC, Leiden, [3]WAKZ, LUMC, Leiden, [4]Nefrologie en LUMC Transplant Center, LUMC, Leiden, Nederland.

28. Non-invasive, fast and accurate quantification of body composition in transplantation patients: The Future is Now! (p. 127)
T.D.A. Swaab[1], L.B. Westenberg[2], M. Zorgdrager[3], E.E. Quint[4], A.R. Viddeleer[3], S.J.L. Bakker[5], R.A. Pol[4], [1]Chirurgie - Orgaandonatie en Transplantatie, Universitair Medisch Centrum Groningen , Groningen, [2]Chirurgie - Orgaandonatie en Transplantatie, Universitair Medisch Centrum Groningen, Groningen, [3]Radiologie, Universitair Medisch Centrum Groningen, Groningen, [4]Chirurgie - Orgaandonatie en Transplantatie, Universitair Medisch Centrum Groningen, Groningen, [5]Interne Geneeskunde, Universitair Medisch Centrum Groningen, Groningen, Nederland.

29. A prior asymptomatic SARS-CoV-2 infection increases the magnitude of humoral and cellular responses in patients with chronic kidney disease, on dialysis, or living with a kidney transplant (p. 128)
S.R.K. Malahe[1], D. Geers[2], C.H. GeurtsvanKessel[2], M.M.L. Kho[1], C.C. Baan[1], M.E.J. Reinders[1], R.D. De Vries[2], [1]Interne Geneeskunde, Nefrologie en Transplantatie, Erasmus MC, Rotterdam, [2]Viroscience, Erasmus MC, Rotterdam, Nederland.

30. Multicenter long-term evaluation of post-transplant lymphoproliferative disease in adult liver transplantation: risk factors and prevention by Epstein-Barr viral load monitoring strategy (p. 129)
B.N. Ruijter[1], R. Wolterbeek[2], M. Hew[1], M. van Reeven[3], D. van der Helm[1], J. Dubbeld[4], M.E. Tushuizen[1], H. Metselaar[5], A.C.T.M. Vossen[6], B. van Hoek[1], [1]Gastroenterologie en Hepatologie, LUMC, Leiden, [2]Medische Statistiek, LUMC, Leiden, [3]Heelkunde, Erasmus MC, Rotterdam, [4]Heelkunde, LUMC, Leiden, [5]Gastroenterologie en Hepatologie, Erasmus MC, Rotterdam, [6]Medische Microbiologie, LUMC, Leiden, Nederland.

31. The dynamics of trans-renal oxidative stress during living donor kidney transplantation (p. 130)
N.A. Spraakman[1], A.M. Coester[2], A.R. Bourgonje[3], V.B. Nieuwenhuijs[4], J.S.F. Sanders[5], H.G.D. Leuvenink[2], H. van Goor[6], G.J. Nieuwenhuijs-Moeke[1], [1]Dept. of Anaesthesiology, University Medical Centre Groningen, Groningen, [2]Dept. of Surgery, University Medical Centre Groningen, Groningen, [3]Dept. of Gastroenterology and Hepatology, University Medical Centre Groningen, Groningen, [4]Dept. of Surgery, Isala Zwolle, Zwolle, [5]Dept. of Internal Medicine, Division of Nephrology, University Medical Centre Groningen, Groningen, [6]Dept. of Pathology and Medical Biology, University Medical Centre Groningen, Groningen, The Netherlands.

Parallel Sessie XII – Klinische/Basale abstracts — Hooglandse Kerk

Voorzitters: *Prof. dr. Teun van Gelder, hoogleraar Drug discovery & development, LUMC*
Dr. Aiko de Vries, internist-nefroloog, LUMC, Leiden

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

13.30 Tacrolimus withdrawal after mesenchymal stromal cell therapy is associated with donor-specific antibody formation in kidney transplant recipients (p. 131)
S. Bezstarosti[1], M.E.J. Reinders[2], J.W. de Fijter[2], S. Heidt[3], [1]Dept. of Immunology and Dept. of Internal Medicine (Nephrology), Leids Universitair Medisch Centrum, Leiden, [2]Dept. of Internal Medicine (Nephrology), Leids Universitair Medisch Centrum, Leiden, [3]Dept. of Immunology, Leids Universitair Medisch Centrum, Leiden, The Netherlands.

13.40 Impact of donor-specific antibodies in (highly-) immunized living donor kidney transplant recipients (p. 132)
T. Tramper[1], D.L. Roelen[2], M.E.J. Reinders[3], M.G.H. Betjes[3], J. Van de Wetering [3], J.I. Roodnat[3], M.M.L. Kho[3], S.H. Brand-Schaaf[2], J.A. Kal - van Gestel [3], A.E. De Weerd[3], [1]Dept. of Internal Medicine, Erasmus MC, Rotterdam, [2]Dept. of Immunology , HLA Laboratory, Leiden University Medical Centre, Leiden, [3]Dept. of Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, The Netherlands.

13.50 Clinically Relevant versus Irrelevant donor epitope specific HLA Antibodies in Predicting Kidney Transplantation Risk (p. 133)
D. Senejohnny, H. Otten, CTI, UMCU, Utrecht, The Netherlands.

14.00 CIAT: a major contribution to the number of transplantations in highly immunized patients and incompatible pair recipients compared to other available transplant programs (p. 134)
M. de Klerk[1], J. Kal[1], D. Roelen[2], M. Betjes[1], J. van de Wetering[1], A. de Weerd[1], M. Reinders[1], M. Kho[1], K. Glorie[3], J. Roodnat[1], [1]Internal Medicine, Erasmus MC Transplant Institute, Rotterdam, [2]Immunohematology and Blood Transfusion, LUMC, Leiden, [3]Econometrics, Erasmus Q-Intelligence EUR, Rotterdam The Netherlands.

14.10 PROCARE 2.0: Towards clinical prediction of kidney graft survival through immunelogical profiling (p. 135)
L.C. Reteig[1], H.G. Otten[1], [1]Center for Translational Immunology, University Medical Center Utrecht, Utrecht, On behalf of the PROCARE 2.0 consortium, PROCARE 2.0, The Netherlands.

14.20 Clinical and molecular profiling to develop a prediction model for the response to alemtuzumab therapy for severe or glucocorticoid-resistant kidney transplant rejection (p. 136)
D.M. Hullegie-Peelen[1], L. van Vugt[1], M. Van der Zwan[2], M.C. Clahsen-van Groningen[3], D.A.M. Mustafa[3], S.J. Baart[4], M.E.J. Reinders[1], C.C. Baan[1], D.A. Hesselink[1], [1]Interne geneeskunde - Nefrologie & Transplantatie, Erasmus MC, Rotterdam, [2]Nefrologie, Amsterdam Universitaire Medische Centra, Amsterdam, [3]Pathologie, Erasmus MC, Rotterdam, [4]Biostatistiek, Erasmus MC, Rotterdam, Nederland.

14.30 High alemtuzumab exposure is associated with delayed lymphocyte recovery in kidney transplant recipients (p. 137)
S. Bezstarosti[1], T.C. Zwart[2], F.R. Achini[3], M.W. Schilham[3], D.J.A.R. Moes[2], M.E.J. Reinders[4], J.W. de Fijter[4], S. Heidt[5], [1]Dept. of Immunology and Dept. of Internal Medicine (Nephrology), Leids Universitair Medisch Centrum, Leiden, [2]Dept. of Clinical Pharmacy and Toxicology, Leids Universitair Medisch Centrum, Leiden, [3]Dept. of Paediatrics, Leids Universitair Medisch Centrum, Leiden, [4]Dept. of Internal Medicine (Nephrology), Leids Universitair Medisch Centrum, Leiden, [5]Dept. of Immunology, Leids Universitair Medisch Centrum, Leiden, The Netherlands.

14.40 PIRCHE-II score is independently associated with the incidence of antibody-mediated rejection in a long-term follow-up cohort of kidney transplant recipients (p. 138)
M.G.H. Betjes[1], J. Kal-van Gestel[2], D.L. Roelen[3], M. van Agteren[2], E. Spierings[4], E.T.M. Peereboom[4], H.J. Otten[4], [1]Nephrol;ogy and Transplantation, Erasmus MC, Rotterdam, [2]Nephrology and Transplantation, Erasmus MC, Rotterdam, [3]Dept. of Immunology, Leiden University MC, Leiden, [4]Center for Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands.

15.00 Koffie- / theepauze

Parallel Sessie XIII – Klinische abstracts **Grote Zaal (Weeshuis)**

Voorzitters: *Drs. David Lam, chirurg, LUMC*
Dr. Remco van Dijk, MDL arts, LUMC

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

13.30 Electronic nose for distinguishing chronic lung allograft dysfunction phenotypes (p. 139)
N. Wijbenga[1], R.A.S. Hoek[1], B.J. Mathot[1], L.S. Seghers[1], D. Bos[2], O.C. Manintveld[3], M.E. Hellemons[1], [1]Respiratory Medicine, Erasmus MC, Rotterdam, [2]Radiology & Nuclear Medicine, Erasmus MC, Rotterdam, [3]Cardiology, Erasmus MC, Rotterdam, The Netherlands.

13.40 Prolonged preservation by hypothermic machine perfusion facilitates logistics in liver transplantation: a European observational cohort study (p. 140)
I.M.A. Brüggenwirth[1], M. Mueller[2], V.A. Lantinga[1], S. Camagni[3], R. de Carlis[4], L. de Carlis[4], M. Colledan[3], D. Dondossola[5], M. Drefs[6], J. Eden[7], D. Ghinolfi[8], D. Koliogiannis[6], G. Lurje[9], T.M. Manzia[10], D. Monbaliu[11], P. Muiesan[5], D. Patrono[12], J. Pratschke[9], R. Romagnoli[12], M. Rayar[13], F. Roma[5], A. Schlegel[7], P. Dutkowski[7], R.J. Porte[1], V.E. de Meijer[1], [1]HPB-surgery an Livertransplantation, University Medical Center Groningen, Groningen, The Netherlands. [2]Surgery and Transplantation, University Hospital Zürich, Zürich, Swiss. [3]Dept. of Organ Failure and Transplantation, ASST Papa Giovanni XXIII, Bergamo, Italy. [4]Dept. of General Surgery and Transplantation, ASST Grande Ospedale Metropolitano Niguarda, Milaan, Italy. [5]General and Liver Transplant Surgery Unit, University of Milan, Milaan, Italy. [6]Dept. of General, Visceral, and Transplant Surgery, University Hospital of Munich, München, Italy. [7]Dept. of Surgery and Transplantation, University Hospital Zürich, Zürich, Swiss. [8]Division of Hepatic Surgery and Liver Transplantation, University of Pisa Medical School Hospital, Pisa, Italy. [9]Dept. of Surgery, Universitätsmedizin Berlin, Dept. of Surgery, Campus Charité Mitte, Berlijn, Germany. [10]Hepato-Pancreato-Biliary and Transplant Unit, University of Rome Tor Vergata, Rome, Italy. [11]Dept. of Abdominal Transplant Surgery and Transplant Coordination, University Hospital Leuven, Leuven, Belgium. [12]AOU Città della Salute e della Scienza di Torino, University of Turin, Turijn, Italy. [13]Service de Chirurgie Hépatobiliaire et Digestive, CHU Rennes, Rennes, France.

13.50 Factors influencing access to Kidney transplantation (FIAT): An integrative multiphasic stakeholders' perspective (p. 141)
R.G. van Merweland[1], J.J. van Busschbach[1], J. van de Wetering[2], S.Y. Ismail Sohal[1], [1]Medische Psychologie, Erasmus MC, Rotterdam, [2]Nefrologie, Erasmus MC, Rotterdam, The Netherlands.

14.00 Early endocrine function after total pancreatectomy with islet autotransplantation (p. 142)
M.C. Tol[1], I.P.J. Alwayn[2], B.A. Bonsing[2], J. Dubbeld[2], M.A. Engelse[1], A. Haasnoot[1], M.D. Hellinga[3], J.E. van Hooft[4], V.A.L. Huurman[2], J.S.D. Mieog[2], M. Niesters[3], M.F. Nijhoff[1], E.J.P. de Koning[1], [1]Interne Geneeskunde, LUMC, Leiden, [2]Heelkunde, LUMC, Leiden, [3]Anesthesiologie, LUMC, Leiden, [4]Maag-, Darm- en Leverziekten, LUMC, Leiden, Nederland.

14.10 Development and determinants of health-related quality of life in elderly kidney transplant recipients (p. 143)
S.E. de Boer, D. Kremer, T.J. Knobbe, A.W. Gomes Neto, S.J.L. Bakker, S.P. Berger, J.S.F. Sanders, Nefrologie, UMCG, Groningen, Nederland.

14.20 Histological score of regulated necrosis executor phosphorylated MLKL is associated with increased risk for early allograft dysfunction after liver transplantation (p. 144)
S. Shi[1], I.J. Schurink[1], E. Bonaccorsi-Riani[2], M. Doukas[3], M.M.A. Verstegen[1], H.P. Roest[1], J.N.M. IJzermans[1], J. de Jonge[1], L.J.W. van der Laan[1], [1]Dept. of Surgery, Erasmus MC Transplant Institute, University Medical Center, Rotterdam, The Netherlands. [2]Abdominal Transplant Unit, Cliniques Universitaires Saint Luc, Université Catholique de Louvain, Brussels, Belgium. [3]Dept. of Pathology, Erasmus MC-University Medical Center, Rotterdam, The Netherlands.

14.30 Employment Status and Work Functioning among Kidney Transplant Recipients: Results of the TransplantLines Biobank and Cohort Study (p. 145)
T.J. Knobbe[1], D. Kremer[1], C. Annema[2], S.P. Berger[1], G.J. Navis[1], S.F. van der Mei[3], U. Bultmann[2], A. Visser[2], S.J.L. Bakker[1], [1]Nefrologie, UMCG, Groningen, [2]Gezondheidswetenschappen, UMCG, Groningen, [3]Gezondheidswetenschappen, UMCG, Groningen, Nederland.

14.40 The risks of endoscopic retrograde cholangiopancreatography after liver transplantation (p. 146)
K. Ghambari[1], D.M. de Jong[1], W. Polak[2], L.M.J.W. Van Driel[1], M.J. Bruno[1], C.M. den Hoed[1], [1]Maag-, darm- en leverziekten, Erasmus Medisch Centrum, Rotterdam, [2]Transplantatiechirurgie, Erasmus Medisch Centrum, Rotterdam, Nederland.

15.00 Koffie- / theepauze

Parallel Sessie XIV - Datagedreven zorg in transplantatieveld - Blauwe Vogelzaal Weeshuis

Voorzitters: *Dr. Paul van der Boog, internist-nefroloog, LUMC*
Dr. Martijn van den Hoogen, internist-nefroloog, Erasmus MC

13.30 Home monitoring with the SElf Care after REnal Transplantation (SECRET) kit in the COVID-19 pandemic (p. 147)
M.W.F. van den Hoogen, T. Both, M.C. de Haan-van Buren, M.N. Houthoff, L. Maasdam, M.E.J. Reinders, M. Salih, M. Tielen, J. van de Wetering, Inwendige Geneeskunde, sectie nefrologie en transplantatie, Erasmus MC Transplantatie Instituut, Rotterdam, Nederland.

13.55 Keuze nierfunctievervanging op basis van uitkomstdata
Prof. dr. Stefan Berger, internist-nefroloog, UMC Groningen

14.15 Dashboarding van NTS-data
Cynthia Konijn, Nederlandse Transplantatie Stichting

14.35 Up to date geïnformeerd over complicatiebeloop van transplantaties
Dr. Paul van der Boog, internist-nefroloog, LUMC

15.00 Koffie- / theepauze

Donderdag 16 juni 2022

Plenaire Sessie IV **Hooglandse Kerk**

Thema: Artificial Intelligence in de zorg

Voorzitters: *Dr. Dave Roelen, immunoloog, LUMC, Leiden*
Dr. Niels van der Kaaij, cardiothoracaal chirurg, UMC Utrecht

15.30 Artificial Intelligence in de zorg: van krantenkop naar klinische praktijk
Prof. dr. ir. Boudewijn Lelieveldt, hoogleraar Biomedische beeldvorming, LUMC, Leiden

Prijsuitreikingen **Hooglandse Kerk**

Voorzitters: *Prof. dr. Ian Alwayn, chirurg, voorzitter organisatiecomité LUMC*
Dr. Niels van der Kaaij, cardiothoracaal chirurg UMC Utrecht, voorzitter NTV

16.00 **Uitreiking LWTV Innovatie-Kwaliteitsprijs 2022**
door Marjo van Helden, voorzitter LWTV

Presentatie winnaar LWTV Innovatie-Kwaliteitsprijs 2021
Project: Waarden gedreven zorg evaluatie van magnetische blackstar JJ-catheter na nier-transplantatie
Esther Nijgh, nurse practioner, LUMC, Leiden

Jon J. van Roodprijs 2022
Uitgereikt door Prof. dr. F.H.J. Claas

Presentatie winnaar Jon J. van Roodprijs 2022
Immunomodulation of brain death-induced lung injury
Dr. Judith van Zanden, chirurg i.o., Medisch Spectrum Twente

Uitreiking NTV Wetenschapsprijs 2022
Uitgereikt door Dr. N.P. van der Kaaij, voorzitter NTV

Presentatie winnaar NTV Wetenschapsprijs 2021
Regenerative Medicine of the Liver; How to grow organoids in decellularized scaffolds
Dr. Monique Verstegen, Assistant professor, Erasmus MC

16.45 Sluiting Bootcongres 2022

Erythropoietin, renin and vitamin D release from human donor kidneys during normothermic machine perfusion: predictors of post-transplantation outcome?

Erythropoietin, renin and vitamin D release from human donor kidneys during normothermic machine perfusion: predictors of post-transplantation outcome?

Z. Du[1], H. Lin[2], S. Bouari[3], E. Rijkse[3], A.H.J. Danser[4], R.C. Minnee[3], M.J. Hoogduijn[1], [1]Dept. of Internal Medicine, Erasmus MC Transplant Institute, University Medical Center Rotterdam, Rotterdam, [2]Dept. of Internal Medicine, Vascular Medicine and Pharmacology, University Medical Center Rotterdam, Rotterdam, [3]Dept. of Surgery, division of HPB & Transplant Surgery, Erasmus MC Transplant Institute, University Medical Center Rotterdam, Rotterdam, [4]Dept. of Internal Medicine, Vascular Medicine and Pharmacology, University Medical Center Rotterdam, Rotterdam, The Netherlands.

Background: Normothermic machine perfusion (NMP) is a promising preservation strategy for donor kidneys before transplantation. Unlike hypothermic machine perfusion (HMP), NMP restores cellular metabolism which will potentially contribute to improvements on donor kidney function assessments.
Methods: We investigated three of the main hormones produced by kidneys including erythropoietin (EPO), prorenin/renin, and vitamin D. Ten donor kidneys were perfused using HMP followed by 2h of end- ischemic NMP before transplantation. NMP perfusate samples were collected at three time points (0h, 1h, 2h). Ten HMP perfusate samples were collected for the same measurements.
Results: EPO was secreted by kidneys on both HMP (13 mIU/min) and NMP (29 mIU/min) without significant differences. Between the first hour and the second hour of NMP, EPO release rate was maintained at similar levels (30 mIU/min). During the first hour of NMP, the release rates of prorenin (2500 pg/min) and renin (3000 pg/min) were 52-fold and 8-fold higher than that in HMP perfusates respectively ($p \leq 0.05$ and $p \leq 0.01$). The release rates of renin were downregulated two-fold during the second hour of NMP as compared to the first hour. Active Vitamin D was undetectable in HMP perfusate samples, while there was an average vitamin D secretion of 42 and 35 pmol/hour in the first and second hour of NMP respectively. By comparing the donation after circulatory death (DCD) kidneys to the donation after brain death kidneys on NMP, a significant 2. 6-fold higher renin release rate was detected in DBD kidneys compared to DCD kidneys during the second hour of NMP ($p \leq 0.01$). Renin release rate and the age of the donors showed a positive correlation ($r = 0.64$, $p = 0.047$) during the second hour of NMP treatment. Furthermore, the renin release rate was lower in the first hour of NMP when the donor kidney had longer duration of cold ischemia time (CIT) ahead of NMP ($r = -0.68$, $p=0.03$). Vitamin D release rate in first hour of NMP showed a positive correlation with donor age ($r = 0.607$, $p = 0.0628$). EPO release rate showed no correlation with age or CIT. Interestingly, during the second hour of NMP, vitamin D release rates were significantly correlated with delayed graft function (DGF) duration ($r=0.94$, $p \leq 0.001$).
Conclusions: These data show the functional hormone restoration by donor kidneys on NMP and provide a group of hormone levels for measurement during NMP to predict graft outcomes, which will be crucial for the refinement of NMP techniques.

Normothermic machine perfusion of diseased explanted livers of patients undergoing liver transplantation as novel preclinical model to study hepatic pharmacokinetic processes

L.J. Stevens[1], J. Dubbeld[1], J.B. Doppenberg[2], B. van Hoek[3], W.H.J. Vaes[4], C.A.J. Knibbe[5], E. van de Steeg[4], I.P.J. Alwayn[1], [1]Dept. of Surgery, Leiden University Medical Centre (LUMC), Leiden, [2]Heelkunde, Leiden University Medical Centre (LUMC), Leiden, [3]MDL, Leiden University Medical Centre (LUMC), Leiden,[4]Metabolic Health Research, TNO, Leiden, [5]Division of Systems Biomedicine and Pharmacology, Leiden Academic Centre for Drug Research (LACDR), Leiden, The Netherlands

Background: The prediction of hepatic clearance and biliary excretion is of high importance to assess the pharmacokinetics (PK) of drugs. This is particularly important in patients with hepatic diseases where altered liver function can result in an altered PK profile of the administered drugs. We therefore aim to develop a physiologically relevant human pre-clinical model to investigate drug PK utilizing normothermic machine perfusion (NMP) of explanted livers in patients undergoing liver transplantation. The aim of this study was to determine feasibility and to achieve stable NMP of these livers for at least 6 hours.
Methods: Up till now, eleven inclusion have been performed; seven cirrhotic livers (1xPrimary Biliary Cirrhosis (PBC), 3xNon-alcoholic Steatohepatitis (NASH), 3xAlcoholic Liver Disease (ALD) and four non-cirrhotic livers (1x Hepatocellular carcinoma with Hepatitis B viral disease (HBV+HCC) and three marginal livers declined for transplantation). After removal of the diseased liver, during liver transplantation, the portal vein and the hepatic artery were immediately flushed with a cold preservation solution. Back table reconstruction and cannulation of the portal vein and left and right hepatic artery was performed. Pressure controlled dual portal and arterial was initiated using the LiverAssist device at 37°C. Livers underwent NMP for 360 min. After 120 min, a bolus of a drug cocktail (rosuvastatin, metformin and furosemide) was applied to study drug pharmacokinetics. Samples from the perfusate and bile were taken at prespecified times
Results: Major differences were observed in the portal flow between the cirrhotic (543±283mL/min) and non-cirrhotic livers (1745±55mL/min). A relation was shown between the MELD score of the patient and the perfusate lactate levels, where livers with a lab MELD score >14, perfusate lactate remained increasing during the pefusion. Clearance of rosuvastatin showed to be decreased in the cirrhotic livers (AUC 8529±5020ng/mL) versus non-cirrhotic livers (AUC 175±69ng/mL). Biliary clearance of rosuvastatin varied between all livers from 4.55% in 120 min (HBV+HCC non-cirrhotic liver) to 0.12% in the NASH liver. Furosemide clearance was also decreased in cirrhotic livers (AUC 5680±1532ng/mL) vs non-cirrhotic livers (AUC 3174±1532 ng/mL). Regarding metformin, minor differences were observed in metformin clearance in cirrhotic livers (AUC 475±112ug/mL) vs non-cirrhotic livers (AUC 358±20ug/mL). Biliary clearance did not differ between the groups.
Conclusions: Here we demonstrate for the first time the use of NMP of explanted as a novel preclinical model to study hepatic clearance, biliary excretion under specific disease circumstances.

Single-cell sequence analyses of circulating T follicular helper cells during antibody-mediated rejection

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Background: T follicular helper (Tfh) cells play an important role during the development of antibody-mediated rejection following organ transplantation by stimulation of antibody-secreting B-cell proliferation and differentiation. Circulating T follicular helper (cTfh) cells, which are considered to represent a memory Tfh cell population, have previously been shown to promote B-cell differentiation and antibody secretion. In the current study, we aimed to unravel the functional phenotype of these cTfh cells using single-cell analyses.
Methods: $CD3^+CD4^+CXCR5^+PD1^+$ cTfh cells and $CD3^+CD4^+CXCR5^-$ T cells were isolated via FACS sorting from PBMCs of a renal allograft recipient who experienced antibody-mediated rejection. To analyze the RNA expression patterns of these T cells, single-cell RNA sequencing (scRNAseq) was performed. In addition, single-cell TCR sequencing was performed to link the scRNAseq data to TCR clonotypes.
Results: Compared to $CD3^+CD4^+CXCR5^-$ T cells, cTfh cells expressed high levels of several genes including *FOS* and *JUN*, transcriptional factors that play a vital role in effector T-cell differentiation, proliferation, and function, and *JUNB*, which has previously been shown to be highly expressed by cTfh cells. Clustering of the cTfh cells showed four clusters, three of which clustered together and one separate cluster. Compared to the rest of the cells and to the $CXCR5^-$ T cells, this separate cluster was observed to be more clonal. In addition, a high expression of cytotoxic genes such as *GZMK*, *GZMA*, and *NKG7* was observed, which might suggest cytotoxic capacity.
Conclusions: In conclusion, our preliminary data provide the first deep insight into the functional phenotype of cTfh cells during antibody-mediated kidney allograft rejection.

Extracellular Vesicles released during Normothermic Machine Perfusion are Associated with Human Donor Kidney Characteristics

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Background: Extracellular Vesicles (EV) represent stable, tissue specific nano-sized particles that reflect the conditional state of their tissue of origin. Here, the dynamic release and phenotype of kidney EV was characterized and quantified during Normothermic Machine Perfusion (NMP) of Expanded-Criteria Donor (ECD) kidneys to examine whether EV could function as a potential biomarker for assessing kidney quality before transplantation.
Methods: Eight discarded ECD kidneys (~13 ± 5 hours of cold ischemia, age 68 ± 7 (mean ± standard deviation), all male) were perfused in a closed system at 37 ^{0}C for 6 hours. Perfusates were taken before and at 1, 3 and 6 hours of NMP and examined with Nanoparticle Tracking Analysis (NTA) and Imaging Flow Cytometry (IFCM). For IFCM, perfusates were stained with the tetraspanins CD9, CD63 or CD81 (general EV markers), or a mix of these three markers in combination with CFDA-SE (a non-fluorescent molecule that acquires fluorescent properties after cleavage by intravesicular esterases) to identify, quantify and characterize EV.
Results: Analysis of perfusates with NTA revealed that the majority of nanoparticles present in the perfusates are <300 nm. For CFSE and the mix of tetraspanin double-positive EV, we observed a ~700 / 740 / 560 fold increase compared to EV levels before perfusion at 1, 3 and 6 hours of NMP, respectively. Analysis of EV concentrations with crude donor characteristics (e.g. age, cold ischemia time (CIT), kidney weight) and NMP viability characteristics (renal flow, renal flow resistance, urine production) revealed that double-positive EV are negatively correlated with CIT whilst positive correlations were found with donor age after the first hour of NMP. Furthermore, tetraspanin CD81 was found to represent the majority (~75%) of the excreted double-positive EV (CD9: ~16% / CD63 ~8%).
Conclusions: EV <300 nm are released by ECD kidneys during NMP with highest excretion levels during the first hour of perfusion. Tetraspanin CD81 is predominantly present on these EV, and EV concentrations were shown to be correlated with well-established indicators of kidney quality such as donor age and CIT. The characterization of the excreted EV as well as their correlation with clinical parameters provide a starting point to study their role as potential biomarkers of kidney quality.

Accumulation of individual cyto-/chemokines in perfusate during human ex vivo lung perfusion differs significantly per donor

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Background: To increase the supply of available donor lungs, ex vivo lung perfusion (EVLP) has been used to optimize marginal donor lungs for transplantation. Inflammatory cytokines/chemokines are present in perfusate during EVLP. However, there is little known which variables influence this cyto-/chemokine accumulation and the correlation with short term graft outcome is unknown. In this study, we have evaluated cyto-/chemokine production during EVLP time.
Methods: Between April 2019 and March 2021, 12 EVLP runs were performed. In 11 cases, perfusate samples were taken at t=0, 10, 30, and 45 minutes, and thereafter hourly until the end of perfusion. Supernatant was collected via centrifugation. Inflammatory cyto-/chemokines were quantitatively measured using Luminex.
Results: From the selected cyto-/chemokines, 13 (e.g., interleukin (IL)-1b, -6, -8, -10, -12, -18, C-C chemokine ligand (CCL) -2, -5, -19, -22, tumor necrosis factor alpha, thymus and activation regulated chemokine (TARC), and granulocyte colony-stimulating factor (G-CSF)) were present at least at one time point. We observed remarkable differences in cyto-/chemokine accumulation between each EVLP, e.g. some donors produced high levels of IL6 whereas others mainly produced CCL2. Some cyto-/chemokines were already present early (t=240 minutes) (IL18 and G-CSF). Preliminary results showed that lungs perfused in the supine position seemed to have higher concentrations of IL6. Primary graft dysfunction grade ≥1 seemed to be associated with higher levels of IL6, IL8 and IL18.
Conclusions: In conclusion, accumulation of individual cyto-/chemokines in perfusate during EVLP differed per donor, both in time and in degree. Although the sample size is rather small, concentrations of specific cyto/chemokines seemed to be correlated to early transplant outcome. We will evaluate in more detail if those differences could be correlated to other variables like donor characteristics and graft performance during EVLP.

Validation of the preclinical models for renal ischemia reperfusion injury. A systematic review.

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Background: Ischemia and subsequent reperfusion is inevitable during organ transplantation. Ischemia reperfusion injury, the paradoxical increase of tissue damage following reperfusion, is a major contributor to early graft dysfunction and compromises long-term outcomes. Despite decades of intense research and numerous preclinical successes, no intervention has been successfully translated to the clinic, an observation that implies a profound translational gap.
We recently identified metabolic failure as the mechanism underlying clinical renal ischemia reperfusion injury (delayed graft function). Similar conclusions were also reached for acute kidney injury following major surgery. These clinical leads now provide an opportunity to evaluate preclinical models. We therefore performed a systematic review of the preclinical studies that reported on metabolic aspects in the context of renal ischemia reperfusion injury, in order to identify parallels and incongruences between preclinical models and clinical context.
Methods: Systematic literature searches were performed in PubMed, EMBASE and Web of Science.
Results: The systematic searches identified 35 preclinical studies that reported (aspects of) the post-reperfusion metabolome. Most studies were performed in rats or mice, four in pigs, and two in dogs. A systematic inventory of these preclinical studies pointed to a series of translational hurdles.
Conclusions: This systematic review identified profound methodological inadequacies in preclinical studies of renal ischemia reperfusion injury. Altogether, inconsistencies amongst preclinical studies as well as profound translational gaps between preclinical and clinical studies provide a rationale for the failure to translate preclinical successes. Optimisation of the experimental models and consensus on optimal methodological practices is urgently needed.

Early exposure to tacrolimus is associated with BK-viremia in kidney transplant recipients

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Background: Evidence on the association of exposure to tacrolimus (Tac) or mycophenolic acid (MPA) and the incidence of BK viremia is absent. We investigated the association between therapeutic drug measurements (TDM) of Tac and MPA and consecutive BK viremia development.
Methods: 713 kidney transplant recipients (KTRs) transplanted at our center between 2013-2018 and treated with Tac, MPA and prednisolone, were selected from the local transplant database. Both trough levels (C_0) and area-under-the-curve (AUC) measurements of Tac and BK viral loads were determined according to local protocol. Exposure measurements were carried backwards to assess exposure on landmarks: month 1.5, 3 and 12. Patients with no measurement of Tac or MPA exposure were excluded, leaving 508 patients for analysis. The incidence and time to BK viremia (with load > limit of detection (LOD) and load > log 4) in the first year post-transplantation were the outcomes of interest. Hazard ratios (HR) of exposure of Tac and MPA were assessed and adjusted for confounders such as donor and recipient age and gender, number of human leukocyte antigen (HLA) mismatch, days on dialysis, induction therapy, and type of transplantation.
Results: In total, 83 out of 508 (16%) KTRs developed a BK viremia in their first year post-transplant. Tac exposure (both C_0 and AUC) on day 45 was significantly associated with subsequent development of BK viremia (load > LOD & load >log 4) with respectively unadjusted and adjusted HRs of 1.08 (95% CI: 1.02-1.14) and 1.08 (95% CI: 1.01-1.15) for 1 μg/L increase in C_0 and 20 mg*h/L increase in $AUC_{0\text{-}12h}$. Exposure of Tac on day 90 and 120 were not associated with incidence of BK viremia. No association between exposure to MPA and BK-viremia was found. Moreover, HR for Tac remained unchanged when adjusted for MPA exposure.
Conclusions: In KTR, Tac exposure on month 1.5 is associated with the incidence of BK viremia in a dose-dependent manner. This was not found for MPA. The explanation for this finding could be that tacrolimus is a more potent suppressor of Th-lymphocytes which play a vital role in boosting viral immunity and memory. To our knowledge, this is the first time that exposure to immunosuppressive drugs has been associated with the incidence of BK viremia. Future research is necessary to investigate causative and predictive impact of Tac exposure on BK-incidence, which may aid physicians balance between toxicity and efficacy within the first year of transplantation.

Tacrolimus 4-hour monitoring in liver transplant patients is non-inferior to trough monitoring: the randomized controlled FK04 trial.

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Background: After liver transplantation (LT), tacrolimus and ciclosporin treatment can lead to, partially concentration-dependent, chronic kidney disease. Monitoring ciclosporin after LT with two-hour levels reduced overexposure and led to better renal function than trough-monitoring (C0). For tacrolimus after LT, a four-hour level (C4) can give a reasonable approximation of total drug exposure. We evaluated whether monitoring tacrolimus in stable patients after LT by four-hour level (C4) was superior to C0 regarding renal function, rejection and metabolic parameters.
Methods: This was an open label randomized controlled trial in which C4 monitoring of tacrolimus BID (Prograft) was compared to trough (C0) monitoring in stable LT recipients. The target range for C4 of 7.8-16 ng/ml was calculated to be comparable with target C0 of 4-8 ng/ml. Primary endpoint was the effect on renal function and secondary endpoints were the occurrence of treated biopsy-proven acute rejection, blood pressure and metabolic parameters, during 3 months of follow-up.
Results: Fifty patients were randomized to C0 (n=25) or C4 (n=25) tacrolimus monitoring. There was no difference in renal function between the C0 and the C4 group ($p = 0.98$ and $p = 0.13$ for CG and MDRD at 3 months). Also, the creatinine levels in a 24h urine sample and the amount of proteinuria were similar ($p = 0.82$ and $p = 0.59$). None of the patients suffered from graft loss or was treated for rejection. Metabolic parameters did not differ between the two groups.
Conclusions: Tacrolimus 4-hour monitoring in stable LT patients is not superior to trough monitoring, regarding the effect on renal function, but is safe for use to facilitate tacrolimus monitoring in an afternoon outpatient clinic.

Intracellular Tacrolimus Concentration in CD3 T Lymphocytes and CD14 Monocytes and Association with Kidney Transplant Rejection

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Background: The intracellular tacrolimus concentration in peripheral blood mononuclear cells (PBMCs) (TAC[PBMC]) was proposed to better represent the active concentration than the pre-dose whole blood concentration (C_0). However, previous studies' results were inconsistent and did not correlate well with acute rejection. Since tacrolimus acts within T cells and other white blood cells such as monocytes, we investigated the association between the tacrolimus concentration in CD3 T lymphocytes and CD14 monocytes, and acute rejection after kidney transplantation.
Methods: A total of 37 kidney transplant patients who underwent a for-cause biopsy was enrolled in this case-control study. Sixteen of these had a biopsy-proven acute rejection (rejection group) and 21 patients had no rejection (control group). PBMCs that are used in this study were collected from both cryopreserved samples (retrospectively) and fresh samples (prospectively). CD3 and CD14 were isolated from PBMCs and measured for the intracellular tacrolimus concentration.
Results: The correlation between whole blood and the intracellular tacrolimus concentrations were poor, with a correlation coefficient of r=0.33 for PBMCs, r=0.54 for CD3, and r=0.67 for CD14. Remarkably, TAC[CD3] was significantly lower than TAC[CD14] (13.3(9.8-18.2) vs 72.8(57.3-101.7) pg/million cells (pg/m);p<0.001). Patients with rejection had a comparable whole blood $C_0$to those without rejection (mean 9.8±2.9 vs 8.8±3.3 ng/mL; p=0.32). Also, no difference was found between the rejection group and control group regarding the TAC[PBMC] (36.0(22.8-48.5) vs 34.0(32.0-45.5) pg/m;p=0.82), TAC[CD3] (13.1 (9.9 -15.7) vs 11.4 (8.3-13.3) pg/m;p=0.19), and TAC[CD14] (74.8 (58.6-105.1) vs 62.3 (51.0-78.8) pg/m;p=0.19). However, PBMCs that were freshly isolated showed significantly higher TAC[PBMC] compared with PBMCs from the cryopreserved samples (91.5(60.5-113.75) vs 34.5(28.1-47.0) pg/m;p<0.001). Subgroup analysis of the intracellular tacrolimus concentration from freshly isolated cells again did not show difference between the rejectors and non-rejectors.
Conclusions: Poor correlation between whole blood and intracellular tacrolimus concentration was found, necessitating the intracellular concentration measurement. The difference of TAC[CD3] or TAC[CD14] between patients with and without acute rejection could not be demonstrated. However, further optimization of the cell isolation process is needed since the difference between TAC[PBMC] from fresh and cryopreserved cells exists.

Effect of Epstein Barr Virus infection on pharmacokinetics of tacrolimus; report of a single center study

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Background: Liver transplantation in children is highly successful with a 20-years patients' survival of > 80%. Nowadays research in pediatric liver transplantation focuses on optimization of the long-term outcomes. One of the long-term outcomes is prevention of post-transplant lymphoproliferative disease by adjustment of tacrolimus in patients with high Epstein Barr Virus (EBV) viral load. Studies have shown a relationship between virus infections (like CMV and BK virus) and differences in tacrolimus pharmacokinetics. However, the effect of active EBV infection on tacrolimus pharmacokinetics is unknown. Therefore, the aim of the study is to investigate the tacrolimus pharmacokinetics, expressed as concentration-dose ratio, of pediatric liver transplantation patients before and during an EBV-infection.
Methods: All patients with active EBV replication, transplanted between 2008-2019 and aged at transplantation below the age of two years were included. The patients had a follow-up of one year. The EBV infection was considered active if EBV DNA was detected in whole blood by routinely screening of all our liver transplantation patients, using quantitative PCR. As part of routine screening blood was taken for both EBV PCR and tacrolimus trough levels at the same time. Patient characteristics such as reason for transplantation, age at transplantation and serostatus prior to transplantation were recorded from the clinical case records. The concentration (tacrolimus through level)-dose (tacrolimus daily dose) ratio was calculated from every patient. The concentration-dose ratio was compared before and during an EBV infection using the Wilcoxon test.
Results: Twenty-six patients were included. The main indication for liver transplantation was biliary atresia (77%) and were transplanted with a living donor (73%). Median age at transplantation is 0.69 years and median age at EBV infection is 1.05 years. Patients did not receive medication which could influence tacrolimus pharmacokinetics.
The median Tacrolimus concentration-dose ratios in the study population before and during EBV-infection were 2.71 and 2.37 and was not significantly different (p=0.18).
Conclusions: In our population of young liver transplantation patients EBV-infection had no effect on the pharmacokinetics of tacrolimus and this result can be used in the protocol for tacrolimus adjustments during the start of the EBV infection. This result is different to the reports of tacrolimus pharmacokinetics and other virus infections (CMV, BK virus) and our findings point towards a difference between viral immunological effects on hepatic CYP-enzymes.

The Effect of FK-binding Protein 12 and P-glycoprotein on the Intracellular Tacrolimus Concentration in CD3 T Lymphocytes and CD14 Monocytes

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Background: Little is known about the pharmacokinetics of intracellular tacrolimus, particularly in CD3 T lymphocytes and CD14 monocytes. In a previous study we demonstrated a significantly higher intracellular tacrolimus concentration in CD3 (TAC[CD3]) compared with CD14 (TAC[CD14]). Our objective was to investigate the role of 2 important proteins involved in intracellular tacrolimus distribution, namely FK-binding protein 12 (FKBP12) and P-glycoprotein (P-gp) to explain these differences in intra-cellular tacrolimus concentrations.
Methods: The experiments were conducted in samples from healthy volunteers. Rhodamine (Rh), which is also a substrate of P-gp (like tacrolimus), was used to determine the P-gp activity in CD3 and CD14. Western blot and flow cytometry were used to semi-quantify FKBP12 and P-gp expression between CD3 and CD14. To confirm the effect of P-gp on intracellular tacrolimus concentration, verapamil, a P-gp inhibitor, was added to the kidney transplant recipient's blood samples before the cell isolation process and intracellular tacrolimus measurement. Results were compared with the same blood samples not treated with verapamil.
Results: CD3 showed significantly lower percentage of Rh-positive cells after 2 hours incubation at 37 ◦C (61±14%) and 25 ◦C (80±9%) compared with 4 ◦C (94±4%) ($p<0.001$) . Adding verapamil completely negated this temperature effect. These results demonstrate that tacrolimus might leak from CD3 if the cells are not processed at 4 ◦Cor without P-gp inhibitor. In contrast, CD14 did not show any difference of the percentage of Rh-positive cells regardless of temperature or the addition of verapamil (98-99%). Flow cytometric analysis revealed a significantly higher expression of P-gp on CD3 than CD14 (mean fluorescence intensity: 793(606-863) vs 664(466-718); $p=0.012$) and a lower intensity of FKBP12 in CD3 than CD14 (182(70-232) vs 595(332-851); $p=0.012$). Western blot confirmed that CD3 had higher P-gp and lower FKBP band density than CD14. By adding verapamil to patient samples, TAC[CD3] was 53-100% higher than samples from the same patients in the absence of verapamil.
Conclusions: The higher activity of P-gp and the lower concentration of FKBP-12 explain the lower TAC[CD3] compared with TAC[CD14]. A substantial amount of tacrolimus is lost from CD3 during the cell isolation process if P-gp is not properly inhibited. Adding verapamil prevents tacrolimus leakage from these cells and lead to more reliable measurements of the tacrolimus concentration.

Ferric carboxymaltose and SARS-CoV-2 vaccination-induced immunogenicity in iron-deficient kidney transplant recipients: the EFFECT-KTx randomized, placebo-controlled clinical trial

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Background: Kidney transplant recipients (KTRs) have an impaired immune response after vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Iron deficiency (ID) impairs vaccine efficacy and is highly prevalent among KTRs. We aimed to investigate whether ID correction by ferric carboxymaltose (FCM) treatment improves humoral and cellular responses after SARS-CoV-2 vaccination in iron-deficient KTRs.
Methods: In this secondary analysis of an ongoing randomized, double-blind, placebo-controlled clinical trial, iron-deficient KTRs received one to four doses of 500 mg intravenous FCM or placebo with six-week intervals. In the primary intention-to-treat analysis we determined the effect of ID correction on anti-SARS-CoV-2 antibody titers (ELISA) and T-lymphocyte reactivity against SARS-CoV-2 (ELISPOT) following SARS-CoV-2 vaccination with mRNA-1273 (N=43) or mRNA-BNT162b2 (N=5).
Results: Out of the 48 trial participants (median age 53 (interquartile range 44-65) years, 53% male), 26 were assigned to receive FCM and 22 to receive placebo. FCM treatment efficiently restored iron status: serum ferritin levels increased from 49 (26-79) µg/L at baseline to 464 (272-621) µg/L at four weeks after the second vaccination (P<0.001 vs baseline; P<0.001 vs placebo group) and TSAT from 21±8% to 34±12% (P<0.001 vs baseline; P<0.001 vs placebo group), while ID persisted in the placebo group. At four weeks after the second vaccination, anti-SARS-CoV-2 IgG titers tended to be lower in the FCM arm (66.51 (12.02-517.59) BAU/mL; placebo arm: 115.97 (68.86-974.67) BAU/mL, P=0.07). SARS-CoV-2 specific T-lymphocyte activation did not differ between the study arms (FCM arm: 93.3 (0.85-342.5) IFN-ɣ spots per 10^6 PBMCs, placebo arm: 138.3 (0.0-391.7) IFN-ɣ spots per 10^6 PBMCs, P=0.83). SARS-CoV-2 IgG titer and T-lymphocyte reactivity against SARS-CoV-2 significantly correlated with each other (Spearman's rho 0.44, P=0.002), but not with ferritin levels at four weeks after the second vaccination (ferritin vs SARS-CoV-2 IgG titer, Spearman's rho -0.15, P=0.33; ferritin vs T-lymphocyte reactivity against SARS-CoV-2, Spearman's rho -0.01, P=0.98). Results were similar in a per-protocol analysis and in sensitivity analyses after exclusion of individuals with low total IgG levels at baseline or after exclusion of patients receiving mRNA-BNT162b2 vaccinations.
Conclusions: FCM treatment efficiently restored iron status in KTRs but did not improve the humoral or cellular immune response against SARS-CoV-2 after two vaccinations. (Funded by Dutch Kidney Foundation and Vifor; COVAC-EFFECT/EFFECT-KTx ClinicalTrials.gov number, NCT03769441)

A comparison between combined liver kidney transplants to liver transplants alone: the Dutch experience

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Background: Combined liver kidney transplant (CLKT) appears to be a straightforward treatment modality for patients with end stage liver disease and renal disease necessitating renal replacement therapy (RRT). However, it is less well-defined for patients with mild or moderate kidney dysfunction, where kidney dysfunction is (partly) reversible and the kidney transplant can be avoided.
The aim of this study is to compare clinical outcomes and post-transplant renal function between patients who received CLKT and patients who received liver transplantation alone (LTA), stratified by pre-transplant estimated glomerular filtration rate (eGFR).
Methods: The Dutch Organ Transplantation Registration (NOTR) database consists of 881 patients who received from January 1st 2000 to January 1st 2020 a CLKT (N = 52; 5.9%) or LTA (N = 829; 94.1%). All patients were stratified into groups according to the KDIGO guidelines based on eGFR at transplant.
Results: The pre-transplant eGFR was significantly lower in the CLKT group as compared to the LTA group (22.6 ml/min/1.73m² and 87.6 ml/min/1.73m², P < 0.001, respectively). The overall patient survival for the CLKT group was not significantly better in comparison with the LTA group (P = 0.245). Patients with Chronic Kidney Disease (CKD)-stadia 5 or receiving RRT at time of transplant had better patient survival in comparison with the LTA group (P=0.05). Patient survival between other CKD stadia (3a/3b/4) was non-significant. The patients of the CLKT group with CKD-stadia 5 or receiving RRT had statistically higher liver graft survival compared to the LTA group (P=0.035). Liver graft survival between other CKD stages was non-significant.
Conclusions: Patients with CKD-stadium 5 or receiving RRT appear to benefit most from CLKT over LTA. A stricter allocation policy when a patient should be placed on a waiting list for CLKT would reduce unnecessary kidney transplantation.

Living kidney donation in Blacks and possible barriers

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Background: Living kidney transplantation remains the best possible treatment for patients with end stage renal failure (ESRD). Blacks are at increased risk of ESRD but seem less likely to receive a living kidney transplant. This systematic review investigates the extent to which blacks with ESDR lag behind to whites to receive a living donor kidney and what the barriers are.
Methods: We searched the following databases: MEDLINE, EMBASE, the World Health Organisation, The Cochrane Library and Google Scholar.
Titles and/or abstracts of the studies retrieved were screened independently by two review authors. Quality of the studies was assessed by the Joanna Briggs Institute Critical Appraisal Tool.
Results: 9675 articles were retrieved, based on abstract and title articles 547 were selected, after full text screening 75 articles were used.
Most studies are from the Unites States of America. Blacks indeed participate less often to living kidney programs. Of all the living kidney transplants in 2019 blacks accounted for 13,1% versus whites 63,9%. Whereas in the OPTN/SRTR 2019 Annual Data report blacks account for 32,3% on the kidney transplant waiting list in comparison to 35,5% whites.
Reported barriers to living kidney transplantation are decreased coping with kidney disease and thereby rejection of a disease role, and an information gap and poor communication between patients, donors and health care professionals.
An imported factor is mistrust in the health care system, including in doctors and hospitals.
Furthermore, socio-economic barriers consisting of lower income, lack of financial support for transplantation medication and adequate financial planning pre and post transplantation also contribute to these barriers.
Medical barriers include obesity with a BMI > 35 for recipient and candidate donors, and a high prevalence of hypertension.
Literature on the situation of blacks in the UK and in Europe appears sparse, but here disparities are also present among different ethnic groups for living kidney donation. In the UK in 2019-2020 only 18% of living kidney donation recipients were ethnic minorities nevertheless they constitute 36% of the kidney transplant waiting list. In an analysis of our center in the Netherlands among kidney transplant recipients only 23% of the black patients received a living kidney transplant versus 59% of the whites.
Conclusions: In the United States blacks as compared to whites lag behind in participation to living kidney programs, the reasons why are multifaceted and include mistrust of the medical system, lack of communication, socioeconomic and medical factors. In Europe and the UK a similar disparity exists, but solid data are missing.

Experiences of the first cohort of unspecified living kidney donors in [name of Dutch transplantation centre] – indicators for improvement of care?

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Background: Unspecified living kidney donation (UKD) has been carried out in the Netherlands since 2000 and the number of unspecified kidney donors (UKDs) has grown ever since. The aim of this large retrospective qualitative study was to explore and analyse experiences of the first cohort of UKDs in [name of Dutch transplantation centre]. Information from this study could help improve the (follow-up) care for this group.
Methods: All UKDs who donated a kidney in [name of Dutch transplantation centre] between 2000-2016 were invited to participate. 106 UKDs participated (response rate 84%). Semi-structured interviews were conducted, recorded and transcribed verbatim. Topics were experiences with preparation, hospital admission, recovery and aftercare, reactions from others, and experiences with anonymity. Interviews were independently coded by 2 researchers in NVivo using an inductive approach.
Results: Reported experiences were: Satisfaction with donation process, Uncertainty about donor approval, Life on hold during workup, Donation requires perseverance and commitment, Interpersonal stress, Normalization of donation, Becoming an advocate for donation, Appreciation of anonymity, Persistent curiosity about donation outcome, Ample social support, and Dissatisfaction about hospital care. The latter theme included a perceived lack of empathy form the hospital staff, frustration about donation-related expenses and insufficient knowledge among general practitioners about living with one kidney.
Conclusions: UKDs are generally satisfied with the donation process and still feel good about the donation and helping a kidney patient. Although anonymity was highly appreciated by most donors, receiving anonymous feedback about the outcome of the transplantation was important for them. Some of the financial frustrations are less relevant due to changes in reimbursement since these donations took place, however ongoing education for healthcare professionals might help increase understanding of this type of donation and empathy towards these donors.

Illness perceptions and medication nonadherence to immunosuppressants after successful kidney transplantation: a cross-sectional study

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Background: Medication nonadherence to immunosuppressants is a well-known risk factor for suboptimal health outcomes in kidney transplant recipients (KTRs). The potential of illness perceptions as a treatment target for medication nonadherence in this population has not been well studied. Therefore, we examined this relationship in prevalent Dutch KTRs and whether this relationship depended on the time since their kidney transplantation.
Methods: Eligible KTRs transplanted in Leiden University Medical Center before April 2019 were invited to participate in this cross-sectional study. The Brief Illness Perception Questionnaire and the Basel Assessment of Adherence to Immunosuppressive Medication Scale were used to measure illness perceptions and medication nonadherence. Associations between illness perceptions and medication nonadherence were investigated using multivariable logistic regression models while adjusting for potential confounders.
Results: Of the 1700 invited patients, 627 participating KTRs were included in our analyses. 203 (32.4%) KTRs were considered nonadherent to their immunosuppressive treatment, with 'taking medication more than 2 hours from the prescribed dosing time' as the most prevalent nonadherent behaviour (n=171; 27.3%). Three illness perceptions were significantly associated with medication nonadherence: *illness identity* (adjusted odds ratio [OR_{adj}]=1.07; 95% confidence interval [CI], 1.00-1.14), *concern* (OR_{adj}=1.07; 95%CI,1.00-1.14), and *illness coherence* (OR_{adj}=1.11; 95%CI,1.01-1.22). The relationships between illness perceptions and medication nonadherence did not differ depending on time since transplantation *(*p-values ranged from 0.48 to 0.96).
Conclusions: Stronger negative illness perceptions are associated with medication nonadherence to immunosuppressants. Targeting negative illness perceptions by means of psychoeducational interventions could optimize medication nonadherence and consequently improve health outcomes in KTRs.

The influence of the donation procedure on the mental health of unspecified kidney donors

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Background: Unspecified kidney donation (UKD) makes a valuable contribution to the living donor pool, but the mental health of unspecified kidney donors and their motivation for donation remain the topic of much debate. Qualitative studies on these topics are scarce. In this large retrospective qualitative study, we explore how UKDs describe their mental health and the influence of the donation on their mental health.
Methods: All UKDs who donated a kidney in [a transplantation centre in the Netherlands] between 2000-2016 were invited to participate. 106/126 UKDs emi-structured interviews on various topics including their motivation for donation and mental health before, during and after the donation. Interviews were audio-recorded, transcribed verbatim and independently coded by 2 researchers in NVivo using an inductive approach.
Results: 41 participants reported having mental health problems before the donation. Eleven of these appeared to have ongoing or chronic psychiatric disorders. All other donors reported to be in good mental health before and after surgery. Motivations for donation included: Desire to help others, Affinity with kidney patients or donors, Triggered by (social) media, and Psychological gain. Mental health themes after donation included: Satisfaction and happiness, Empowering experience, Life-changing experience, Brief psychological distress, Persistent negative emotions, and Regret. In one case, the persistent negative emotions appeared to be related to the chronic mental health problems of this donor.
Conclusions: UKDs were mainly motivated to donate by a desire to help somebody. A small group of donors hoped to gain psychological benefits from donation. This was mainly expressed by donors with chronic psychiatric disorders or donors who experienced traumatic life events in the past. Apart from having (had) mental health problems, the donation did not seem to harm the mental health of our donors. Many donors reported a positive influence of the donation on their happiness and self-esteem. A handful of donors still experiences negative emotions when thinking about the donation and two donors regret the decision to donate. These findings make an important contribution to the ongoing discussion about whether donors with mental health problems should be allowed to donate.

Heart donation and transplantation of circulatory death donors: The Dutch experience

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Background: The significant shortage of donor hearts in the Netherlands can be reduced by the use of hearts of circulatory death donors. At the end of 2015, just after the first DCD heart transplants were performed in Australia and the UK, initiatives were undertaken to also start a DCD heart transplantation program in the Netherlands. On the 15th of March 2021, a national program, using the Direct Procurement and Perfusion approach, started with reimbursement of the Dutch government. Here we report the early outcome of DCD heart transplantation in the Netherlands.
Methods: After confirmation of death and respecting the five minute no touch period, donors were transferred to the OR, a sternotomy was performed, blood was collected, cardioplegia administered and the heart excised. Hearts were normothermically reperfused in the donor hospital with donor blood on the Organ Care System (OCS) of Transmedics. Hearts were transferred on the OCS to the recipient centers and implanted with conventional techniques. All essential time points from withdrawal of life support until reperfusion of the heart in the recipient were recorded. The following donor and recipient parameters were collected: Donor age, transplantation date, recipient age, underlying disease, recipient history of cardiac surgery, presence of a ventricular assist device (VAD), survival, incidence of primary graft dysfunction (PGD), postoperative extra corporeal life support (ECLS) and acute kidney injury (AKI) requiring dialysis.
Results: Between March and November 2021, 22 donor procedures were attended of which 1 did not proceed to donation. Of the remaining 21 donors, all hearts were placed on the OCS. Four hearts were declined for transplantation; two because of technical issues, one due to the suspicion of an abdominal malignancy and one due to vascular size mismatch. Seventeen hearts were transplanted resulting in a retrieval rate of 77%. Mean recipient age was 46 years and 10 patients were bridged with a long-term VAD (59%). The survival rate post-transplant was 100% at a maximal follow-up interval of 225 days. Two patients (12%) developed a severe PGD requiring veno-arterial ECLS (1 and 6 days) whereafter their cardiac function recovered to normal. Grade 2 rejection was found in one patient (6%) which was treated with solumedrol. Five patients developed AKI (29%) requiring short term dialysis.
Conclusions: Implementation of a DCD heart donation and transplantation program in the Netherlands resulted in 17 extra heart transplantations within a period of 8 months with an excellent survival. The incidence of recorded complications (PGD, ECLS support and rejection) were lower than the reported incidence in the UK and Australian cohort.

Short- and long-term maternal and pregnancy outcomes after orthotopic liver transplantation in the Netherlands

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Background: Pregnancy after orthotopic liver transplantation (OLT) potentially puts the mother, transplanted organ and child at risk. We performed a retrospective multicenter cohort study to evaluate maternal and pregnancy outcomes after OLT. Secondary aim was to assess predictors for adverse pregnancy outcomes.
Methods: Descriptive statistics, regression analysis, Kaplan Meier and generalized estimating equation analysis were used.
Results: We included 60 women with 94 pregnancies >20 weeks. In 86% (n=79) of the pregnancies a calcineurin inhibitor was used. In 23% of pregnancies hypertension and in 11% preeclampsia occurred. Live birth rate was 86%; 33% was born preterm and 22% with low birth weight (LBW). On univariable regression analysis pre-pregnancy serum creatinine >90 umol/L and pre-existent hypertension increased the composite adverse outcome risk (hypertension during pregnancy, preeclampsia, LBW, preterm birth, NICU admission) (OR 6.8, 3.2 respectively). On multivariable regression analysis only higher BMI increased the composite outcome risk (OR 1.135). Thirteen mothers (22%) died (median 8 years [IQR=4-12] after delivery), of which two within one year after delivery. Long-term follow-up (median 9 years [IQR=4-14]) showed a small increase in serum creatinine ($p<0.001$) and small decrease in bilirubin ($p=0.033$).
Conclusions: In conclusion, pregnancy after OLT leads to increased risk for short-term pregnancy complications, but these do not lead to long-term adverse outcomes. However, of importance for pre-pregnancy counseling, a substantial proportion of mothers does not see their child reach adulthood. This is probably mostly a result of complications from the OLT itself.

Long term outcomes of pancreas-after-kidney and islet-after-kidney transplantation

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Background: Pancreas-after-kidney (PAK) or islet-after-kidney (IAK) transplantation are treatment options in patients with type 1 diabetes and a previous kidney transplantation. Here we compare the long-term outcomes.
Methods: All consecutive subjects who had received a PAK or IAK transplantation between 2004 and 2019 with at least 1 year follow-up were included. The primary outcome was allograft function as defined by the Igls classification: 1) insulin independence, 2) good function (i.e. HbA1c <53 mmol/mol, reduced insulin requirement, no hypoglycemic events, C-peptide positive), 3) poor function (C-peptide positive but not 'good'), 4) graft failure (C-peptide negative). Treatment success was defined as a score of 1 or 2.
Results: There were 31 PAK (17M/14F) and 29 IAK (19M/10F) recipients with a mean follow-up of 5.4±3.2 years. PAK recipients were younger than IAK recipients (42.1±5.2 versus 51.9±10.3 years, p<0.001) and had a better kidney graft function (eGFR 52±10.1 versus 45.7±13.1 mL/min/1.73m^2, p=0.04). Baseline HbA1c was 68.5±21 versus 64±12.8 mmol/mol Hb, respectively (p=0.33).
One-year success rate was 68% in PAK versus 72% in IAK (insulin independence 65% versus 28%, complete graft failure 29% versus 10%, P<0.001)). Seven-year success rate was 60% (PAK) vs 57% (IAK) (p=0.6), insulin independence 47% versus 14% (p<0.001) and complete graft failure 33% versus 0%, (p=0.05). At seven years, HbA1c declined to 44.3±13.7 mmol/mol Hb (PAK; p=0.002) and 51.1±13.3 mmol/mol Hb (IAK (p=0.05) (PAK versus IAK p = 0.28). Estimated GFR declined from 52.0 to 30.6 mL/min/1.73m^2 (PAK; p=0.001) and from 45.7 to 29.0 mL/min/1.73m^2 (IAK; p=0.12) (PAK versus IAK p =0.85).
Mortality was 22.5% in PAK and 20.1% in IAK (p=0.38), predominantly due to cardiovascular disease.
Conclusions: Treatment success rates (Igls 1 and 2 categories) are comparable between PAK and IAK transplantation after 7 years. A greater proportion of PAK recipients achieved insulin independence but also complete graft failure.

Recent outcomes of liver transplantation for Budd Chiari Syndrome – Analysis of the European Liver Transplant Registry (ELTR) and affiliated centres - For the European Liver and Intestine Transplant Association (ELITA).

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Background: The management of Budd-Chiari Syndrome (BCS) has improved the last decades. However, no recent studies focusing on the outcomes after liver transplant for patients with BCS in Europe have been published. Therefore, the main objective of this study is to evaluate the post-liver transplant outcomes in Europe since 2000.
Methods: Data from all transplanted BCS patients till 2020 was obtained from the European Liver Transplantation Registry (ELTR). Patients age <16, secondary BCS and hepatocellular carcinoma were excluded. Patient survival (PS) and graft survival (GS) before and after 2000 were compared. Multivariate Cox regression-analysis identified predictors of PS and GS after 2000. Supplementary data was requested from all ELTR-affiliated centres and received from 44.
Results: 293 patients were transplanted before 2000 and 808 between 2000-2020. The median age was 37yrs, 63% was female, the median MELD-score was 18 and 30% had High Urgency (HU) listing. The 1-, 5- and 10-year PS before vs. after 2000 were 71%, 66% and 61% vs. 84%, 77% and 69% (p<0.01). GS was 63%, 58% and 52% vs. 78%, 71% and 62% (p<0.01). Since 2000, 12% received a re-transplant. Older recipient age (HR:1.03; 95%CI:1.01-1.04,p<0.01) and higher MELD-score (HR:1.03; 95%CI:1.00-1.05,p=0.03) were associated with worse PS. HU-listing was associated with improved PS (HR:0.58; 95%CI:0.36-0.94,p=0.03). Recipient gender (male) had no impact on GS (HR:0.69; 95%CI:0.46-1.04,p=0.08). Increased donor age was the only independent predictor of worse GS (HR:1.01; 95%CI:1.00-1.02,p<0.01). Of the 353 patients (44%) with supplementary data, 31% had myeloproliferative disease, 20% received TIPS pre-LT and 84% used anticoagulation post-LT. In this group, OAC post-LT was associated with better PS (HR:0.38; 95%CI:0.15-0.98,p<0.01) and GS (HR:0.51; 95%CI:0.29-0.92,p=0.03).
Conclusions: LT for BCS results in excellent patient- and graft survival, which have improved since 2000. Older recipient age and higher MELD result in poorer survival. HU listing appears to select patients with the most favourable outcome and long-term anticoagulation seems beneficial.

Machine perfusion or cold storage in deceased-donor kidney transplantation - A 10-year follow up analysis

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Background: In 2009 we reported the results of an international randomized controlled trial in which one kidney of each deceased donor was randomly assigned to hypothermic machine perfusion, and the contralateral organ was assigned to static cold storage. We observed that machine perfusion significantly reduced the risk of delayed graft function and that graft survival at 1 year was significantly better, as compared with static cold preservation. In 2012 the follow up period was extended, showing a significant superior overall 3-year graft survival for machine-perfused kidneys, especially in kidneys recovered from expanded criteria donors.
Methods: For this 10-year analysis, we contacted all 59 original participating transplantation centers to obtain data on graft survival, patient survival, serum creatinine level and glomerular filtration rate. This analysis included 672 recipients in the main data set (kidneys donated after brain death or after cardiocirculatory death), plus 80 recipients of kidneys donated after cardiocirculatory death in the extended data set.
Conclusions: At the moment of the deadline for this abstract we have reached a 93% data completeness and are awaiting the results of only two more participating centers. Given the potential impact of the outcomes of this long term follow up, no preliminary data analysis could be conducted for the purpose of this abstract. We will, however, be able to present these important and unique 10-year follow-up data for the first time to the Dutch transplant community during the upcoming Bootcongres.

Randomized controlled trial of dual hypothermic oxygenated machine perfusion in donation after circulatory death liver transplantation

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Background: Transplantation of livers from donation after circulatory death (DCD) donors is associated with an increased risk of non-anastomotic biliary strictures. Hypothermic oxygenated machine perfusion of livers may reduce the incidence of biliary complications, but data from prospective controlled studies are lacking.
Methods: In this multicenter, controlled trial we randomly assigned patients undergoing transplantation of a DCD liver to receive that liver after dual hypothermic oxygenated machine perfusion or conventional static cold storage alone (control group). The primary end point was the occurrence of non-anastomotic biliary strictures within 6 months after transplantation. Secondary end points included other graft-related and general complications.
Results: A total of 156 patients were enrolled; 78 participants received a machine perfused liver and 78 received a liver after static cold storage only. Non-anastomotic biliary strictures occurred in 6% of the patients in the machine perfusion group and 18% of the controls (risk ratio, 0.36; 95%CI, 0.14 to 0.94; P=0.03). Post-reperfusion syndrome occurred in 13% of the recipients of a machine perfused liver and in 27% of the controls (risk ratio, 0.43; 95%CI, 0.20 to 0.91; P=0.03). Early allograft dysfunction occurred in 26% of machine perfused livers vs. 40% of controls (risk ratio 0.61; 95%CI, 0.39 to 0.96; P=0.03). Cumulative number of treatments for non-anastomotic biliary strictures was 4-fold lower after machine perfusion, compared to controls. There were no significant differences in adverse events.
Conclusions: Hypothermic oxygenated machine perfusion reduced the risk of non-anastomotic biliary strictures after DCD liver transplantation by two-third.

Real-life tacrolimus targets are associated with biopsy-proven acute rejection after the first year post-transplantation in kidney transplant recipients

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Background: There is limited evidence to support immunosuppressive therapeutic target concentrations to balance efficacy and toxicity of immunosuppression after the first year of kidney transplantation (KT). We analyzed real-life data on therapeutic drug measurements (TDM) of Tac and MPA in kidney-only transplant recipients (KTRs) beyond the first year.
Methods: All 1862 KTRs, who used Tac, MPA, and Pred after the first year post-transplantation were selected from the local KT-database. Both trough levels (C_0) and area-under-the-curve (AUC) measurements of Tac were determined according to protocol. Patients without TDM between 6-18 months were excluded, leaving 475 patients for analysis. Intra-patient variability (IPV) of Tac C_0 levels were assessed for all KTRs and categorized in low (IPV < median) and high (IPV > median). Primary outcome was the incidence of biopsy-proven acute rejection (BPAR) between year 1-3 post-KT. Hazard ratios (HRs) of exposure of Tac and MPA were assessed and adjusted for human leukocyte antigen (HLA)-mismatch, and other transplant characteristics.
Results: In total, 16 out of 475 (3.4%) KTRs on triple therapy with Tac, MPA, and Pred suffered from BPAR between year 1-3 post-KT. Incidence of BPAR in KTRs with high IPV was 5% vs 1.3% in KTRs with low IPV (P=0.01).
Both $AUC_{0\text{-}12h}$ and C_0 of Tac were significantly associated with BPAR within 1 and 3 years posttransplant with an unadjusted HR of 0.55 (95% CI: 0.42-0.73; p<0.000) and adjusted HR of 0.44 (95% CI: 0.30-0.66; p<0.000) for every 20 mg*h/L increase in $AUC_{0\text{-}12h}$ and an unadjusted HR of 0.61 (95%CI: 0.49-0.76; p<0.000) and adjusted HR of 0.54 (95%CI: 0.40-0.70; p<0.000) for every 1 mg/L increase in Tac. $AUC_{0\text{-}12h}$ of MPA was not associated with BPAR. The probability of BPAR exponentially increased when AUC or C_0 levels of Tac go below respectively 75 mg*h/L or 5 μg/L. Higher levels did not result in meaningful reduction in BPARs. KTRs with low IPV had a lower risk of rejection with similar exposure compared to KTRs with high IPV. AUC measurements showed better association with BPAR as compared to C_0 measurements.
Conclusions: In KTR, BPAR after the first year post-transplantation is relatively uncommon in patients on triple therapy with Tac C_0 > 5 μg/L. There is little evidence to target a C_0 higher than 6-7μg/L since the impact on incidence of BPAR between year 1-3 year post-transplant is minimal, and risk of toxicity will increase. The association found between Tac and BPAR seems independent of HLA mismatch or other transplant characteristics. To our knowledge, this is the first study that investigates impact of simultaneous Tac and MPA TDM beyond the first year after KT which may help in defining long-term exposure.

Randomized trial of ciclosporin with two hours post-dose monitoring versus tacrolimus with trough level monitoring in first liver transplantation; the DELTA study

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Background: Calcineurin inhibitors ciclosporin and tacrolimus are the backbone of immunosuppression following liver transplantation (LT), but it is unclear whether ciclosporin is (non)inferior to tacrolimus.
Methods: This open-label parallel group randomized controlled trial aimed to demonstrate superior or equal efficacy, tolerability and safety of ciclosporin with 2-hour monitoring (C2) versus tacrolimus with trough monitoring (T0) after first LT. Primary endpoint was treated biopsy-proven acute rejection (tBPAR) at 3 months.
Results: 171 patients were randomized to C2 (N=85) or T0 (N=86). Cumulative incidences C2 vs T0: tBPAR at 3 months 17.7% (CI 9.3-26.1) vs 8.4% (CI 2.5-14.3)(HR 2.088 [CI 0.866-5.026], p=0.104); at 6 and 12 months 21.9% (CI 12.7-31.1) vs 9.7% (CI 3.4-16.0)(p=0.049) (HR=2.269 [CI 1.003-5.155], and HR= 2.275 [CI 1.003-5.155] at 6 and 12 months); For 1-year mortality 15.5% (CI 7.9-22.1%) vs 5.9% (CI 0.8-11.0%) (HR=2.704 [CI 1.005-7.284], p=0.049); for death-uncensored graft failure 23.8% (CI 14.8-32.8%) vs 9.4% (CI 3.1-15.7%)(HR=2.662 [CI 1.197-5.916], p=0.015). Serum creatinine, creatinine clearance, fasting blood glucose and incidence of hypertension were similar. Serum triglyceride (p=0.025) and LDL-cholesterol (p=0.013) were lower with T0 than C2. T0 vs C2 had a higher incidence of infection (51% vs. 49%,) and diarrhea (64% vs 31%, P=<0.001), less early (104 vs 127)(p=0.049) but more late infections (100 vs 63)(p=0.002), for other adverse and serious adverse events it was comparable.
Conclusions: The first 3 months after LT, C2 was non-inferior to T0 regarding tBPAR. However, at 6 and 12 months after LT tacrolimus (T0) was superior to ciclosporin (C2) for preventing tBPAR, and at 12 months also regarding mortality and re-transplantation-free survival.

T-cell epitopes shared between immunizing and donor HLA associate with kidney allograft failure

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Background: T-helper cells play an important role in alloimmune reactions following transplantation by stimulating humoral and cellular responses, which might lead to allograft failure. Previously, it has been shown that graft failure is more frequent in patients with non-donor-specific HLA antibodies as compared to patients without HLA antibodies. Possibly, this could be explained by the presence of donor-HLA-reactive memory T-helper cells from a previous immunizing event, which can potentially be reactivated by exposure to donor HLA mismatches sharing T-cell epitopes with the initial immunizing HLA. In this study, the effect of pre-transplant donor HLA-reactive memory T-helper cells on kidney allograft failure was investigated using the predicted overlap of T-cell epitopes between immunizing and donor HLA.
Methods: For 190 kidney transplant recipients with non-donor specific HLA antibodies, i.e. HLA-antibody-positive but DSA-negative, the immunizing HLA alleles were identified by means of a Luminex SAB assay. The potential T-cell epitopes originating from these immunizing HLA alleles as well as from the donor HLA were determined using the Predicted Indirectly ReCognizable HLA Epitopes (PIRCHE-II) algorithm. Subsequently, the overlapping PIRCHE-II load was calculated for each recipient and the effect of this PIRCHE-II overlap score on the 10-year risk of kidney graft failure was univariately and multivariably studied in a Cox proportional hazards model.
Results: The natural logarithm-transformed PIRCHE-II overlap score was significantly associated with the 10-year risk of kidney graft failure in the multivariable analysis with a hazard ratio of 1.48 (p=0.015). In addition, recipients with a low number of shared T-cell epitopes were shown to have a significantly higher cumulative incidence of graft failure as compared to recipients with a higher number of shared T-cell epitopes (p=0.014). Finally, it was suggested that over time, the number of shared T-cell epitopes between immunizing and donor HLA remains associated with an increased risk of graft failure.
Conclusions: We here show for the first time that the theoretical amount of shared T-cell epitopes between immunizing and donor HLA significantly correlates with kidney graft failure. Our findings suggest that the PIRCHE-II overlap score might be a strong indicator for the risk of allograft failure and that the presence of pre-transplant donor-HLA reactive memory T-helper cells might play an important role in the development of graft failure.

T-cell cytokine profiles after mRNA-1273 COVID-19 vaccination in kidney patients

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Background: T-cells are fundamental in the control and clearance of viral infections and contribute to protective immunity by long-term immunological memory. The mRNA-1273 COVID-19 (Moderna) vaccine induces durable SARS-CoV-2 Spike (S) specific $CD4^+$ and $CD8^+$ T-cell responses. However, little is known about the phenotype of these S-specific T-cells over time in kidney patients with a potentially disturbed immune system. Here, we investigated the cytokines produced by T-cells obtained from mRNA-1273 vaccinated kidney patients after *ex vivo* stimulation.
Methods: Patients on dialysis (n=41), with chronic kidney disease (CKD, n=39), kidney transplant recipients (n=69) and controls (n=45) were vaccinated twice with the mRNA-1273 COVID-19 vaccine. Whole blood obtained pre-vaccination, and 28 days and six months after second vaccination, was stimulated with peptides covering the S protein in a commercially available IFN-γ release assay (QuantiFERON, QIAGEN). After stimulation, cytokines (IL-2, 4, 5, 6, 9, 10, 13, 17A, 17F, 22, IFN-γ and TNF-α) were measured in plasma by a multiplex bead assay and ELISA (IL-21). Patients were clustered over time to identify cytokine production profiles via unsupervised clustering.
Results: After *ex vivo* stimulation with peptides covering the S protein a specific production of IFN-γ, IL-2, IL-5, and IL-13 response was found in all cohorts. Particularly, the Th1 cytokines (IFN-γ, IL-2) could still be detected six months after vaccination. Clustering analysis revealed no difference in cytokine profile between kidney patients and controls. Cytokine production was significantly lower in kidney transplant recipients compared to the other cohorts at 28 days and 6 months after vaccination ($p<0.01$). However, S-specific T-cell responses were still detectable in 81% of kidney transplant recipients based on the production of IL-2.
Conclusions: Our study shows that after mRNA-1273 COVID-19 vaccination, kidney transplant recipients have fewer S-specific T-cells, based on a multiplex cytokine assay. However, we were able to detect cytokines produced by SARS-CoV-2-specific T-cells even after six months in 81% of the kidney transplant recipients.

Donor-specific hyporesponsiveness following kidney transplantation is explained by progressive loss of donor-reactive polyfunctional CD4+ effector memory T cells and could guide lowering of immune suppressive medication

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Background: After kidney transplantation, donor-specific hyporesponsiveness (DSH) develops which is defined as a lowered response of alloreactive T cells to donor antigen while retaining response to a third party antigen. A better understanding of how changes in donor-reactive T cells after transplantation underlie DSH could guide lowering of immunosuppressive medication.
Methods: This study integrates multiparameter flow cytometry-based assays to characterize phenotype and function of circulating donor-reactive (vs third party-reactive) CD4+ and CD8+ T cells over time. Paired samples were taken from stable kidney transplant recipients (N=46) before, at 3-5 years and more than 5 years after transplantation. Donor-reactive T cells were identified at the single cell level by CD137 expression and data on T cell differentiation status and transcription factor expression were evaluated by unsupervised clustering. Proportions of polyfunctional donor-reactive CD137+ T cells capable of producing multiple pro-inflammatory cytokines were characterized as well as proliferation towards donor-antigen.
Results: The data point to progressive and specific loss of activated donor-reactive T cells capable of producing pro-inflammatory cytokines after transplantation. The number of circulating CD4+ donor-reactive T cells declined within the first 3-5 years after transplantation and became virtually undetectable in the years thereafter. The donor-reactive CD8+ T cells declined substantially only after >10 years. The decrease in donor-reactive CD4+ T cells is primarily within the effector memory subset and within T cells capable of producing two or more pro-inflammatory cytokines (TNF-α, IFN-γ and IL-2). This reduction in polyfunctional donor-reactive CD4+ T cells was strongly correlated with the reduced proliferation of CD4+ T cells following kidney transplantation. Importantly, the frequency of third party-reactive T cells did not alter significantly in time after transplantation indicative of a donor-specific effect and not an aspecific effect of immunosuppressive medication.
Conclusions: This study detected a decline in highly active donor-reactive T cells capable of producing multiple pro-inflammatory cytokines from the circulation in a time-after transplantation dependent fashion. The loss of polyfunctional donor-reactive effector memory CD4+ T cells likely plays an important role in the development of DSH in kidney transplant recipients.

Trained immunity determines long-term kidney allograft survival

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Background: Ischemia-reperfusion injury (IRI) is associated with chronic rejection and poorer long-term allograft survival. However, the immunological mechanisms that may explain this are poorly understood. We hypothesize that damage-associated molecular patterns (DAMPs) released into the circulation during IRI may induce long-term memory in innate immune cells, termed "trained immunity." This enhances their capacity for cytokine production and stimulate adaptive immune responses.
Methods: An *in vitro* trained immunity assay was used in which human peripheral blood mononuclear cells (PBMCs) are stimulated, and after five days of rest, re-stimulated with lipopolysaccharide (LPS). IL-6 and TNF are measured in the supernatant as a readout of the trained immunity response. We screened a library of DAMPs to determine if they can induce trained immunity. We performed ChIP sequencing of PBMCs obtained before and one week after transplantation from ten kidney transplant recipients to assess epigenetic modulations at the IL-6 and TNF gene locus. Sera from 96 kidney transplant recipients obtained one week after transplantation were used to stimulate PBMCs in trained immunity assays to assess the effect of post-transplant circulating DAMPs on trained immunity and how this is related to long-term graft outcome.
Results: We found that DAMPs can either induce (HMGB1, histones, IL1-β) or suppress (vimentin, ATP and C1q) trained immunity. ChIP sequencing analysis of PBMCs from kidney transplant recipients before and after transplantation shows distinct dynamics in the H3K4me3 histone marks at the IL-6 and TNF gene locus. Stimulation of PBMCs with sera from kidney transplant recipients induced trained immunity with a heterogeneous effect between patients. Trained immunity was not associated with delayed transplant function, acute rejection, de novo donor-specific antibody formation, or infection rates within the first two years after transplantation. However, trained immunity was strongly associated with long-term (>8 years) death censored graft survival ($p=0.002$ in a Kaplan-Meier analysis for serum induced trained immunity tertiles).
Conclusions: We have shown that trained immunity can be induced by DAMPs, and that it is associated with long-term graft survival. In doing so, we have identified innate immune memory as a novel and relevant immunological mechanism in organ transplantation.

Effects of Natural Killer cell alloreactivity on allograft failure in kidney transplantation

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Background: HLA mismatches between donor and recipient may facilitate Natural Killer (NK) cell alloreactivity upon kidney transplantation through the lack of interaction between donor HLA molecules and inhibitory killer immunoglobulin-like receptors on the NK cells of the recipient, a condition called "missing-self".
Methods: In this study, we investigated the effect of NK alloreactivity on kidney transplant failure. From the Dutch PROCARE consortium database, containing extended patient and donor information from kidney transplantations with at least 10 years follow-up, we selected 4024 patients without pretransplant donor-specific antibodies. We determined NK alloreactivity based on the Bw4, Bw6 and C1, C2 typing of patients and donors. The patients were divided in a non NK-alloreactive group (group 0, N=2693), an alloreactive group with 1 missing-self HLA ligand (group 1, N=1179) and an alloreactive group with 2 missing-self HLA ligands (group 2, N=152). We checked for potential confounders such as age, sex and type of kidney donor but these did not influence the results we found.
Results: NK cell alloreactivity protected against graft failure during the first year post-transplant, and the protective effect was stronger for group 2 (HR=0.3, p=0.002) than for group 1 (HR=0.7, p=0.001). However, after 5 years, this protection disappeared. The effect was most pronounced for group 2, where HRs (group 2 vs. 0) increased from 0.3 (T=1y) to 0.6 (T=5y) or 1.2 (T=10y). After 15 years, the risk for graft failure was even higher in group 2 than in the non-alloreactive group, though this was not significant (HR=1.5, p=0.3, group 2 vs. 0). In the group with 1 missing-self HLA ligand, the risk for graft failure after >5 years was almost comparable to non-alloreactive group (HR_{T5}= 1.0, p=0.9; HR_{T10}= 1.1, p=0.5; HR_{T15}=0.8 p=0.3).
Conclusions: In conclusion, we found that NK alloreactivity temporarily protects against graft failure, but after 5 years, this effect disappears and the hazard ratio of failure slowly increases.

HLA-DQ-specific recombinant human monoclonal antibodies allow for in-depth analysis of HLA-DQ eplets

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Background: HLA-DQ donor-specific antibodies (DSA) are the most prevalent type of DSA after renal transplantation and have been associated with eplet mismatches between donor and recipient HLA molecules. Eplets are theoretically defined configurations of surface exposed amino acids on HLA molecules that need verification to confirm that they can truly be recognized by alloantibodies. While human HLA-specific monoclonal antibodies (mAbs) are the most convincing tool for antibody-verification, only a limited number of HLA-DQ eplets have been antibody-verified due to a lack of HLA-DQ mAbs. In this study, we demonstrate the generation and reactivity analysis of HLA-DQ-specific recombinant human mAbs.
Methods: HLA-DQ specific memory B cells were isolated by flow cytometry from alloimmunized individuals using soluble biotinylated HLA-DQ monomers. After expansion, RNA from HLA-specific-antibody positive memory B cell clones was isolated and used to generate recombinant human HLA-DQ-specific mAbs. These mAbs were tested with luminex single antigen bead assay to determine their specificity, which was confirmed with flow cytometry and complement dependent cytotoxicity assays. Reactivity patterns were analyzed with the HLA Epitope Mismatch Algorithm (HLA-EMMA) to identify amino acids that were uniquely shared by the reactive HLA alleles and were mapped to known eplets.
Results: Overall, 15 HLA-DQB1-specific mAbs with six different specificities were generated. The HLA-DQB1*03:01-specific mAb LB_DQB0301_A and the HLA-DQB1*03-specific mAb LB_DQB0303_C supported the antibody-verification of eplets 45EV and 55PP respectively, while mAbs LB_DQB0402_A and LB_DQB0602_B verified eplet 55R on HLA-DQB1*04/05/06. The reactivity pattern analyses of the HLA-DQB1*02-specific mAb LB_DQB0201_A, the HLA-DQB1*02/03/04-specific mAb LB_DQB0303_A and the DQB1*03/04-specific mAb LB_DQB0303_B resulted in the identification of multiple uniquely shared residues, warranting further studies to define the inducing functional epitope and corresponding eplet.
Conclusions: This is the first study in which recombinant human HLA-DQ-specific mAbs were generated through isolation of HLA-specific-memory B cells from alloimmunized individuals using soluble biotinylated HLA-DQ monomers. This unique set of HLA-DQ specific mAbs will be further expanded and will facilitate the in-depth analysis of HLA-DQ eplets, which is relevant for further studies of HLA-DQ alloantibody pathogenicity in transplantation.

Novel Avenue of Allograft Monitoring: Direct Measurement of Donor-Specific Extracellular Vesicles in Human Plasma

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Background: Extracellular Vesicles (EV) - regarded as "snapshots" of their cell of origin - represent promising liquid biomarkers to monitor allograft function post transplantation. Recently, we developed an imaging flow cytometry (IFCM) based protocol to identify and characterize EV ≤240 nm in molecularly complex samples such as human plasma *without* prior isolation of EV. Using this protocol, we measure allograft derived EV based on HLA phenotype as a first step to detect allograft specific EV in the circulation of kidney transplant (KTx) recipients.
Methods: EDTA blood samples from kidney transplant donors (HLA-A2+, n=21) and recipients (HLA-A2-, n=33) were collected before transplantation as well as 3 days, 7 days, 6 months and during 'for-cause' biopsies (recipients only) after transplantation. Platelet-poor plasma (PPP) was stained with a donor-specific HLA antibody (HLA-A2) in combination with a common EV marker (tetraspanin CD9) and measured using standardized IFCM.
Results: Quantification and comparison of CD9+/HLA-A2+ double-positive EV showed $1.1E^7 \pm 8.9E^6$ vs $3.5E^5 \pm 2.5E^5$ objects/mL for donor and recipient (pre-KTx) EV respectively, with recipients A2- EV concentrations representing background level of the machine. CV values for inter- and intra-assay variability were 16% and 11%, respectively. Serial dilution of A2+ PPP in A2- PPP (n=5) showed a linear reduction in the numbers of CD9+/HLA-A2+ EV according to the dilution rate whilst total CD9+ EV levels remained unchanged. The lower limit of detection of IFCM was defined as the dilution at which point CD9+/HLA-A2+ EV dropped below baseline (A2- PPP) and was determined to be ~1%. Measurement of longitudinally collected recipient samples revealed the detection of allograft derived EV as soon as 3 days – but up to at least 6 months – after KTx.
Conclusions: Here we demonstrate for the first time the detection of allograft derived EV in the circulation of KTx recipients in unprocessed human plasma samples. Identification, quantification and characterization of these EV opens up the possibility to monitor these EV over time after transplantation, and may prove to be a minimally-invasive biomarker.

T cell mediated immune rejection of kidney organoids transplanted in a humanized mouse model

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Background: In the past years knowledge about induced pluripotent stem cells (iPSCs) and their derived cell types and tissues has increased substantially. Among others iPSCs can be differentiated to kidney organoids containing multiple nephron structures, such as glomeruli and proximal tubules. After transplantation in mice, the kidney organoid becomes vascularized and matures. Therefore iPSC-derived kidney organoids have the potential to be used as clinical therapy to improve kidney function in patients. However, a major challenge in the transplantation field is the risk of allograft rejection. In this study we developed a humanized mouse model to study immune rejection of transplanted human iPSC-derived kidney organoids. This enables us to investigate innovative approaches that prevent immune rejection of transplanted tissues in the future.
Methods: Human iPSC-derived kidney organoids were transplanted under the renal capsule of immunodeficient mice. One week later the mice were injected with human peripheral blood mononuclear cells (PBMCs) isolated from buffy coats to reconstitute a human immune system. Blood is taken at multiple timepoints to quantify the composition of human derived leukocytes in the mouse peripheral blood. Five weeks after transplantation, the mice were sacrificed and organs collected for further analysis.
Results: Flow cytometric analysis of mouse peripheral blood after injection of human PBMCs showed that human T cells were able to engraft, survive and proliferate in the mice for at least 4 weeks after injection. Other cell types that were present at the time of injection such as B cells, monocytes and NK cells were not detected in peripheral blood at 1 and 4 weeks after injection. Immunohistochemical staining of the collected tissues showed that human T cells were attracted to the human kidney organoid. Both $CD4^+$ and $CD8^+$ T cells were present in the kidney organoid. Part of the T cells were proliferating indicated by $KI67^+$ staining and a portion of the $CD8^+$ T cells were positive for Granzyme B. Finally, cytotoxicity and active immune rejection was visible by kidney tubule dedifferentiation and nephron structure atrophy in the kidney organoid.
Conclusions: Our findings show that human T cells were attracted to and actively rejected the transplanted kidney organoid. We therefore conclude that this humanized mouse model can be used to study immune rejection of transplanted iPSC-derived human kidney organoids.

High humoral response in relation to immunosuppressive blood levels in liver transplant recipients after SARS-CoV-2 vaccination: an observational, cohort study

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Background: Several studies show that the humoral responses to SARS-CoV-2 vaccines in solid organ transplant (SOT) recipients is reduced, with positive serology ranging from 30% - 65%. Until now, no study evaluated the effect of immunosuppressive blood levels on the IgG SARS-CoV-2 anti-spike antibody response after SARS-CoV-2 vaccination.
Methods: In this observational, cohort study, we determined the antibody response to SARS-CoV-2 vaccination in liver transplant (LT) recipients in relation to the immunosuppressive blood levels after the 2nd dose of mRNA vaccines or the vector vaccine ChAdOx1 nCoV19.
Results: A total of 476 LT recipients were included: 430 Moderna® mRNA-1273 vaccine, 25 Pfizer® BNT162b2 mRNA vaccine and 21 AstraZeneca® ChAdOx1 nCoV19 vector vaccine. We found a positive IgG SARS-CoV-2 serology test in 79·0% (376/476) of our LT recipients. LT recipients vaccinated with the mRNA-1273 vaccine had significantly higher IgG SARS-CoV-2 anti-spike antibody levels compared to the other two vaccines, p<0·001. The use of mycophenolic acid (MPA), regardless the blood level, suppresses the IgG SARS-CoV-2 anti-spike antibody response to below the threshold for an effective vaccination, whereas the other immunosuppressive agents did not have that effect.
Conclusions: We found a high efficacy for the SARS-CoV-2 vaccination in our LT recipient cohort. The mRNA-1273 vaccine produces a superior IgG SARS-CoV-2 anti-spike antibody response. MPA suppresses the IgG SARS-CoV-2 anti-spike antibody response to below the cut-off for an effective vaccination, regardless the blood levels of MPA. Discontinuation of MPA and the switch to another class of immunosuppressive drugs not acting on the B lymphocytes at least 6 weeks before a booster vaccination for every patient on MPA is suggested to achieve an optimal humoral response.

Longevity of antibody and T cell responses after COVID-19 vaccination in patients with chronic kidney disease, on dialysis, or living with a kidney transplant

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Background: The availability of effective COVID-19 vaccines is of great importance for kidney patients. In our recent study, especially kidney transplant recipients (KTR) were shown to have a poor immune response at 28 days following the second vaccination, and to a lesser extent also patients with chronic kidney disease (CKD G4/5) or on dialysis. In this follow-up report, we studied antibody and T cell responses in these patients 6 months after COVID-19 vaccination.
Methods: This investigator driven, prospective, controlled multicenter study included 155 participants with CKD stages G4/5 (eGFR <30 mL/min/1.73m^2), 145 participants on dialysis, 277 kidney transplant recipients and 185 controls. Participants received two doses of the mRNA-1273 COVID-19 vaccine (Moderna). SARS-CoV-2 Spike S1-specific IgG antibodies, neutralizing antibodies and SARS-CoV-2 specific T-cell responses in whole blood were measured at baseline, 28 days and 6 months after the second vaccination. For S1-IgG a threshold of ≤10 BAU/mL was adopted to indicate seronegativity.
Results: The seroconversion rates at day 28 after the second vaccination were 100% and 99.3% in patients with CKD G4/5 and on dialysis, respectively, of whom 1.3% and 4.2% became seronegative at 6 months. In KTRs the seroconversion rate was 57% of whom 14.6% became seronegative at 6 months. Controls had a seroconversion rate of 100% and none became seronegative at 6 months. In all four groups antibody titers declined significantly from day 28 to month 6 (CKD G4/5 2345 (1235-4583) to 314 (194-750) BAU/mL; dialysis 1585 (695-3089) to 155 (71.5-341) BAU/mL; KTR 24.4 (2.52-416) to 16.1 (1.64-115) BAU/mL; controls 3022 (1994-4856) to 386 (226-712) BAU/mL; all P<0.001). At 6 months, antibody titers in dialysis and transplant patients were significantly lower when compared to controls (both P<0.001). For neutralizing antibodies similar trends were observed. At 28 days and at 6 months a high SARS-CoV-2-specific T cell response was observed in 69.4% and 50% of CKD G4/5 patients, 65.8% and 47.4% of dialysis patients, 15.6% and 7.8% of kidney transplant recipients and 85.7% and 73.8% of controls, respectively (all P<0.001).
Conclusions: Although at month 6 after vaccination seroresponse did not change much, waning of antibody levels was observed in all 4 groups, with antibody levels being significantly lower in dialysis and especially kidney transplant recipients, when compared to controls. T-cell responses also declined in all groups, with persistently low responses in kidney transplant recipients. These data suggest that third vaccination and alternative vaccination strategies are warranted to obtain long-lasting immunogenicity in dialysis and transplant patients.

Stronger antibody response after vaccination with mRNA-1273 as compared to BNT162b2 and AZD1222 in patients with chronic kidney disease, dialysis patients, and kidney transplant recipients - results from the prospective RECOVAC Antibody Study

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Background: Patients with kidney disease are at high-risk of severe COVID-19. Recent literature demonstrates an impaired immune response to vaccination in kidney transplant recipients (KTR), and to some extent in dialysis patients and patients with CKD stages G4-G5. In the present study, we analysed the antibody response and safety after mRNA-1273, BNT162b2 and AZD1222 vaccination in these patients.
Methods: During the Dutch SARS-CoV-2 vaccination programme, we prospectively enrolled patients with CKD stages G4-G5 (n=418), dialysis patients (n = 590) and KTR (n=2584). Blood samples were obtained 1 month after complete vaccination by at-home collection of capillary blood via finger prick and analysed for the presence of IgG antibodies against the receptor binding domain (RBD) of the spike protein of SARS-CoV-2 using ELISA. Immunogenicity and safety of different vaccines were compared. Seroconversion was defined as reaching an anti-RBD IgG concentration > 50 BAU/mL.
Results: Seroconversion rates were high in patients with CKD stages G4-G5 (95.7%), and dialysis patients (92.4%), but markedly lower in KTR (52.6%). In KTR, mRNA-1273 resulted in a higher seroconversion rate in comparison to BNT162b2 and AZD122 (53.9% vs. 38.5% and 29.1%, P=0.001 and P<0.001 resp.). There was no significant difference in seroconversion rates between these vaccines in dialysis patients and patients with CKD stages G4-G5. However, in all patient groups mRNA-1273 resulted in higher antibody levels (P<0.001) compared to BNT162b2 and AZD122 (KTR: 72.4 (8.83-638) BAU/mL vs. 21.0 (5.36-131) BAU/mL and 18.3 (2.75-95.1) BAU/mL, resp.; Dialysis: 1656 (572-3032) BAU/mL vs. 606 (193-1416) BAU/mL and 196 (144-429) BAU/mL, resp.; CKD stages G4-G5: 2879 (1369-5335) BAU/mL vs. 1063 (385-1895) BAU/mL and 206 (88.2-333) BAU/mL, resp.).
Systemic adverse events (AEs) after vaccination, were reported in 54.4% of patients with CKD stages G4-G5, 26.9% of dialysis patients and 25.8% of KTR. This percentage was significantly higher for mRNA-1273 compared to BNT162b2 but did not differ between mRNA-1273 and AZD122 in dialysis patients and KTR. In patients with CKD stages G4-G5 systemic AEs were more prevalent for mRNA-1273 compared to BNT162b2 and AZD122.
Conclusions: Only about 50% in KTR seroconvert after SARS-CoV-2 vaccination, in contrast to dialysis patients and patients with CKD stages G4-G5, in which more patients seroconvert. The mRNA-1273 vaccine is most effective in terms of antibody response in these high-risk kidney patient groups. Systemic AEs are more often reported for mRNA-1273. Our data suggest that mRNA-1273 may be the preferred SARS-CoV-2 vaccine in high-risk kidney patients.

SARS-CoV-2 vaccination response in tacrolimus treated kidney transplant recipients with and without mycophenolate mofetil: follow-up of a randomized controlled trial.

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Background: Immunosuppression is a risk factor for severe SARS-CoV-2 infection and insufficient vaccination responses in kidney transplant recipients. Mycophenolate mofetil (MMF) has been associated with low vaccination responses. However, data from a controlled study are currently lacking.
Methods: A randomized controlled trial in immunologically low risk kidney transplant recipients was performed (EudraCT nr.: 2014-001372-66). Patients were randomized to standard Tacrolimus (TAC)/MMF or to TAC monotherapy (TACmono) from 9 months onwards, without steroids. Data on COVID-19 disease were extracted from the electronic patient file and by telephone interviews. Antibody based immune responses to SARS-CoV-2 vaccination were investigated as part of the RECOVAC Antibody study (EudraCT nr.: 2021-283 001520-18). A central laboratory (Sanquin) performed the anti-SARS-CoV-2 receptor binding domain IgG ELISA assay 2-8 weeks after the second COVID-19 vaccination. Patients were classified as non-responders (≤50 BAU/mL), low-responders (50-300 BAU/mL) and responders (>300 BAU/mL).
Results: Between 2015 and 2018, 79 recipients were randomized to TAC/MMF (n=41) and to TACmono (n=38). At the outbreak of the COVID-19 pandemic in early 2020, 67 patients were alive with a functioning graft (TAC/MMF n=35,TACmono n=32). Ten recipients had symptomatic COVID-19 disease before vaccination (TAC/MMF n=7, TACmono n=3, p=0.3). Four TAC/MMF patients were admitted, of whom one died and one was admitted to the ICU. Two TACmono patients were admitted, of whom one to the ICU. In 28 patients without prior COVID-19 disease, vaccination responses were measured. 26 patients received mRNA-1273 and 2 BNT162b2 vaccination (TAC/MMF n=1 and TACmono n=1). Patients were 63 (43-75) years of age, median time after transplantation was 4.2 (3.0-6.5) years and eGFR was 54 (36-105) ml/min/1.73m^2. TAC trough levels were 6.7 (±0.3) µg/L in both groups. MMF dose was 1000 mg daily (500-2000) in TAC/MMF. In TAC/MMF, vaccination response was 37.3 BAU/ml (median; 5 non, 7 low, 1 responder) and for TACmono 1016.4 BAU/ml (median; 1 non, 6 low, 8 responders, p =0.016).
After second vaccination, 1 TAC/MMF and 1 TACmono patient developed COVID-19. Both recovered without admission. As of November 2021, 31 TAC/MMF and 30 TACmono patients are alive with a functioning graft.
Conclusions: In this controlled study mycophenolate mofetil on top of tacrolimus severely hampered serological SARS-CoV-2 vaccination response.

Mucosal antibody responses following SARS-CoV-2 infection and vaccination in kidney patients and healthy controls

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Background: Vaccination against SARS-CoV-2 with mRNA vaccines has demonstrated to be highly efficacious in the general population and induces high levels of neutralizing serum antibodies against the spike protein. At present it is unclear how serum antibody levels are related to the level of mucosal antibodies, which are crucial in the prevention of infection. We examined the induction and persistence of mucosal and serum antibodies against SARS-CoV-2 following vaccination in patients with severely impaired kidney function, dialysis patients, and kidney transplant recipients. Additionally, we compared the antibody response to vaccination with response to infection.
Methods: Serum and nasal mucosal lining fluid (MLF) were collected from 212 participants of the RECOVAC-IR study in which the immunogenicity and safety of Spikevax (previously mRNA-1273; Moderna) was investigated in patients with chronic kidney disease (stages 4 and 5), dialysis patients, kidney transplant patients, and a control group. Samples were collected at baseline and 28 days and 6 months after the second dose. For the post-infection study, the MuCo-study, MLF was collected in 108 hospital care workers with COVID-19 at study inclusion, shortly after a positive PCR test, and MLF and serum were collected at 28 days, 9 months and 15 months following infection. Serum and MLF IgG and IgA levels against nucleocapsid (N), receptor-binding domain (RBD) and spike protein (S) of SARS-CoV-2 were quantified by multiplex immunoassay.
Results: At 28 days post-vaccination, a strong increase in mucosal and serum IgG antibodies against RBD and S was observed. Whereas mucosal IgG levels were similar in controls and CKD4/5 patients, lower levels were observed in dialysis patients and kidney transplant patients. In contrast to IgG, a minor and variable increase in mucosal IgA was observed across the vaccination groups. Preliminary analysis suggests that vaccination induces high levels of mucosal IgG but low levels of IgA at 28 days, whereas infection induces both mucosal IgG and IgA. Analysis of mucosal antibody levels at later follow-up timepoints and their relation to serum levels is in progress.
Conclusions: The reduced mucosal antibody responses observed in kidney transplant patients, and to a lesser extent in dialysis patients, suggest that these patients remain at high risk of infection. The absence of mucosal IgA post-vaccination suggests that systemic vaccination with Spikevax does not induce mucosal immune memory responses, in contrast to infection. Analysis of the persistence of mucosal antibodies over time, the impact on risk of infection and disease, and the response to booster vaccination are key priorities for further research.

Influence of COVID-19 vaccination on the presence and level of HLA antibodies in patients with chronic kidney disease, on dialysis, or living with a kidney transplant

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Background: HLA antibodies can be induced by pregnancy, transplantation or transfusion. Induction of HLA antibodies or increase in pre-existing HLA antibodies has been reported after vaccination. This can theoretically increase the risk of rejection in patients after kidney transplantation. Recently, COVID-19 mRNA vaccines have been introduced with high vaccine efficacy in healthy controls. However, these new vaccines have not yet been studied for induction of HLA antibodies in risk populations. Therefore, the aim of this study was to investigate the change in HLA antibody status of kidney patients after COVID-19 mRNA vaccination.
Methods: The historical HLA antibody status of 118 of 213 patients included in the RECOVAC study was available from patient records (excluding 50 controls and 45 patients not yet registered at Eurotransplant). All patients that had current or pre-existing HLA antibodies (n = 38) and patients that had current and historically negative HLA antibody data were included (n = 37).
In these 75 patients with chronic kidney disease (CKD) stage G4/5 (n = 21) , on dialysis (n = 22) or living with a kidney transplant (n = 32) HLA antibody screening was performed before vaccination and 28 days after the second mRNA-1273 COVID-19 vaccine (Moderna) using Luminex screening (Immucor). Specificity was determined in positive samples using Luminex single antigen beads (LSA, Immucor). Background corrected MFI values of the LSA assays of positive patients were compared before and after vaccination using a paired T test.
Results: In 37 of 75 RECOVAC patients there were no pre-existing HLA antibodies and no HLA antibodies after vaccination. In 38 patients current and/or pre-existing HLA antibodies were present. Of these 38 patients 12 were historically positive but negative before and after vaccination, 25 were positive historically and after vaccination. There was no statistical significant difference in the background corrected MFI values of the LSA assays of positive patients before and after vaccination (p=0,18). All positive patients were also analyzed individually. Changes in HLA antibody levels before and after vaccination were present in both directions e.g. higher before or higher after vaccination. All changes could be explained by the presence of HLA antibodies around the cutoff point of the assay, by the normal variation of the assay or by changes in immunosuppression of the patient.
Conclusions: The mRNA-1273 COVID-19 vaccinate did not induce de novo HLA antibodies and did not result in an increase of HLA antibodies in kidney patients with or without pre-existing HLA antibodies.

Humoral response to SARS-CoV-2 infection among liver transplant recipients

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Background: Immunosuppressive agents are known to interfere with T- and/or B-lymphocytes, which are required to mount an adequate serologic response. Therefore, we aim to investigate the antibody response to SARS-CoV-2 in liver transplant (LT) recipients after COVID-19.
Methods: Prospective multicenter case-control study analyzing antibodies against the nucleocapsid-protein and spike protein of SARS-CoV-2 in LT recipients with confirmed SARS-CoV-2 infection (COVID-LT) compared to immunocompetent patients (COVID-immunocompetent) and liver transplant patients without COVID-19 symptoms (non-COVID LT).
Results: Overall, 35 LT recipients were included in the COVID-LT cohort. 35 and 70 subjects fulfilling the matching criteria were assigned to the COVID-immunocompetent and non-COVID LT cohort, respectively. We showed that LT recipients, despite the use of immunosuppressive drugs and less symptoms, mounted a detectable anti-nucleocapsid antibody titer in 80% of the cases, although the level was significantly lower in comparison to the level detected in the COVID-immunocompetent cohort (3.73 vs. 7.36, $p<0.001$). When analyzing the anti-spike-protein antibody response, no difference in positivity rates was found between the COVID-LT and the COVID-immunocompetent cohorts (97.1% vs. 100%, $p=0.314$).
Conclusions: Our findings suggest that the humoral response of LT recipients is only slightly lower than expected compared with that of COVID-19 immunocompetent controls. Anti-nucleocapsid antibodies, although specific for SARS-CoV-2 when tested alone, may erroneously lead to an underestimation of the immune response in this population. Testing for anti-spike antibodies adds sensitivity. Altogether, routine antibody testing against separate SARS-CoV-2 antigens shows that LT patients are capable of mounting an adequate antibody response against SARS-CoV-2.

COVID-19 vaccination induces a poor IL-21 memory T-cell response in kidney transplant recipients

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Background: COVID-19-related morbidity and mortality is high among kidney patients. Several studies recently suggested low humoral and cellular immune responses after two doses of mRNA-1273 (Moderna) in these patients. Interleukin (IL)-21 is key in orchestrating an effective immune response against viral infections, is mainly produced by activated CD4+ T-cells and stimulates both humoral and cellular immunity. However, T-cell function may be impaired in kidney patients and this may explain the poor response to vaccination. Currently, there is limited data available on the vaccine-induced IL-21 memory T-cell response in these patients. We studied the induction of SARS-CoV-2-specific IL-21 memory T-cell response after mRNA-1273 vaccination in 3 groups of kidney patients.
Methods: 102 participants were randomly selected from a prospective controlled multicenter cohort study, including 34 controls, 19 chronic kidney disease (CKD) stages G4/5 (eGFR <30 mL/min/1.73m2), 17 dialysis and 32 kidney transplant patients. All participants received 2 doses of mRNA-1273. To assess the vaccine-induced IL-21 memory T-cell response, we performed an IL-21 ELISpot (per 3.105 PBMCs) in these participants at baseline and 28 days after the second vaccination. SARS-CoV-2 S1-specific IgG antibody levels were already measured in the context of the multicenter cohort study.
Results: Kidney transplant recipients had a significantly lower number of SARS-CoV-2-specific IL-21 producing memory T-cells when compared to controls (median of 46 versus 151, P<0.001). Participants with CKD G4/5 or on dialysis also had reduced SARS-CoV-2-specific IL-21 producing memory T-cells compared to controls (median of 128 [19-658] and 108 [7-462] versus 151 [10-635], p=0.48 and p=0.23, respectively), but the difference was less pronounced. In addition, a positive correlation was found between the number of SARS-CoV-2-specific IL-21 producing memory T-cells and SARS-CoV-2 S1-specific IgG antibody levels for all groups (Pearson correlation coefficient of 0.2, p=0.028).
Conclusions: Kidney transplant recipients have an impaired antibody response after two doses of mRNA-1273 (Moderna), which correlates with poor SARS-CoV-2-specific T-cell reactivity. These findings suggest that poor IL-21 memory T-cell response might hamper protection against COVID-19.

SARS-CoV-2 spike-specific IFNγ T-cell response after COVID-19 vaccination in Patients With Chronic Kidney Disease, on Dialysis, or Living With a Kidney Transplant

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Background: The availability of effective COVID-19 vaccines is of great importance for kidney patients. In our recent study, kidney transplant recipients were shown to have a poor humoral immune response at 28 days following the second vaccination, in contrast to patients with chronic kidney disease or on dialysis. In this study we investigated the cellular immune response following COVID-19 vaccination in different cohorts of kidney patients compared to controls.
Methods: In our prospective controlled study we vaccinated patients with chronic kidney disease (CKD) stage G4/5 (eGFR <30 ml/min/1.73m^2), on dialysis, living with a kidney transplant and controls with 2 doses of the mRNA-1273 COVID-19 vaccine (Moderna). Subjects with a previous COVID-19 infection were excluded (by history or by presence of nucleocapsid antibodies). Blood was drawn before and 28 days after the second vaccination. Peripheral blood mononuclear cells (PBMCs) were isolated from 50 mL of venous blood and SARS-CoV-2 specific T cells were measured using an IFNγ ELISPOT assay.
Results: A positive SARS-CoV-2 specific T-cell response was observed in 56/80 (70%) CKD G4/5, 42/77 (54.5%) dialysis, and 60/141 (42.6%) kidney transplant recipients compared to 70/92 (76.1%) control subjects (p=0.99, p=0.01, p<0.001, respectively). Previously, similar results were found for the humoral response. In kidney transplant recipients log-transformed humoral and cellular response showed a poor correlation (r = 0.27; p = 0.01). The use of calcineurin inhibitors was associated with a poor cellular response, whereas mycophenolate mofetil was associated with a poor humoral response.
Conclusions: Dialysis and especially kidney transplant recipients show a reduced humoral and cellular immune response after mRNA SARS-CoV-2 vaccination. A third vaccination, possibly with temporary withdrawal of immunosuppression in transplant recipients, seems warranted.

Kidney graft immunogenicity on normothermic machine perfusion

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Background: Ex situ normothermic machine perfusion (NMP) is a promising method of organ preservation, allowing donor kidneys to be reconditioned and assessed prior to transplantation. The long-term outcome of transplantation is partially determined by the initial graft immunogenicity. The aim of this study is to determine the immune and inflammatory status of discarded donor kidneys on NMP. Ultimately, this could aid the assessment of the graft immunogenicity to predict outcomes or even to enable immunomodulatory interventions prior to transplantation.
Methods: Discarded deceased donor kidneys (n=23) were perfused in a closed system at 37°C for 6h with a red blood cell-based perfusion solution. Of these grafts, cytokine/chemokine release, cellular efflux, and the total amount and localization of resident immune cells were analyzed. For this, perfusate samples were collected before and at 1, 3 and 6h after NMP in which released cytokines were quantified using a 27-plex Luminex panel. Leukocytes were characterized in the similar sequential perfusate by flow cytometry for monocytes (CD14), NK cells (CD56), T cells (CD3, CD4 and CD8) and B cells (CD19). Biopsies were collected for quantification and localization of resident immune cells using imaging mass cytometry.
Results: All kidneys displayed stable perfusion parameters on NMP. Throughout perfusion there was a continuous increase in pro-inflammatory cytokine levels in the perfusate, resulting in high concentrations of IL-8 (8.7±7.5 ng/ml), IL-6 (7.2±3.3 ng/ml), IP-10 (2.5±1.6 ng/ml), G-CSF (1.3±0.7 ng/ml), and MCP-1 (0.6±0.3 ng/ml) at the end of perfusion. During perfusion there was considerable release of leukocytes from the kidney (baseline: $4.3x10^3 \pm 2.4x10^3$ cells, 6h of perfusion: $13.1x10^6 \pm 5.6x10^6$ cells). Cell populations detected at 6h of NMP in this analysis consisted primarily of monocytes, and minor populations of natural killer (NK) cells and CD8+ T cells ($3.2x10^6 \pm 3.6x10^6$, $2.2x10^6 \pm 2.2x10^6$ and $1.4x10^6 \pm 2.6x10^6$ percentage of leukocytes, respectively). Resident leukocytes visualized in biopsies appeared to decrease the end of NMP.
Conclusions: Graft quality and initial immunogenicity determine, at least in part, the success of organ transplantation. We demonstrate that *ex situ* NMP initiates the efflux of monocytes and NK cells and release of several pro-inflammatory cytokines. The immunological contribution of the graft as observed may be beneficial when initiated during perfusion, rather than exposing these events to the recipient. A better understanding of these immunological features during NMP may provide useful assessment markers and novel therapeutic targets to modulate and allow enhancement of the graft during NMP.

Functional differences between in vivo and ex vivo renal tissue oxygenation assessed with magnetic resonance imaging

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Background: Renal normothermic machine perfusion (NMP) is a promising method for pre-transplant graft quality assessment. Although its potential is increasingly being recognized, it remains unclear which pathophysiological mechanisms could convey information about graft viability. Functional magnetic resonance imaging is a class of imaging methods developed to demonstrate regional, time-varying changes in metabolism and function. To broaden our understanding about the physiological processes during NMP, we combined non-invasive MRI with renal normothermic perfusion. This project aimed to determine the differences between *in vivo* and *ex vivo* regional renal tissue oxygenation by means of T2* mapping.
Methods: Pigs (n=7) were anaesthetized and brought into a clinical grade MRI scanner (Siemens Skyra 3T). In vivo MRI scans were performed to provide information about regional tissue oxygenation using T2* mapping (slice thickness 4 mm, voxel sizes 1.4 x 1.4 mm, 7 TE's from 4 to 42 ms). Subsequently, a bilateral nephrectomy was performed to retrieve 14 kidneys (7 pairs), which were randomly assigned to either a minimal warm ischaemia (WI) group or a 75 min WI group. After WI and 300-500 min of cold machine perfusion preservation, both kidneys were simultaneously connected to an MRI compatible NMP circuit and perfused for 6 hours. Hourly, T2* maps were acquired from both kidneys. Regions of interest (ROIs) were drawn in the cortex and medulla to calculate the mean signal intensity.
Results: In vivo mean T2* corticomedullar (CM) signal ratio (1.60±0.30) differed significantly from the mean ex vivo CM ratio of the minimal WI group (0.43±0.13, $P < 0.0001$) and the 75 min WI group (0.49±0.19, $P < 0.0001$). When the minimal and the 75 min WI groups were compared, differences in CM ratio, as well as those between cortical and medullar signal intensities, did not reach statistical significance. Oxygen consumption during NMP in the 75 min WI group had a moderate correlation with medullar T2* signal ($r = -0,525$ $P < 0.021$), but not with the minimal WI group.
Conclusions: These results provide the first evidence for the existence of relevant differences in regional tissue oxygenation between a physiological in vivo environment and during ex vivo normothermic perfusion. These differences highlight that tissue oxygen kinetics during ex vivo perfusion do not resemble what we expect from our in vivo reference frame indicating that conventional assessment strategies might need to be weighted carefully.

A droplet digital PCR-based indel quantification method for the detection of circulating donor-derived cell-free DNA as biomarker for acute kidney transplant rejection

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Background: Donor-derived cell-free DNA (ddcfDNA) is a promising minimally invasive biomarker for acute rejection (AR) in kidney transplant recipients. To assess the diagnostic value of ddcfDNA as marker for AR, ddcfDNA was quantified at multiple time points after kidney transplantation with a novel high-throughput droplet digital PCR (ddPCR) indel method that allowed for the absolute quantification of ddcfDNA.
Methods: In this study, ddcfDNA in plasma samples from 223 consecutive kidney transplant recipients was analyzed pre-transplantation, and at 3, 7 and 180 days after transplantation, and at time of for-cause biopsies obtained within the first 180 days after transplantation.
Results: Median (interquartile range [IQR]) ddcfDNA concentration was significantly higher on day 3 (58.3 [17.7-258.3] copies/mL) and day 7 (25.0 [10.4-70.8] copies/mL) compared to day 180 after transplantation (4.2 [0.0-8.3] copies/mL; $p<0.001$ and $p<0.001$, respectively). At time of biopsy-proven AR (BPAR), between day 11 and 180 after transplantation, ddcfDNA concentration was significantly higher (50.0 [25.0-108.3] copies/mL) compared to those when biopsies showed non-AR (0.0 [0.0-15.6] copies/mL; $p<0.05$). ddcfDNA concentration within the first 10 days after transplantation showed no significant difference between recipients with BPAR and those with non-AR in their biopsy or between recipients with BPAR and ddcfDNA measured at day 3 and day 7.
Conclusions: Unfortunately, ddcfDNA concentration is not a good biomarker to detect AR within the first 10 days after transplantation. However, BPAR occurring after 10 days after transplantation can be detected in kidney transplant recipients by ddcfDNA using a novel and unique, high-throughput ddPCR indel method.

Galunisertib suppresses fibrosis in an ex vivo renal transplantation model

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Background: Circulatory death donor (DCD) kidneys undergo ischemia/reperfusion injury, increasing the chances of developing late transplant renal failure due to fibrosis. One of the most important cytokines involved in the onset of fibrosis is transforming growth factor β (TGF-β), that causes phosphorylation of SMAD2/3 via the TGF-β type I receptor kinase. Galunisertib is an inhibitor of this receptor kinase and could therefore be a promising drug candidate for targeting renal fibrosis. However, this has neither been tested in a whole organ, nor in a transplant setting. Our aim was to observe the antifibrotic effects of galunisertib during normothermic machine perfusion (NMP).
Methods: To address our aim, we created an *ex vivo* kidney fibrosis model by combining NMP and PCKS. Porcine kidneys were subjected to 30min of warm ischemia, 24h of oxygenated hypothermic machine perfusion, and 6h of NMP with treatment (control, TFG-β, galunisertib, or TGF-β+galunisertib; n=8). To determine whether effects persisted upon ceasing treatment, precision-cut kidney slices (PCKS) were prepared from respective kidneys and incubated for 48h with treatment continued and discontinued.
Results: Macroscopically, no abnormalities or infections were observed. With regard to general viability, we observed that kidneys perfused with galunisertib were marked by an increased oxygen consumption, elevated ATP levels and attenuated tubular dilation and necrosis. No significant differences in renal function or injury markers were observed. Galunisertib altered inflammation markers by causing a significant increase in gene expression of TNF-α, and a significant decrease of *IL-6* after 6h NMP. This was supported by IL-6 protein expression. Continued TGF-β supplementation promoted fibrogenesis as shown by significantly increased mRNA expression of *TGF-ß, ACTA2, COL1A2, FN-1, SERPINE1, SERPINH1* after 48h of incubation. Continued treatment with galunisertib, however, clearly attenuated the expression of all tested fibrosis-related genes after 48h incubation. Picrosirius red staining showed no significant differences in fibrosis formation.
Conclusions: In conclusion, our findings suggest that galunisertib affected mitochondrial activity, tissue integrity and expression of fibrogenesis-related genes. Galunisertib therefore appears to be a promising drug for further research, and may ultimately be implemented during machine perfusion in a clinical setting as treatment to suppress the onset fibrosis in DCD kidneys.

A novel immunosuppressive compound (79-6) that targets BCL6 prevents the humoral alloresponse

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Background: BCL6, is a transcription factor involved in B cell activation and differentiation. BCL6-expressing B cells play a crucial role in the development and maintenance of germinal centers, which are essential for the development of a humoral response. Targeting BCL6-mediated responses has the potential to prevent humoral alloreactivity. Here, a small molecule BCL6 inhibitor named 79-6 was tested *in vitro* and its effect on plasma blast formation and IgG production was investigated.
Methods: The following experiments were performed in the presence and absence of the small molecule BCL-6 inhibitor 76-9 (range 25-100 µg/mL): (1) Polyclonally-activated B cells (anti-IgM/anti-CD40 and IL-21) from healthy controls were studied for differentiation, plasma cell formation and IgG-production. (2) To study 79-6's inhibitory effect on B cell differentiation stages, circulating TfH cells and B cells were stimulated with alloantigen, and 79-6 was added at different time points (day 0, 3, and 7).
Results: After polyclonal stimulation, a median of 7.4% of the B cells differentiated into plasmablasts. In the presence of 79-6, plasmablast formation was significantly inhibited by 91% and the proportion of class switched memory B cells dropped by 22%, both $p<0.01$). Production of IgGs was measured in culture supernatants (median of 600 ng/ml), After inhibition by 79-6, IgG-concentrations were significantly reduced (91%, $p <0.01$).
After stimulation with alloantigen, B cells successfully differentiated into plasma blasts (median 9.8%). Early addition of 79-6 (day 0, day 3) resulted in inhibition of plasma blast formation (median inhibition: 97% and 73%, respectively), while addition of 79-7 at day 7, when B cells have differentiated into plasmablast, did not result in significant inhibition of plasma blast formation.
Conclusions: 79-6 effectively inhibits differentiation of B lymphocytes into immunoglobulin-producing plasmablasts, whereas it does not inhibit Ig production once plasmablast formation is established. This implies that the timing of 79-6 administration in clinical practice is crucial.

The Anti-Inflammatory Effect of Perfusate from Prolonged Normothermic Machine Perfused Discarded Human Donor Kidneys on Monocyte derived Dendritic Cells

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Background: Dendritic cells (DCs) are potent antigen presenting cells and form the bridge between the innate and adaptive immune system. Toll like receptors allow DCs to sense damage associated molecular patterns (DAMPs) that are released upon ischemia reperfusion injury. Currently, information about the immunological state of the kidney during machine perfusion is lacking. We hypothesize that the immunogenicity of the organ might be reflected by the release of DAMPs in the perfusate. We developed a model using monocyte-derived DCs to monitor DAMPs being released by analysing the DC activation state. This model was used to analyse the immunogenicity of donor kidneys during prolonged normothermic machine perfusion (NMP).
Methods: Perfusate (n=11) was obtained from the PROPER trial where discarded human donor kidneys were perfused for 6h at 37°C. Monocytes were isolated from buffy coats and cultured with IL-4 and GM-CSF for 5 days to allow differentiation into DCs. DCs were incubated for 24h with 4x diluted perfusate from 4 timepoints (before the kidney is attached, after 1, 3 and 6h of perfusion). DC supernatant was analysed for IL-10 and TNF-α with ELISA. Cells were analysed with flow cytometry for expression of co-stimulatory markers CD80, CD83, CD86 and HLA-DR. Luminex analysis with a 27 cytokine panel was used to analyse the DC supernatant from the 6h perfusion samples.
Results: Incubation of DCs with perfusate had no effect on viability or activation with lipopolysaccharide. With increased perfusion time, exposure to DCs showed a decrease of costimulatory marker CD86 compared to the start of perfusion. Pro-inflammatory TNF- α could only be detected when DCs were incubated with perfusate collected early (1h) after the start of perfusion, but not at later time points. In contrast, release of the anti-inflammatory IL-10 by DCs increased when exposed to 6h perfusates. Luminex analysis showed an increase of IL-10, but also growth factor G-CSF and chemokine IL-8 were produced by DCs upon exposure to 6h perfusate.
Conclusions: Addition of perfusate from prolonged NMP of discarded human donor kidneys to human monocyte-derived DCs leads to a more anti-inflammatory DC phenotype as shown by a decrease in costimulatory marker CD86 and an increase in anti-inflammatory cytokine IL-10. This is further supported by Luminex analysis of the perfusate. Further studies should investigate the functional changes of these DCs and identify the compound(s) responsible for this anti-inflammatory DC profile.

Is urine the new blood? - Similarity of venous and urine pO2 values could lead to a new non-invasive clinical evaluation tool of renal oxygen consumption

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Background: Ex vivo kidney perfusion is a relatively new technique developed to preserve and evaluate kidneys, and normothermic machine perfusion (NMP) offers the possibility to investigate the organ in a metabolically active state. NMP not only allows to assess viability, but also to mimic pathological conditions and study renal physiology. Arterial and venous blood gas analyses are commonly performed during ex vivo perfusion, but urine samples are usually not subjected to gas analysis. This study aimed to compare arterial, venous, and urine pO2 parameters in a minimal warm ischemia time (WIT) versus 75 minutes WIT NMP experiment setup.
Methods: Nineteen pigs were anesthetized and underwent bilateral nephrectomy. Each kidney pair was randomly assigned to either a minimal WIT group or a 75 WIT group, after which kidneys were flushed with preservation solution and submitted to an average of 4 hours of oxygenated cold machine perfusion. Next, both kidneys were simultaneously connected to an NMP setup and perfused for 6 hours with a 95% O_2/5% CO_2 mixture. Arterial, venous, and urine gas analyses were performed at 1, 3, and 6 hours of perfusion.
Results: In the 75 WIT group, venous pO_2 (kPa) (27.01±4.35 at 1h, 24.75±5.08 at 3h, 23.37±5.4 at 6h) and urine pO_2(22.89±1.93 at 1h, 23.53±2.41 at 3h, 25.48±2.07 at 6h) were very similar throughout perfusion (*P*=0.611), as well as for the minimal WIT group venous pO_2 (23.41±4.11 at 1h, 25.41±6.39 at 3h, 26.26±6.54 at 6h) and urine pO_2 (21.43±1.86 at 1h, 23.07±2.25 at 3h, 25.55±2.31 at 6h) (*P*=0.077). We found no statistically significant difference between the urine pO_2 of the two WIT groups (*P*=0.303).
Conclusions: In order to calculate oxygen consumption of the kidney during machine perfusion, parameters such as arterial and venous pO_2 and arterial flow are necessary. However, in the clinical in vivo setting, obtaining renal venous samples is a laborious and invasive procedure. The striking similarity of urinary and venous pO_2 that we found in this study suggests that the urinary partial pressure of oxygen may adequately reflect the renal venous effluent pO_2 state. Although further studies are necessary for validation, these results show first evidence that urine samples from patients, in combination with an arterial blood gas and ultrasound-based renal flow measurement, could provide clinicians with an easy non-invasive tool to estimate renal oxygen consumption in vivo.

Changes in expression of bile-acid dependent transporters and cholesterol metabolism during hepatic normothermic machine perfusion

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Background: Normothermic machine perfusion (NMP) of organs is proven to be an excellent platform to study drug pharmacokinetic (PK) processes. As hepatic uptake and excretion of compounds into bile or blood is controlled by several transporter proteins, their expression and activity greatly affects drug plasma levels and elimination and is therefore of interest when studying PK processes. The expression of some important transporters is dependent on bile acid, however the effect of perfusion on transporter expression and the bile acid synthesis pathway has not been studied before. Therefore, we aim to study the effect of NMP on transporter expression levels and bile acid synthesis pathway.
Methods: Porcine livers biopsies were obtained from slaughterhouse pig livers that were applied for NMP studies (n=5) and were taken at t=0 and t=6h. Human liver biopsies were obtained from diseased explanted human livers and discarded research livers on NMP at t=0 and t=6h (n=6). RNA sequencing was performed on the biopsies using paired-end (2 x 150 bp reads) sequencing, with 20 million reads per sample. Expression was normalized based on total counts per sample.
Results: Expression of enzymes involved in bile acid synthesis showed to be decreased after 6 hours; cytochrome P-450 CYP27A1 expression (human:0.6x, p=0.05; pig:0.5x, p=0.01). HMG-CoA reductase, rate limiting enzyme for cholesterol synthesis, was increased after 6h (human:1.7x, p=0.006; pig:3.3x, p=0.07). Similarly, the expression of low-density lipoprotein receptor (LDLR), involved in cholesterol uptake, was strongly increased in porcine livers (3.4x, p=0.01) while the expression of ABCG8, which exports cholesterol into bile, decreased over time (human:0.5x, p=0.05; pig:0.4x, p=0.002). The gene expression of bile acid dependent transporters like the Organic Anion-Transporting Polypeptide (OATP)2B1 and the Organic Anion Transporter (OAT)2 showed to be reduced (human:0.5x, p=0.03; pig:0.3x, p=0.01), (human:0.4x, p=0.02; pig:0.4x, p=0.01) respectively. Also, the expression of bile salt export pump (BSEP), involved in biliary efflux, strongly decreased during NMP (human:0.5x, p=0.03; pig:0.3x, p=0.005).
Conclusions: Taken together, these changes in gene expression are suggestive of adaptive mechanisms to increase de novo cholesterol synthesis by the liver during NMP. Results indicate that during NMP the bile acid synthesis from cholesterol in the liver is exhausted, since the enterohepatic circulation of bile acids is missing. Therefore, we will study cholesterol levels and relative bile acid abundance in perfusate, liver biopsies and bile to further understand the underlying processes and to ultimately optimize perfusate composition during NMP.

Belevingsonderzoek bij nabestaanden van donoren.

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Background: Onderzoek naar de beleving van nabestaanden gedurende de donatieprocedure is van belang om goede zorg te leveren. De huidige inzichten in deze beleving zijn beperkt, maar wel van belang voor optimalisatie van de donatieprocedure vanuit het perspectief van nabestaanden. Vanuit het NTS programma Bouwen aan Donatiezorg (BaD) is daarom een onderzoek gestart met als doel het verbeteren van de organisatie van donatie vanuit het perspectief van de donor en diens omgeving.
Doel: Inzicht in de beleving van nabestaanden gedurende het donatieproces geeft input voor optimalisatie van de communicatie en omgang met nabestaanden en scholing voor professionals. De inzichten leveren tevens een bijdrage aan twee pilotprojecten(BaD) waarin een vaste contactpersoon nabestaanden gedurende de hele procedure begeleidt.
Methods: Onderzoeksbureau Excap, gespecialiseerd in belevingsonderzoek, heeft twee nabestaandenreizen in kaart gebracht (van orgaan- en weefseldonatie). Het onderzoek bestaat uit semigestructureerde diepte-interviews van 60-90 minuten via videobellen met 24 respondenten. 13 deelnemers zijn nabestaanden van orgaandonoren (n=3 in combinatie met weefseldonatie) en 11 nabestaanden van weefseldonoren. De respondenten zijn geselecteerd via de Patiëntenfederatie, Orgaandonatiecoördinatoren (ODC) en een oproep in het NTS magazine Nabestaandencontact.
Results:
Algemene inzichten:
• Oprechtheid en echte aandacht voor nabestaanden is belangrijk gedurende de hele procedure.
• Nabestaanden delen graag hun perspectief en beleving over het donatieproces om onwetendheid bij een breder publiek weg te nemen.
• Donatie kan betekenis geven aan het verlies van een dierbare, zoals troost en trots.
Inzichten in specifieke momenten van de nabestaandenreis:
• Het weerzien met de donor na de donatie kan impactvol zijn en hangt samen met verwachtingen en voorbereiding van nabestaanden.
• Nabestaanden weten onvoldoende wat ze qua informatievoorziening kunnen verwachten na de donatie.
• Vanaf het moment dat de ODC er was kwam er rust.
• Confrontatie met het transplantatieteam of vervoer kan impactvol zijn.
• De brief met resultaten van donatie en transplantatie is een kostbaar bewaardocument.
• Een bedankbrief van een ontvanger is van grote waarde.
Conclusions: De resultaten uit het onderzoek geven nieuwe inzichten die bewustwording creëren en/of de communicatie en omgang met nabestaanden kunnen verbeteren. Daarmee wordt bijgedragen aan de positieve beleving van nabestaanden rondom de donatie van hun dierbare.

The Dutch National Focal Point for Organ Trafficking

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Background: Trafficking of human beings for the purpose of organ removal (THBOR) and trafficking in human organs (THO) is a global problem impacting the safety of the donor and patient population. According to the WHO, 5–10% of all transplants performed worldwide are conducted illegally[1]. Since the Declaration of Istanbul on Organ Trafficking and Transplant Tourism in 2008[2], the Council of Europe (CoE) has taken steps formulating policy towards combatting and preventing transplant related crimes. In a resolution in 2013, on establishing procedures for the collection and dissemination of data on transplantation activities outside a domestic transplantation system[3], the CoE called on memberstates to install a National Focal Point for Organ Trafficking (NFP). In January 2021, the Dutch Ministry of Health (VWS) has asked the Dutch Transplant Foundation (NTS) to implement this resolution in The Netherlands, thereby joining the already existing NFP network by January 2022.

1: https://www.europarl.europa.eu/RegData/etudes/STUD/2015/549055/EXPO_STU(2015)549055_EN.pdf

2: Declaration of Istanbul. Available online: https://www.declarationofistanbul.org/

3: https://www.edqm.eu/sites/default/files/medias/fichiers/resolution_cmres201355_on_establishing_procedures_for_the_collection_and_dissemination_of_data_on_tr.pdf

Methods: The NFP will support the national efforts against transplant related crimes by regularly collecting anonymized data on potentially illicit transplantation activities and creating awareness among transplant professionals. The collected data will be reported and disseminated within the international network and will contribute to our understanding of the prevalence and scale of THBOR and THO in the Netherlands. As of now, the NTS is consulting with data and legal experts on the best method to collect and safely report the data.

Results: It is our aim to provide the transplant field with a safe, user-friendly and legally sound reporting protocol, with clear guidelines, on how to act when encountering a potential THBOR/THO case. NTS will provide regular reports on the data collected. The goal of the NFP network is to gain insight in trafficking routes and to identify complicit brokers, not to prosecute individual patients. The NFP will also work towards building and maintaining a relationship network of relevant national and international parties.

Conclusions: To make our national contribution to the NFP network a success, it is crucial that transplant professionals recognize and acknowledge the need for an NFP and know where to find us. At the Bootcongress we will provide background information and demonstrate methods and guidelines on how to act when there is a case in a hospital.

Radiological screening methods in deceased organ donation: an overview of guidelines worldwide

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Background: Organ transplantation is performed worldwide, but policies regarding donor assessment and imaging are not uniform. An overview of the policies in different regions of the world is missing. This study aims to investigate the various protocols worldwide on radiological screening in deceased organ donation.
Methods: An online survey was created to determine the current policies in different countries regarding radiological screening in deceased organ donation. Competent transplant authorities were approached through email and asked to fill out the questionnaire based on their current protocols.
Results: A total of 29 countries filled out the questionnaire (43 countries were approached, response rate 67%). In 17% of the countries no abdominal imaging is required prior to procurement. In 48% an abdominal ultrasound (US) is performed to screen the abdomen and in 21% an enhanced abdominal Computed Tomography (CT). In 13% of the countries both an unenhanced abdominal CT scan and abdominal US is performed. In 38% of the countries a chest radiographic (CXR) is performed to screen the thorax, in 28% only a chest CT and in 34% both a CXR and a chest CT is performed.
Conclusions: Policies regarding radiologic screening in deceased organ donors show a great variation between different countries. Consensus on which diagnostic imaging method should be applied is missing but a uniform approach will contribute to quality and safety, which does justice to the national and international exchange of donor organs.

Preliminary results evaluation Quality Standard Donation – Dutch new donor law

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Background: In July 2020 the new donor law was implemented and the government started to send letters to citizens who were not registered in the Donor Register (7 million people). In case of no response the person will be registered with 'no objection' against donation, which means the same as 'consent' for donation. This new law could only pass after a necessary amendment to develop a 'Quality Standard Donation'. This standard gives information on new items of the donor law; a) how to approach donor families in case of 'no objection' in the Donor Register, b) the possibility for families to make clear that 'consent' or 'no objection' registration does not match with the known wishes of the donor. The use of the Quality Standard Donation is evaluated in practice. The first preliminary results are available.
Methods: Data are based on: 1) evaluation forms for physicians who approached donor families for organ or tissue donation, 2) a national application (NovaNORD) where information on donation from all hospital deaths is registered, from January – October 2021.
In total 165 evaluation forms for organ donation are analyzed from 28 hospitals, covering the period of January – October 2021. Additionally, 116 evaluation forms for tissue donation from 9 hospitals are analyzed, from July – October 2021.
Results: *Evaluation forms – no donation:*
- *Organ donation:* in case of 'consent' (n=46) 3 times (6,5%) families made clear that the registration did not match with the known wishes of the donor, in case of 'no objection' (n=34) this was 15 times (44%).
-*Tissue donation:* in case of 'consent'(n=32) 6 times (19%) families made clear that the registration did not match with the known wishes of the donor, in case of 'no objection' (n=41) this was 24 times (59%).
Data NovaNORD:
-*Organ donation:* in case of 'consent' (n=194) 33 times (17%) families made clear that the registration did not match with the known wishes of the donor, in case of 'no objection' (n=137) this was 78 times (57%).
-*Tissue donation:* in case of 'consent'(n=2044) 455 times (22%) families made clear that the registration did not match with the known wishes of the donor, in case of 'no objection' (n=1288) this was 758 times (59%).
Conclusions: These preliminary data give a first insight in how the Quality Standard Donation works in practice in approaching families for organ and/or tissue donation. A difference is seen in the outcome of the donor conversation between 'consent' and 'no objection'. Updated data and detailed information will be shown at the congress.

The effect of contrast-enhanced Computed Tomography in deceased kidney donors on transplantation outcomes

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Background: In 17-18% of the deceased donors in The Netherlands a CT scan is performed, in some cases using intravenous contrast medium (ICM) for enhancement. However, ICM administration has been associated with acute kidney injury. The effect of donor administered ICM on graft function has been poorly studied and subjected to selection bias. The Dutch donor population is known for its high number of donors after determination of circulatory death (DCD), generally yielding kidneys more at risk for ischemia-reperfusion injury and delayed-graft function (DGF) and thus more susceptible to ICM nephropathy.This study aims to investigate the effect of the administration of ICM during CT in deceased kidney donors from the Dutch population on transplant outcomes in kidney recipients.
Methods: A retrospective analysis of all Dutch donors, reported to Eurotransplant between 2014 – 2018, and the concomitant kidney recipients, was performed. Donor characteristics and follow up data on kidney recipients were obtained from the Eurotransplant and Dutch Transplantation Foundation Database respectively. For each kidney transplant, the donor record was reviewed for ICM exposure. DGF was defined as the requirement of dialysis within 7 days after transplantation
Results: Between 2014 – 2018, 1464 kidney donors were reported and procured, of which 174 donors with a preoperative CT scan had to be excluded due to missing data on ICM administration. This resulted in the inclusion of 1289 donors, of which 141 were exposed to ICM, who donated their kidneys to 2000 recipients.
Age, BMI, pre-procurement creatininelevel and gender did not differ significantly between the two donor groups. The number of DCD donors was significantly higher in the donors who were exposed to ICM (65% in the ICM group vs 47% in the non-ICM group, $p<0.0001$). There was a skewed distribution in the two groups regarding hypertension (22% in the ICM group vs 31% in the non-ICM group, $p=0.002$) and history of diabetes (5% in the ICM group vs 8% in the non- ICM group, $p=0.006$). In the recipients groups, age and gender were equally distributed.
Exposure of the donor to ICM was not significantly associated with DGF rate (40.3% in the ICM group vs 35.3% in the non-ICM group, p=0,669). Also, no significant differences were seen in creatinine serum levels at 3 months, one year, two years, and three years after transplantation.
Conclusions: The preliminary results of this study show that intravenous contrast medium administration appears to have no effect on early midterm graft function after transplantation. This outcome is particularly noteworthy due to the higher number of DCD donors in the ICM group.

Successful kidney transplantation in patients with hyperoxaluria: 7 years experience

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Background: The success rate of kidney transplantation (KT) in hyperoxaluria patients is low because of recurrent calcium-oxalate deposition and nephrolithiasis. Seven years ago we established a protocol to reduce plasma oxalic acid levels peri-transplantation based on intensified dialysis and low oxalic acid intake to improve transplant function and survival.
Methods: 26 patients received 28 KTs with the hyperoxaluria protocol. Patients had extensive comorbidity including four heart transplants, one liver transplant, one lung transplant, seven others were second opinions rejected elsewhere because of complexity. Twelve were retransplants.
The causes of hyperoxaluria were: 2 primary hyperoxaluria, 2 pancreatic insufficiency, 6 gastric bypasses, 11 bowel resections (2 Encapsulating Peritoneal Sclerosis), 3 high output stoma, 3 other. Serum oxalic acid levels were >40 umol/l in all but 1 patient (mean 66 umol/l). Median time on dialysis was 28 months (range 3.1-215). Mean age at transplantation was 52.5 years (26-74).
Low oxalic acid diet was started at diagnosis. When possible, dialysis was intensified in the week before transplantation (primarily LD recipients) and this was continued after transplantation until urine production>2L/day. After KT, tube feeding was started. As the protocol is quite a burden, it was eased. Intensified dialysis before transplantation was omitted, and intensified dialysis and tube feeding after transplantation were stopped at 2 weeks from patient 14 onwards. Then regular dialysis and low oxalic acid diet was restarted.
Results: Transplant function was direct in 11, 13 had DGF and 4 NFG.
8/10 patients (primarily LD) with and 3/18 (primarily DD) without intensified dialysis before transplantation had direct function.
In 22 transplants a renal biopsy was done within 3 months after KT. 13 showed ATN, seven rejection, one TMA, one infection, five showed oxalate depositions, three nefrocalcinosis.
After 3 months 19/24 (79%) transplants were functioning with mean eGFR 52 ml/min (24-87 ml/min). Oxalic acid levels were <15 umol/l in all and 8/19 patients had normal values(<5 umol/l).
After 1 year 17/21 (81%) transplants were functioning with mean eGFR 51 ml/min (31 - 94 ml/min).
Conclusions: Patients with hyperoxaluria have many comorbidities and increased failure and death risks. In the large majority of patients KT was successful, in part after a period of DGF. Intensified dialysis in the week before KT may improve results.

Reducing cold ischemia time by donor liver 'back-table' preparation under continuous oxygenated machine perfusion of the portal vein

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Background: Non-anastomotic strictures (NAS) of the biliary tree after liver transplantation are one of the leading causes of graft failure. Donor age and the length of cold ischemia time are well-known risk factors for the development of NAS. End-ischemic hypothermic oxygenated machine perfusion (HOPE) of liver grafts reduces the incidence of NAS, and has the potential to reduce cold ischemia times. We hypothesized that if a part of the back-table procedure could be performed under continuous HOPE, cold ischemia time would be reduced, and the utilization rate of high-risk donor livers would increase.
Methods: The back-table of eight consecutive high-risk, initially declined donor livers was performed with ongoing HOPE. Upon arrival at our transplant center, the remainder part of the adherend diaphragm was removed from the graft. The extrahepatic portal vein was dissected from surrounding tissue and cannulated. Further graft preparation was then continued during HOPE through the portal vein. After at least one hour of HOPE, grafts were rewarmed to 37 degrees and viability of liver and biliary tree was assessed during normothermic machine perfusion. Livers that met the predefined viability criteria were subsequently transplanted.
Results: Compared to 60 similar high-risk donor livers of which the back-table was performed according to standardized fashion in a bowl with ice-cold preservation solution, a back-table procedure with ongoing HOPE led to a decrease in non-oxygenated back-table time from median 74 minutes (IQR 58-92 minutes) to median 23 minutes (IQR 18-32 minutes), $p < 0.01$. Median total cold preservation times were reduced from 279 minutes (IQR 254-297) to 232 minutes (IQR 127-248), $p = 0.01$. Utilization rate of these high-risk livers was higher in the HOPE back-table group than in the non-oxygenated back-table group, but this did not reach statistical significance (88% versus 62%, $p = 0.16$).
Conclusions: Cold ischemia times of liver grafts can be successfully reduced up to an hour using portal vein only HOPE during back-table preparation. This can result in the successful salvage of donor livers that were previously deemed non-transplantable due to excessive ischemic damage.

Chronic active antibody-mediated rejection is the major cause of kidney graft failure long after transplantation: results of a cohort of recipients with a very long-time follow-up after transplantation

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Background: Biopsy-proven causes of graft loss during a very long time of follow-up after kidney transplantation are scarcely documented. In addition, the overall impact of cellular and antibody-mediated rejection in relation to death with a functioning graft is usually not taken into account.
Methods: Patients transplanted between 1995 and 2005 (n=737) in the Erasmus MC were followed on a regular basis until January 2021. The recipients were divided according to age at transplantation into 3 groups; 18-39 years (young), 40-55 years (middle age) and older than 55 years (elderly). For cause renal transplants biopsies were clustered into the categories; rejection, interstitial fibrosis and tubulus atrophy, return original disease and diagnosis of *de novo* kidney disease. Other categories of graft loss were: "death with functioning graft", "unknown" and "other causes of graft loss" (e.g. infection-related acute kidney injury).
Results: In over 95% of cases the cause of graft loss could be classified by kidney biopsy or medical events. Rejection was the main cause of graft failure censored for death in every time period after transplantation. The incidence of cellular rejection became rare 6 years after transplantation while the cumulative incidence of chronic active antibody-mediated rejection (c-aABMR) increased over time (1.1% per year). C-aABMR was not diagnosed anymore beyond 15 years of follow-up in recipients without pre-transplant donor-specific anti-HLA antibodies (DSA). An episode of cellular rejection was associated with an increased incidence of c-aABMR diagnosis in the short-term but did not increase the overall incidence of c-aAMBR in the long-term. Only the presence of pretransplant DSA and no other clinical or demographic factor was associated with the incidence of c-aABMR.
Death as a cause of graft failure became an important competitive risk factor long after transplantation and resulted in a significantly lower frequency of rejection-related graft loss in the elderly group (11% vs 23% in the young group at 15 year follow-up). Recurrence of original disease and *de novo* kidney disease were minor causes of graft failure.
Conclusions: C-aABMR is a major cause of kidney graft loss after long-term follow-up, but time after transplantation, the presence of DSA before transplantation, and age of the recipient determine the relative contribution to overall graft loss.

Systematic review and meta-analysis of TTV load as marker of infection and rejection in solid organ transplantation

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Background: Balancing immunosuppression to prevent infection and rejection in solid organ transplant recipients (SOTx) remains a challenge. Torque teno virus (TTV), a commensal non-pathogenic virus, has been proposed as marker of functional immunity: higher loads may correspond to over-immunosuppression, and lower loads to under-immunosuppression. This review offers an overview of the current literature on the association between TTV loads and infection and rejection in SOTx recipients.
Methods: A systematic search strategy resulted in 548 records. After screening, 24 were included in qualitative assessment, and 13 for quantitative synthesis. Studies were included if the association between TTV load and either infection or rejection in SOTx was studied. Non-original and non-peer-reviewed studies were excluded. The Quality in Prognosis Studies tool was used to assess the risk of bias. Meta-analyses were performed on results with similar analyses and endpoints.
Results: Most studies found evidence that supports an association between TTV load and rejection. Meta-analysis showed lower TTV loads in the rejection group, and a odds and hazard ratio lower than 1 for developing rejection per 1 log TTV load-increase. For infection, the association was less evident. Meta-analysis showed higher TTV loads in patients with infections, and an odds ratio and a non-significant hazard ratio larger than 1 for developing infection, per 1 log load-increase. Qualitative bias assessment showed varying risks of bias between studies.
Conclusions: This systematic review and meta-analysis presents evidence for an association between TTV load and rejection, however the association with infection seems less evident. The inconsistent results between studies on the association with infection may reflect the heterogeneity of the endpoints and/or might signify a limited predictive value of TTV for anticipating infections. Diagnostic tests or prognostic models based on prediction models remain to be built and carefully validated, as these will offer individualized predictions for developing in infection and rejection for SOTx recipients.

Tacrolimus high metabolizers in a cohort of kidney transplants in Amsterdam Retrospective cohort study

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Background: Tacrolimus (Tac) is important as first line immunosuppressant in kidney transplantation (KTx). Underdosing of Tac increases the risk of acute rejection, while overdosing can cause nephrotoxicity. Tacrolimus is a drug with a high intra- and interindividual pharmacokinetic variability. This is partly due to different polymorphisms of the cytochrome P450 (CYP) enzyme. The CYP3A5*1 allele is the subtype leading to fast tacrolimus metabolism and has evidently higher prevalence in the African American (AA) population compared to whites. High doses might be accompanied by higher peak levels, which can adversely affect renal function.The population of this study consists of a relatively high number of patients from African or Caribbean background.With this study, we aimed to identify patients with higher Tac dose requirement and possible fast Tac metabolism and correlate this to ethnicity, rejection incidence and kidney function.
Methods: We retrospectively analyzed data of 260 kidney transplant patients using Advagraf in the AUMC at two and six weeks and three, six and 12 months after KTx to determine Tac concentration (C), dose (D) and kidney function. Based on mean C/D ratio, patients were classified as high metabolizers (HM) (C/D ratio ≤ 1.05 ng/mlx1/mg) or slow metabolizers (SM) (C/D ratio >1.05 ng/mlx1/mg) and we assessed the correlation between C/D ratio, dose and ethnicity to kidney function (creatinine clearance (CrCl)) at six and 12 months and to rejection incidence.
Results: High metabolizers (61%) showed significantly worse graft functions at six months (eGFR HM 44.42 ± 16.41, eGFR SM 50.53 ± 18.60, p=0.007; CrCl HM 56.33 ± 21.45, CrCl SM 63.90 ± 23.02, p=0.030) and notably but not significantly worse at 12 months (eGFR HM 46.40 ± 16.11, eGFR SM 50.70 ± 18.40, p=0.065; CrCl HM 61.39 ± 22.25, CrCl SM 63.87 ± 23.09, p=0.454). Tac trough levels were significantly lower in high metabolizers at two and six weeks (p=0.000). No difference in rejection rate was seen between high and slow metabolizers (p=0.641). High metabolizers comprise of relatively more African/Creoles (ACs) (p=0.000) and less whites (p=0.048). 66 patients required a mean dose >15mg daily in the first year. They showed no poorer kidney function compared to lower dosed patients. Acute rejection rate was similar between all groups.
Conclusions: High tacrolimus metabolism is associated with poorer graft function at six months and initial lower tacrolimus levels and is present in more ACs compared to whites and Asians and in patients classified as high metabolizers. We propose increasing initial Advagraf dosing for ACs to 20mg to achieve target tacrolimus trough levels.

Impact of endoscopic ultrasound in unresectable perihilar cholangiocarcinoma patients in liver transplantation work-up

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Background: For a highly selected group of patients with unresectable perihilar cholangiocarcinoma (pCCA), liver transplantation (LT) is a treatment option with curative intent. Both endoscopic ultrasound (EUS) and surgical exploration are part of the Dutch screening protocol for pCCA, to identify either metastatic lymph nodes (LN) or other abdominal metastases. When metastases are found, survival is very limited and patients are excluded from further LT screening. However, the added value of EUS for LN detection in this protocol that also includes MRI and PET-CT is unclear. Moreover, EUS is currently not performed in a standardized way. Therefore, this study investigates the added value of EUS screening for metastatic LN with tissue acquisition in patients with unresectable pCCA who are potentially eligible for LT.
Methods: In this retrospective, nationwide, multicenter cohort study, patients with suspected unresectable pCCA who underwent an EUS in the screening for LT between 2010 and 2021, were included. Data on EUS- and surgical LN status were collected. During EUS, sampling of suspicious LN was performed if deemed necessary by the endoscopist. The primary outcome of this study was the added value of unstandardized EUS, defined as number of patients not undergoing further screening due to malignant LN identified by EUS. Secondary outcomes were the number of malignant LN found in patients undergoing surgery after EUS.
Results: A total of 84 EUS procedures were performed in 75 patients (63% male, median age of 56 years, 52% with underlying PSC). In 18/75 (24%) patients a total of 31 suspicious LN were identified, with tissue acquisition in 28/31 (90%) LN. Two of the 28 (7%) biopsies in 2/75 (3%) different patients confirmed malignancy and further screening was therefore precluded. Of the remaining 73 patients, 19 (26%) did not undergo any form of surgery because of other reasons such as clinical deterioration or other malignancy found. The first surgical procedure was performed after a median of 44 days after EUS. In total, 44/75 (59%) patients underwent an explorative laparotomy or diagnostic laparoscopy in whom malignant metastatic LN were found in 6/44 (14%) patients precluding further work-up. Finally, LT was performed in 29/38 (76%) patients and no metastatic LN were identified. The final postoperative diagnosis was benign in 7/38 (18%) patients.
Conclusions: This nationwide study showed that the current unstandardized EUS screening of metastatic LN in patients with unresectable pCCA in LT work-up has limited value and LN were missed in 14% of the cases. However, this may improve when systematic survey of all metastatic LN locations is implemented.

Development and validation of a prediction model for nonseroconversion after SARS-CoV-2 vaccination in kidney transplant recipients

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Background: Kidney transplant recipients (KTRs) are still at risk for COVID-19 disease after two doses of SARS-CoV-2 vaccination. A tool for predicting the immune response to vaccination in KTRs could help patient-specific risk stratification. Furthermore a prediction model might expose interactions, that helps to understand the process of the development of a humoral response in these complex patients.
Methods: We developed and internally validated a multivariable logistic regression-based prediction model, derived from the data on KTRs who were prospectively recruited to the Dutch REnal patients COVID-19 VACcination (RECOVAC) consortium. Participants received two doses of the mRNA-1273 COVID-19 vaccine (Moderna). The primary outcome was nonseroconversion, i.e. reaching a SARS-CoV-2 Spike S1-specific IgG antibody concentration at day 28 following the second vaccination of <10 BAU/ml, in which case participants were classified as non-responder.
Results: The final model included 288 KTRs of which 164 responders and 124 non-responders, and comprised 6 predictors for nonseroconversion: increased age, lymphocytopenia, lower estimated glomerular filtration rate (eGFR), shorter time after transplantation, not using steroids and the use of mycophenolate mofetil/mycophenolic acid (MMF/MPA). An interaction between MMF/MPA use and eGFR was found. These variables accurately predicted the response to SARS-CoV-2 vaccination. The optimism-corrected model showed excellent discrimination (area under the curve, 0.84, 95% confidence interval 0.79 to 0.88).
Conclusions: The prediction model is a promising tool to identify KTRs who do not seroconvert after two doses of SARS-CoV-2 vaccination and who may benefit from a third vaccination or passive immunization. These data also give rise to the hypothesis that the interaction between MMF/MPA use and eGFR may explain why MMF/MPA is associated with non-response in populations with kidney patients, but not in patients with rheumatic diseases.

Poor Sleep Quality, Fatigue, Social Participation and Health-Related Quality of Life in Kidney Transplant Recipients

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Background: Fatigue and limited health-related quality of life (HRQoL) are common among kidney transplant recipients (KTR). We hypothesized that both may partly be attributable to poor sleep, yet few studies have addressed sleep quality in this population.
Methods: We used data of KTR (≥1 year after transplantation) and healthy controls (HC) from the TransplantLines Biobank and Cohort Study. Sleep quality was assessed using the validated Pittsburgh Sleep Quality Index. Determinants of poor sleep quality were identified using logistic regression. Associations of poor sleep quality with fatigue, societal participation, and HRQoL were assessed using linear regression. Among a subgroup of KTR, sleep quality was assessed before, at six and twelve months after transplantation, allowing to assess sleep quality trajectories over time.
Results: In total, we included 872 KTR (61.1% male, age 55.7±13.1y) with available data on sleep ≥1 year after transplantation, and 335 HC. In total, 16.7% of male KTR and 31.0% of female KTR reported poor sleep quality, which was significantly higher compared to HC (males: 8.8%, $P_{Chi\text{-}squared}$=0.017 and females: 15.5%, $P_{Chi\text{-}squared}$<0.001). Next to female sex, more anxiety and calcineurin inhibitor usage were main determinants of poor sleep quality. Additional analyses suggested effect modification by age, and subgroup analyses confirmed that calcineurin inhibitors were only significanty associated with increased risk of poor sleep quality in patients <57 years of age(OR 6.14, 95%CI 1.87-20.15). Poor sleep quality was associated with more fatigue (st. β 0.34, P<0.001), lower ability to concentrate (st. β 0.27, P<0.001), poorer societal participation (restriction score: st. β -0.24, P<0.001), and lower HRQoL (physical component: st. β -0.32, P<0.001 and mental component: st. β -0.40, P<0.001) among KTR. All associations remained independent of potential confounders. Longitudinal data in 124 participants showed that sleep quality improved after kidney transplantation in males (P<0.001), but not in females.
Conclusions: Poor sleep quality is common among KTR, and may potentially be a key target to improve fatigue, societal participation, and HRQoL.

Functional recellularized patient derived endothelium; a human vascular graft approach

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Background: In transplantation, the endothelial lining is the first barrier between the donor organ and recipient immune system. Damaged endothelium exposes extracellular matrix (ECM) molecules that can aggravate inflammation and cause graft rejection. Endothelial repair strategies may improve transplant outcomes. Here we prove that re-endothelialization of acellular blood vessels using kidney-vein endothelial cells (EC) generates a functional endothelium with vascular barrier function/innate immune conduit function.
Methods: Human common iliac veins (CIV) (n=19) from deceased healthy donors were decellularized by submersion in Triton X-100 (4%), ammonia (1%) and DNase. Efficiency of decellularization was checked by residual DNA content analysis and histology. Decellularized CIV were subsequently repopulated with human umbilical vein endothelial cells (HUVEC) or patient derived kidney-vein EC. The re-endothelialized veins were analysed using confocal microscopy for EC confluency. Functionality of the EC barrier was analyzed using trans-endothelial electrical resistance (TEER), dextran permeability and nitric oxide production (eNOS). The innate immune barrier function was assessed by co-culture with THP-1 monocytic cells (5:1 ratio) in a transmigration system.
Results: The CIV were fully decellularized, demonstrated by the complete removal of cellular components, and the removal of dsDNA (before: 83.8±29.0 , after:13.0±6.5 ng/mg). Histological integrity was preserved, as well as ECM polysaccharides. Confocal microscopy showed the formation of a confluent monolayer of cells as soon as 24 hours after seeding. After 28 days of culture repopulated CIV scaffolds remained confluent. At day 10, the constructs had TEER measurements above background of 15.1±12.2 $\Omega \cdot cm^2$ (n=4); reduced dextran permeability compared to decellularized CIV; and showed eNOS activity. These results indicated the restoration of a functional EC barrier. The innate immune barrier function was demonstrated by THP-1 cell adhesion and transmigration through the EC monolayer. THP-1 differentiation into M1 inflammatory macrophages and M2 anti-inflammatory macrophages was confirmed via flow cytometry and immunohistochemistry with representative markers.
Conclusions: We developed a procedure to efficiently decellularize human CIV and generated functional and long-term stable re-endothelialized veins using patient derived kidney-vein EC. This provides a new model to study re-endothelialization in-vitro.

Improved nephron maturation and stromal composition upon vascularization of kidney organoids

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Background: Human induced pluripotent stem cell-derived (hiPSC) kidney organoids have the potential to be developed into clinically transplantable auxiliary tissue. However, they lack a functional vasculature and the sparse endogenous endothelial cells are lost upon prolonged culture *in vitro*, limiting maturation and applicability. Here, we aim to develop a scalable model to vascularize kidney organoids through intracoelomic transplantation in chicken embryos.
Methods: HiPSC-derived kidney organoids are transplanted at day 19 of differentiation and harvested 1 and 8 days after transplantation. They are analyzed and compared to untransplanted controls using single cell RNA sequencing, immunofluorescence analysis, and electron microscopy.
Results: In transplanted organoids, we show expansion of human organoid-derived endothelial cells that reorganize into a perfused vascular network. Mesenchymal cells differentiate into perivascular cells supporting this vascular structure, while off target cell populations decrease. Perfused glomeruli display maturation and morphogenesis to capillary loop stage.
Conclusions: Our findings demonstrate the beneficial effect of vascularization on not only nephron cell types, but also the mesenchymal compartment, inducing the formation of ´on target´ pericytes which in turn are necessary for further maturation and stabilization of the neo-vasculature. The capacity of organoid derived endothelial and mesenchymal cells to form a functional vascular structure that promotes glomerular maturation and morphogenesis is very promising for in vitro vascularization attempts.

Creating a kidney-vasculature interaction model using a novel organ-on-chip system.

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Background: Induced pluripotent stem cell (iPSC)-derived kidney organoids have proven to be a valuable model to study kidney development and disease, however the lack of vascularization of this tissue often leads to a necrotic core and prevents organoids from reaching sequential stages of maturation. Although organoid vascularization has previously been achieved *in vivo* by implantation into animal models, this technique fails to provide a human-tissue-derived perfusable vasculature. The aim of our research is to culture kidney organoids in on the chip device together with endothelialized microchannels to mimic vasculature and thereby obtain a research model that more faithfully recreates *in vivo* conditions.
Methods: We used a novel organ-on-chip system consisting of a culturing chamber that connects with three microfluidic channels through a porous membrane. The surface of the device was subjected to plasma ashing and fibronectin coating to make it cell-culture ready. The chip's microfluidic channels were then seeded with green fluorescent protein human umbilical vein endothelial cells (GFP-HUVECs). Kidney organoids were then placed in the upper chamber and subjected to co-culture conditions.
Results: We proved the capacity of GFP-HUVECs to adhere to all surfaces of the channel, creating synthetic vessels. Culture of iPSC under kidney organoid inducing conditions in the chip under continuous fluid flow demonstrated the appearance of nephron structures, namely glomerular ($WT1^+$) and tubular ($Villin^+$, $E\text{-}Cadherin^+$) structures at day 17, therefore demonstrating kidney organoid culture if feasible in a microfluidic device. We analyzed maturation patterns of ECs native to organoid tissue, and observed that under flow conditions, EC populations demonstrate a maturation pattern that more closely resembles native tissue. Moreover, GFP-HUVECs derived from the chip's channels migrated through the pores and proliferated inside the organoid tissue, forming tubular structures presenting an open lumen, reminiscent of vessels.
Conclusions: To our knowledge, we present the first kidney organoids successfully cultured in a microfluidic organ-on-chip device and stablished proof-of-concept for this kidney-vasculature interaction model. Overall, we expect that this research will lead not only to an improvement of kidney organoid maturation by mimicking the interaction of endothelial vessels with kidney tissue, but also open a new door to translational applications such as pre-clinical drug trials.

Large-scale engineering and cryopreservation of hiPSC-derived nephron sheets

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Background: The generation of human induced pluripotent stem cells (hiPSCs) has opened a world of opportunities for stem cell-based therapies in regenerative medicine. Currently, several human kidney organoid protocols are available that generate organoids containing kidney structures. However, these kidney organoids are relatively small ranging up to 0.13 cm^2 and therefore contain a small number of nephrons compared to an adult kidney, thus defying the exploration of future use for therapy.
Methods: Expansion of the 3-dimensional phase of kidney organoid differentiation was performed in 4 hiPSC cell lines by using 2 templates to define the culture site for standardized seeding of differentiating cells.
Results: We show a scalable, easily accessible, and reproducible method to increase the size of the organoid up to a nephron sheet of 2.5 cm^2 containing a magnitude of nephrons. Confocal microscopy showed that the subunits of the nephrons remain evenly distributed throughout the entire sheet and that these tissue sheets can attain ~30,000-40,000 glomerular structures. Upon transplantation in immunodeficient mice, such nephron sheets became vascularized and matured. They also show reuptake of injected low-molecular mass dextran molecules in the tubular structures, indicative of glomerular filtration. Furthermore, we developed a protocol for the cryopreservation of intermediate mesoderm cells during the differentiation and demonstrate that these cells can be successfully thawed and recovered to create such tissue sheets.
Conclusions: The scalability of the procedures, and the ability to cryopreserve the cells during differentiation are important steps forward in the translation of these differentiation protocols to future clinical applications such as transplantable auxiliary kidney tissue.

Bile duct on a chip: engineering a microfluidic platform for studying biliary epithelium in a dish

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Background: Biliary complications that may arise after liver transplantation, such as anastomotic strictures and diffuse biliary strictures, are challenging and can negatively impact the transplant outcome. Ischemia-related cell death and impaired regeneration of damaged biliary epithelium is known to be involved in causing these complications. Intrahepatic cholangiocyte organoids (ICO) allow for the expansion and study of cholangiocyte-like cells, but access to the lumen of the organoids is limited and can only be studied after disrupting the 3D structure. There are currently no *in vitro* models mimicking the circumstances as exposure of bile ducts to warm ischemia time or cold storage, and therefore we aimed to establish a microfluidic bile-duct-on-chip (BDOC) platform for studying the effect of these conditions on biliary epithelium *in vitro.*

Methods: ICO were initiated from human liver biopsies (N=5) obtained during liver transplant procedures. Three-channel BDOC (dimensions; length 1cm, width and height 500µm) were prepared by casting polydimethylsiloxane (PDMS) into a mold. Subsequently, plasma treated PDMS chips were bonded to glass slides. The BDOC channels were filled with collagen type I pre-gel and viscous finger patterning procedures were used to create a lumen inside the collagen hydrogels. ICO-derived cells ($25 \cdot 10^3$ cells/channel) were introduced into the channels and ICO expansion medium was added to the reservoirs. The BDOC were incubated for up to 21 days. Growth of epithelial cells was monitored using confocal microscopy and histology.

Results: The lumen inside the collagen hydrogels were on average 287µm (SD:43µm). ICO-derived cells populated the entire surface of the channels with a single layer of cells within 7 days after seeding. Whole mount confocal imaging revealed that cells were columnar in shape and morphologically looked like biliary epithelium. Zonula Occludens-1 (ZO-1) staining showed cholangiocyte-like polarization of cells in honey comb patterns. The cells express the cholangiocyte markers cytokeratin 7 and 19 on gene and protein level.

Conclusions: The results show that microfluidic approaches combined with cholangiocyte-like (KRT 9 and 19-positive) cells from ICO can be used to create healthy small diameter intrahepatic bile duct structures *in vitro.* This model can allow for detailed analysis of epithelial damage. Subsequently, this BDOC platform can also be used to study the impact of ischemia or reperfusion settings while mimicking the effect of different perfusion techniques, such as oxygenated cold or warm machine perfusion.

Single-cell RNA sequencing of human pancreatic islets reveals a role of pancreatic duct cells as mediator of the inflammation during the early stage of T1D

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Background: Type 1 diabetes (T1D) is an inflammatory disease that is characterized by the autoreactive destruction of pancreatic beta-cells by immune cells. The goal of this study is to investigate the response of human pancreatic cells to pathophysiological conditions associated with T1D, ultimately to unravel the molecular mechanisms driving loss of the functional beta-cell mass in T1D.
Methods: Pancreatic islets from 3 non-diabetic donors were treated with inflammatory stressors (IL1β&IFNγ and IFNα) for 24 and 72h to mimic the physiopathology scenarios that occurs in diabetes. After treatment, islets were processed for single-cell RNA sequencing. In addition, islets from 2 T1D donors and 3 non-diabetic controls were processed for single-cell RNA-seq. Finally, validation experiments were performed with human islets and EndoCBH1 cells treated with human recombinant IL8 or blocking IL8 antibody.
Results: Proinflammatory conditions significantly compromised beta-cell identity and function. A subpopulation of beta-cells (HMOX1+,DDIT3+, SQSTM1+,SLC3A2+) presented lower levels of MHCs when exposed to IL1β&IFNγ treatment. Anti-oxidant defense is increased in islet cells, while duct cells show a clear pro-inflammatory profile. We confirmed the presence of a duct subpopulation presenting a proinflammatory signature in T1D, including increased expression of IL8. Furthermore, we show that IL8 activates NFκB in beta-cells. IL8 treatment compromises primary human beta-cell function, while blocking IL8 prevents cytokine-induced beta-cell failure.
Conclusions: We identified a beta-cell subpopulation that presents an adaptation to an inflammation environment that may represent a protective mechanism to T1D by lowering antigen-presentation capacity, and thereby reducing the risk of recognition by (auto-)immune cells. Furthermore, our data revealed a potential role of the duct cell compartment in the amplification of islet inflammation in T1D. In addition to that, we show that the pro-inflammatory cytokine IL8 can act directly on beta-cells and have a detrimental effect on beta-cell function. Overall, this study sheds new light into the understanding on molecular aspects of the adverse pro-inflammatory processes that are detrimental for beta-cells. Therefore, our efforts will help to develop new immune-therapy strategies that will enhance the survival of beta-cells in islets transplantation.

A novel approach for the generation of substantial numbers of intrarenal T cells from kidney biopsies allows for in-depth characterization at the single cell level

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Background: Chronic active antibody-mediated rejection (c-aABMR) is the most frequent cause of renal allograft loss in the long-term. Biopsies with c-aABMR may show large areas of T cells infiltrates within the interstitium. Function and antigen-specificity of these T cells is currently unknown. The number of intrarenal T cells obtained following enzymatic dissociation of a renal biopsy is in most cases insufficient for detailed characterization. Therefore, we developed a new technique to maximize the number of intrarenal T cells obtained from renal tissue.
Methods: The standard method of enzymatic dissociation of renal tissue (direct isolation) was compared to a novel method of tissue culture allowing T cells to migrate into the medium. In addition, the effect of exogenous IL-2 and IL-15 was studied. T cell numbers were quantified and phenotype of resident T cells ($CD69^{+}CD103^{+/-}$), TCR Vβ repertoire and functional characteristics were analyzed with multi-parameter flow cytometry.
Results: Renal tissue culture for 4 weeks in the presence of exogenous IL-2 and IL-15 yielded higher numbers of T cells ($3.1x10^{4}/mm^{3}$) when compared to cultures without exogenous cytokines ($71/mm^{3}$). Enzymatic dissociation of renal tissue yielded $662/mm^{3}$ T cells ($p<0.05$ compared to renal tissue culture).
T cells from renal tissue cultures with exogenous cytokines were compared with T cells directly isolated from renal tissue. The proportion of T cells with a resident phenotype did not change in the tissue culture, percentages amounted to 53% and 45% respectively. In addition, frequencies of $CD4^{+}$, $CD8^{+}$, $CD4^{-}CD8^{-}$, $TCR\gamma\delta^{+}$ T cells and MAIT T cells remained similar. $CD4^{+}$, but not $CD8^{+}$, T cells had a more differentiated memory phenotype after tissue culture. The TCR Vβ-repertoire analysis was performed to check for clonal expansion of T cells but the distribution of TCR Vβ families remained unchanged. Functional analysis demonstrated that T cells of the renal tissue cultures with exogenous cytokines had a predominant Th1 cytokine secretion profile which was not significantly changed compared to directly isolated T cells from renal tissue.
Conclusions: Renal tissue culture in the presence of exogenous IL-2 and IL-15 allows for a significant increase in number of intrarenal T cells without major effects on composition and functionality. This novel method yields sufficient T cells from kidney biopsies for in-depth characterization.

Towards a GMP-compliant protocol for the differentiation of human pluripotent stem cells to Beta-like cells for the treatment of type 1 diabetes

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Background: The generation of insulin-producing pancreatic Beta-cells from human pluripotent stem cells (hPSC) *in vitro* would provide an unlimited cell source for drug discovery and cell replacement therapy for diabetes. Here we aim to generate Beta-cells under GMP (Good Manufacturing Practice)-compliant conditions that can be used for clinical application.
Methods: We applied a modified seven-stage (30-day) differentiation protocol to generate hPSC-derived insulin-producing Beta-like cells in a 3D microwell and scalable spinner flask culture system. Beta-cell function was evaluated *in vitro* by GSIS (Glucose-Stimulated Insulin Secretion), and *in vivo* by intraperitoneal glucose tolerance tests after transplantation of stage-7 cell clusters in immunodeficient mice and human C-peptide secretion was determined by ELISA. Single-cell RNA sequencing of stage 7 clusters was carried out. The expression profile of developmentally relevant genes and markers across the cell types was assessed.
Results: In the microwell set-up, cells acquired a pancreatic progenitor phenotype at stage 4 (day 12), characterized by the co-expression of PDX1/NKX6.1 (46.7%± 3.5;n=3). At the end of stage 7 (day 30), C-peptide-positive Beta-like cells (49.5%±10.5;n=3) and glucagon-positive alpha-like cells (18.4%±6.1;n=3) were present. The stimulation index upon exposure to glucose was 4.4 ± 3.1(n=5). Following transplantation of day-30 clusters into mice, stimulated human C-peptide levels reached 57.2 pmol/L (n=16), 80.5 pmol/L (n=16) and 391.8 pmol/L (n=9) at day 14, 28 and 60 respectively, indicating further maturation of the cells *in vivo*. Comparable differentiation efficiency was obtained in disposable spinner flasks. Preliminary single-cell transcriptomics data allowed us to identify and characterize all cell types present in the stage 7 clusters.
Conclusions: hPSCs-derived islets are a promising future alternative to donor islets for the treatment of type 1 diabetes. We can generate functional hPSCs-derived Beta-like cells in GMP-compliant conditions *in vitro.* We are currently applying these protocols to a clinical-grade PSC line that we expanded and banked in the GMP facility of our institute.

Prehabilitation of Candidates for Renal transplantation; the PreCareTx project

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Background: Prehabilitation may be an effective intervention to improve the overall fitness of kidney transplant candidates. By offering prehabilitation before the transplant, patients may be more likely to adopt an enduring healthy lifestyle. This may not only improve their overall fitness before the transplant and enhance recovery after transplantation but may also be beneficial for their health and quality of life before and after transplantation. The purpose of the Prehabilitation of Candidates for Renal Transplantation (PreCareTx) project is to develop, implement and test a multimodal prehabilitation program tailored to the needs of kidney transplant candidates (KTCs). The program will be focused on achieving lifestyle changes and will consist of physical training, dietary management, and stress reduction.
Methods: The PreCareTx-project comprises three consecutive phases:
1) Understand: a context analysis using the Context and Implementation of Complex Intervention (CICI) Framework will be performed to gain insight into contextual and implementation factors of influence on prehabilitation for KTCs to guide intervention development and implementation strategy selection by using qualitative (focus group meetings and individual interviews) and quantitative (questionnaire, TransplantLines databank analysis) methods.
2) Co-create: the multimodal prehabilitation program will be developed in co-creation with patients, their significant others and healthcare providers involved in the care for KTCs, using the Behavioral Change Wheel Method.
3) Test: a hybrid effectiveness-implementation study design will be used to examine the effectiveness of the prehabilitation to improve the frailty status of KTCs (primary outcome) and changes in physical and psychological fitness, nutritional status, quality of life and clinical outcomes (secondary outcomes) in a randomized controlled trial (N = 124). Data will be measured at baseline (T0), and at 12 weeks (T1) and 24 weeks (T2) after randomization. Next to this, a mixed-method study will be performed to gain insight into feasibility, barriers and facilitators for (further) implementation in a real-world setting by obtaining process measures regarding enrolment, attrition, safety, program content, intervention adherence, logistic problems and costs.
Results: The PreCareTx project started on the 1st of September 2021 by performing the contextual analysis. Intervention development will start in the spring of 2022. The hybrid effectiveness-implementation study will start in September 2022 and is expected to end in August 2025.

The incidence, predictors and course of fatigue after living kidney donation: a single center retrospective file research.

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Background: Living kidney donation has been considered the best therapeutic option for end-stage renal disease. Globally, a kidney from a living donor is used in almost 50% of all kidney transplants performed annually. Awareness of potential consequences due to a donation is important and donor morbidity should be minimized. Some literature suggests that living donation is associated with increased fatigue, but data is lacking. The aim was to investigate the incidence, predictors and course of fatigue after living kidney donation.
Methods: We performed a single center retrospective file research in which sociodemographic, clinical and surgical variables and self-reported fatigue were collected in 209 donors with 5 years follow-up. Descriptive statistics and the univariable and multivariable generalized linear mixed effect model were used to examine the relationship between the variables and fatigue.
Results: 3 Months post donation 26.8% of all kidney donors reported being fatigued. At 1-year post donation this was 10.7%. After the second year follow up the number of fatigued kidney donors fluctuated between 3.3-7.1%. Significant predictors of fatigue were serum creatine (P=0.0292), hand-assisted surgery compared to laparoscopic surgery P=(0.0412) and psychological medical history (P=0.0202).
Conclusions: The risk of fatigue is at its highest shortly after kidney donation and decreases over time. However, fatigue persists in a small group of kidney donors and does not disappear within the first two months after kidney donation. This is important knowledge to improve donor informed consent and a good implication for more research into high-risk donors and possible preventive interventions.

Nierteam aan Huis, online netwerkvoorlichting ten tijde van COVID-19

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Inleiding: Nierteam aan Huis (NTAH) betreft een voorlichting voor de patiënt en zijn sociale omgeving over alle vormen van nierfunctie vervangende behandeling. De meerwaarde van NTAH is dat het sociale netwerk van de patiënt adequaat geïnformeerd wordt over de impact van nierfalen en verschillende vormen van nierfunctie vervangende behandeling en dat de patiënt geholpen wordt een gesprek over nierdonatie bij leven op gang te brengen waarmee de kans op een vroegtijdige, liefst pre-emptieve transplantatie met een nier van een levende donor wordt vergroot. Ook is het doel van een voorlichting begrip te creëren voor de patiënt en ondersteuning vanuit zijn omgeving te bevorderen. Deze voorlichting vindt plaats bij de patiënt thuis of op een daarvoor geschikte locatie. Ten tijde van COVID-19 zorgden de richtlijnen van de rijksoverheid ervoor dat de voorlichting niet meer thuis en /of op locatie kon plaatsvinden. Hierdoor zijn we op zoek gegaan naar andere mogelijkheden en hier is de online / hybride voorlichting uit voort gekomen.
Methoden: Sinds juli 2020 zijn we gestart met het geven van voorlichting in een online omgeving. Het kennismakingsgesprek voorafgaande aan de voorlichting heeft in sommige gevallen ook online plaatsgevonden. We kennen inmiddels de volgende varianten:
Online kennismakingsgesprek, patiënt en voorlichters
Online voorlichting, zowel de patiënt als de genodigden zijn online aanwezig
Hybride vorm van voorlichting, patiënt en een aantal genodigden op locatie en overige deelnemers online aanwezig.
Resultaten: Door het inzetten van de online mogelijkheid hebben we de voorlichting door NTAH kunnen voortzetten.
We hebben in totaal uitgevoerd:
21 online kennismakingsgesprekken
17 online voorlichtingsbijeenkomsten, waarvan 2 met tolk
4 hybride voorlichtingsbijeenkomsten
We hebben iedere bijeenkomt op een gestandaardiseerde manier geëvalueerd en kregen overwegend positieve feedback. Patiënten hebben bijvoorbeeld aangegeven dat ze het fijn vonden dat er hierdoor geen vertraging op werd gelopen in het traject.
Er zijn ook een aantal patiënten die de bijeenkomst verplaatst hebben, omdat zij geen gebruik wilden maken van een online voorlichting.
13 uitgestelde voorlichtingsbijeenkomsten
Conclusie: Online of hybride voorlichting is een goed alternatief voor een live voorlichting. Belangrijk is dat de voorlichting aan het netwerk van de patiënt kan doorgaan. Deze vorm van voorlichting is ook heel geschikt om in te zetten bij patiënten waarvan de familie op afstand (eventueel in het buitenland) verblijft.

Ervaringen van nierdonoren in de periode vanaf ontslag uit het ziekenhuis tot 3 maanden na donatie: een exploratief kwalitatief onderzoek.

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Background: Als verpleegkundig specialisten kregen we signalen van nierdonoren dat het verblijf op de afdeling en nazorg mogelijk verbetering behoeft. Doel van het onderzoek was erop gericht de ervaringen van nierdonoren inzichtelijk te maken in de periode tussen ontslag uit het ziekenhuis en de follow-up 3 maanden na de nierdonatie om daarmee de kwaliteit van de follow-up, het herstel van de donoren en uiteindelijk in het verlengde hiervan, de kwaliteit van het leven van de donoren te kunnen verbeteren.
Methods: Er werd een exploratief kwalitatief onderzoek uitgevoerd waarbij individuele semigestructureerde online interviews werden afgenomen bij donoren die in 2018 of 2019 hun nier gedoneerd hadden. Deelnemers moesten rechtstreeks aan hun ontvanger gedoneerd hebben, de Nederlandse taal voldoende beheersen en het hele donortraject inclusief follow-up in ons centrum doorlopen hebben.
Donoren die voldeden aan de criteria werden via e-mail benaderd voor deelname aan het onderzoek. Ze kregen een patiënteninformatiebrief en informed consent formulier. De eerste 6 personen die reageerden werden geïncludeerd.
De interviewguide was gebaseerd op literatuurstudie en werd als pilotinterview getest.
Topics waren: herstel, communicatie, informatie en begeleiding.
Tijdens de analyse werd een cyclische werkwijze gehanteerd, waardoor opname en ontslag als topics werden toegevoegd.
Results: Er werden 6 donoren geïnterviewd, 3 mannen en 3 vrouwen, in de leeftijd van 41 tot 71 jaar, de interviews duurden 24 tot 37 minuten.
Donoren ervoeren wisselende lichamelijke klachten, zorgen en onzekerheid t.a.v. wondgenezing en conditioneel herstel en dankbaarheid. De verwachtingen kwamen niet altijd overeen met de belevingen. De begeleiding door de verpleegkundig specialisten in het hele traject werd als prettig ervaren, maar de zorg op de afdeling en de informatie bij ontslag behoeft verbetering.
Conclusions: Op basis van deze resultaten zijn we in de voorlichting sterker gaan benadrukken dat lichamelijke klachten heel individueel bepaald zijn en soms lang kunnen duren. Ook houden we als verpleegkundig specialisten na ontslag intensiever telefonisch contact met de donoren en geven we expliciet dat wij ook de contactpersoon blijven bij vragen en/of klachten na ontslag.
Op basis van deze resultaten zal voorts overlegd worden hoe we samen met de chirurgisch verpleegafdeling de bejegening en begeleiding van de donoren op de afdeling kunnen verbeteren. Ook zal ten behoeve van betere informatie over herstel in de periode kort na ontslag een patiëntenfolder ontwikkeld worden.

Hemofiltration improves the diluted whole blood perfusate of the isolated slaughterhouse porcine heart perfusion model.

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Background: In a normothermic ex situ heart perfusion approach (PhysioHeart™ perfusion system), whole blood from slaughterhouse pigs is collected during exsanguination of the animal for oxygenated perfusion of the heart. After reperfusion, high potassium levels are found in the perfusate that increase over time, interfering with optimal cardiomyocyte repolarization and thus conductance. In this study we aimed to optimize the perfusate composition by adding a hemofiltration system in the PhysioHeart™ perfusion circuit.
Methods: Fourteen hearts were harvested from Dutch Landrace pigs, that were sacrificed for human consumption. All hearts were preserved for 4 hours using static cold storage after which all hearts were reperfused for 4 hours on the PhysioHeart™ platform, a normothermic, oxygenated, diluted whole blood loaded heart model. In seven hearts, a hemofiltration system was added to the perfusion circuit. Prior to mounting of the heart, the perfusion fluid was filtrated for 1 hour with a flow of 1L/hour. After mounting the heart, filtration flow was maintained at 1L/hour. Blood samples and cardiac function were analyzed at multiple time points, with blood samples as primary outcome. Survival was defined as a cardiac output above 3 liters with a mean aortic pressure of more than 60 mmHg.
Results: Hemofiltration resulted in a significantly reduced potassium concentration at all time points ($p < 0.001$), while sodium remained at baseline levels in the later time points ($p < 0.004$). Creatinine and ammonia decreased over time as a result of hemofiltration. Cardiac function showed a lower atrial pressure (14 mmHg vs 11 mmHg, $p < 0.038$) and a reduction of the required dobutamine dose ($p < 0.003$). Survival was improved in the hemofiltration group, although not statistically significant (N=5 86% vs N=4 57 %, $p = 0.286$).
Conclusions: Hemofiltration results in an improved biochemical composition of the whole blood perfusate and might benefit cardiac function during normothermic perfusion, although no statistically significant impact on survival was found.

H2S-enriched flush-out in DBD and non-DBD porcine kidneys

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Background: Kidney extraction time has a detrimental effect on post-transplantation outcome. The hypothesis is that this results from a temperature increase of the kidney when extraction takes longer, which subsequently results in a higher metabolic rate. Lowering temperature or metabolic rate could potentially be protective. This study aims to improve the flush-out and potentially decrease ischemic injury by addition of hydrogen sulphide (H_2S) to the flush medium in kidneys from both brain dead and non-brain dead pigs. H_2S is a gasotransmitter capable of inducing a hypometabolic state and its addition during abdominal flush could therefore help to reduce injury and improve organ quality.
Methods: 22 porcine kidneys (female Danish domestic pigs, +/ 62 kg) were extracted during organ recovery surgery. Prior to donation, pigs underwent brain death induction or a sham operation. The kidneys were stratified in 4 groups: donation after brain death (DBD) control, DBD H_2S, non-DBD control and non-DBD H_2S. Directly after the abdominal flush, kidneys were extracted and flushed with or without H_2S. Next, all kidneys were subjected to 90 min of room temperature ischemia to simulate the increase in temperature during a deceased donor procedure before the kidneys were preserved via static cold storage (SCS) for 13 h. The next day, kidneys were tested using normothermic machine perfusion to evaluate metabolism, renal function, injury markers and histology.
Results: Oxygen consumption was significantly higher in the H_2S treated DBD kidneys compared to the DBD control group ($p=0.03$). The non-DBD kidneys show superiority in creatinine clearance compared to the DBD control group ($p = 0.03$). Significant higher complement activation (C3a) was seen in the urine and after SCS in the DBD control group compared to the living control group ($p=0.004$ and $p=0.03$). Pro-inflammatory cytokines IL-1b and IL-8 were significantly lower in H_2S treated DBD kidneys ($p=0.03$). No difference was seen between all four groups in perfusion parameters, injury markers (lactate, LDH, ASAT, MDA, BAX/BCL2 ratio and NGAL), urine production and proteinuria. All groups showed comparable histological appearance, complement staining will be performed in the near future.
Conclusions: We found an overall trend of better renal function in the non-DBD kidneys compared to the DBD kidneys and a higher complement activation of DBD kidneys. The addition of H_2S during the flush out and SCS showed a reduction of pro-inflammatory cytokines however without affecting renal function or injury markers. Further studies are needed to determine the effect of H_2S on transplant outcome.

The effect of different nutrients on mitochondrial function during long term incubation of precision-cut kidney slices

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Background: Marginal donor kidneys are more susceptible to ischemia-reperfusion injury (IRI). IRI causes the mitochondria to produce reactive oxygen species (ROS) after reintroduction of oxygen. To diminish production and deleterious effects of ROS, mitochondria should be preserved optimally between donation and transplantation. Normothermic machine perfusion (NMP) is increasingly explored to improve quality during preservation. One important question is how to provide metabolic support to kidneys during NMP and which nutrients are best to support mitochondrial energy production. To resemble NMP circumstances, we developed a precision-cut kidney slices model that can study the kidney on a cellular level. The aim of this study is to investigate the effect of different nutrients on mitochondrial function during incubation of precision-cut kidney slices.
Methods: Pig kidneys were procured at a local slaughterhouse. After 30 minutes of warm ischemia kidneys were perfused with hypothermic machine perfusion (HMP) for 3 hours. Thereafter, precision-cut kidney slices were made and incubated for 24 or 48 hours in different incubation media. The basic incubation medium was Dulbecco's Modified Eagle Medium (DMEM) without glucose and pyruvate supplemented with ciprofloxacine (10 µg/mL) and fungizone (0,25 µg/mL). Two control groups contained the basic medium only and the basic medium supplemented with glucose (2mg/mL), glutamine (2 mM) and fatty acids (1,5 mg/mL) (SMOFlipids®). To the experimental groups (n=8) the following nutrients were added to the basic medium: 1) glucose; 2) glucose and glutamine; 3) fatty acids; 4) fatty acids and glutamine; 5) glutamine. At zero, 24 and 48 hours, mitochondrial respiration, using the Oxygraph-2k, was assessed. Therefore, the glycolysis (pyruvate and glutamate) and the beta-oxidation of fatty acids (C16-carnitine) were stimulated. Furthermore, mitochondrial energy status, injury markers in the incubation medium and oxidative stress markers will be analyzed when all experiments are finished.
Results: Preliminary results (n=6) of the mitochondrial respiration show that after HMP the respiratory control ratio (RCR) is best when only glutamate is used to stimulate the respiration. Furthermore, mitochondria were better preserved after 48 hours with the addition of glucose, glutamine and fatty acids compared to no nutrients. More results will be available after all experiments and analysis are finished.
Conclusions: Preliminary data using the precision cut slices model show that nutrient composition impacts on mitochondrial function. These data pave the way to optimize the perfusion solution for NMP of marginal donors.

Hypothermic machine perfusion improves survival of the isolated slaughterhouse porcine heart.

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Background: The aim of this study was to compare functional survival of slaughterhouse porcine hearts using ex situ hypothermic machine perfusion versus static cold storage.
Methods: Twenty-one hearts were harvested from Dutch Landrace pigs, that were sacrificed for human consumption. Fourteen hearts were preserved using static cold storage and seven hearts were connected to the hypothermic machine perfusion system for 4 hours. During hypothermic machine perfusion the heart was perfused with a homemade adjusted Steen Heart Solution with a perfusion pressure of 20-25 mmHg to achieve a coronary flow between 100-200 ml/min. After preservation, all hearts were functionally assessed during 4 hours on the PhysioHeart™ platform, a normothermic, oxygenated, diluted whole blood loaded heart model. Survival was defined as a cardiac output above 3 l/min with a mean aortic pressure of more than 60 mmHg.
Results: Survival was significantly better in the hypothermic machine perfusion group with 100% in comparison to 30% in the static cold storage group ($p = 0.006$). Furthermore, we found that harvesting time was inversely related to survival with a correlation coefficient of -0.561 ($p = 0.019$). This correlation was stronger in the static cold storage group alone (-0.754, $p = 0.038$).
Conclusions: Hypothermic machine perfusion improves survival of the slaughterhouse porcine heart. Optimizing the hypothermic perfusion approach can further improve current results.

Alteration of oxygenation during renal normothermic machine perfusion: hyperoxia versus normoxia

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Background: Normothermic machine perfusion (NMP) of renal grafts provides a platform for graft evaluation and regeneration. However, there is no consensus about the oxygen concentration that should be applied. Typically, a 95%O_2/5%CO_2 gas mixture is used, resulting in a supra-physiological partial oxygen pressure of 60-80 kPa. Such hyperoxia can potentially promote the formation of reactive oxygen species (ROS) and worsen reperfusion injury of the graft. We hypothesized that NMP with normoxia (pO_2 10-20 kPa) may prevent additional ROS-induced renal injury, which could be associated with more favourable perfusion parameters and a better metabolic rate.
Methods: Paired renal grafts from 8 pigs were procured at the local slaughterhouse and stored on oxygenated hypothermic machine perfusion for 10 hours. The left and right kidney were randomized for either 6 hours of NMP with hyperoxia (70kPa, n=8) or 6 hours of NMP with normoxia (10-20 kPa, n=8). Biopsies were taken at the end of HMP and after 1 hour, 3 hours and 6 hours of NMP. Perfusate and urine samples were taken hourly, and perfusion parameters were monitored continuously.
Results: Glucose consumption, lactate flux and urine production were similar for both groups. Likewise, perfusion parameters, such as renal flow, were similar for both groups. Total oxygen consumption tended to be higher in the normoxia group (p=0.08), and tissue ATP levels were similar at all timepoints.
Conclusions: No significant differences in perfusion parameters and metabolic rate were seen between the kidneys exposed to hyperoxia and normoxia during renal NMP, although the normoxia group showed a trend towards a higher oxygen consumption. Further analysis of oxidative stress and damage markers should reveal whether the degree of tissue injury differs between the groups.

Mitochondrial damage and kidney function in DCD porcine kidneys using different flush out solutions

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Background: During organ retrieval a systemic cold flush is performed to cool down organs. After the initial vascular flush and cooling of the kidneys, the temperature of the kidney increases again. Absence of oxygen and nutrients, this results in warm ischemic injury. We hypothesize that the use of prolonged, oxygenated, and/or nutrient enriched flush out solutions could improve organ quality during prolonged extraction times.
Methods: Twelve porcine kidneys, donated after cardiac death (DCD), obtained from a local abattoir were subjected to 30 min warm ischemic time and were stratified in 3 different groups (n=4). Group 1: flush with University of Wisconsin- Cold Storage Solution (UW-CSS). Kidneys were kept on ice. Group 2: flush with 500ml UW-CSS. Kidneys were rewarmed 15 min after the start of the flush. Group 3: flush with 1000ml of oxygenated UW- Machine perfusion solution (UW-MPS). Kidneys were also rewarmed. The rewarming was performed in a temperature-controlled box to mimic a prolonged extraction of the organs with subsequent increase in temperature. After 60 minutes of ischemia all kidneys underwent 4h of oxygenated hypothermic (HMP) and subsequently 4h of normothermic machine perfusion (NMP). Mitochondria were isolated from the cortical kidney tissue to measure mitochondrial activity, quality and injury using multiple analyses. Endothelial cells were isolated to evaluate endothelial injury and the kidneys were tested using NMP to evaluate metabolism, renal function, injury markers, histology and renal cortical microperfusion using laser speckle contrast imaging (LSCI).
Results: No differences in mitochondrial respiration was observed between all 3 groups during the flush, after the flush, HMP or NMP. Mitochondrial membrane potential was similar between all 3 groups. Oxygen consumption during NMP showed similar results, indicating that all 3 groups had a similar metabolic activity. Kidneys that were flushed with oxygenated UW-MPS showed significant higher ATP-levels in biopsies 60 minutes after the flush compared to the UW-CSS groups. After HMP and NMP this effect could not be observed anymore. No differences in fractional sodium function were observed. Mitochondrial -, endothelial - and tubular injury and LSCI measurements are currently being performed.
Conclusions: The first results show a similar mitochondrial respiration and function between all 3 groups over time, but increased ATP-levels 60 minutes after the flush with UW-MPS. Further analysis will reveal whether mitochondrial injury, endothelial injury are affected by different flush-outs at the beginning of a DCD donation setting and/or benefit from early oxygen and nutrient supply during the flush out.

Furosemide but not desmopressin can induce changes in renal function during normothermic machine perfusion that could potentially serve as relevant add-on parameters for pre-transplant viability assessment

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Background: Renal normothermic machine perfusion (NMP) is a promising method for pre-transplant graft quality assessment. Nevertheless, it remains unclear which parameters are relevant for viability assessment during NMP. This study aimed to determine whether the (anti-)diuretics furosemide and desmopressin can induce differences in functional parameters that could serve as a relevant add-on for pre-transplant viability testing during NMP.
Methods: Eighteen porcine kidneys sustained 30 min of warm ischemia and 3-5 hours of oxygenated hypothermic perfusion before being subjected to 6 hours of NMP. Each organ was randomized to receive either no drug, desmopressin (16 μg), or furosemide (750 mg) during NMP (n = 6 per group).
Results: Throughout NMP, renal perfusate flow was significantly lower in the furosemide group compared to the other groups ($P < 0.0001$). Moreover, the urine production and the fractional excretion of sodium as well as potassium were higher in the furosemide group ($P < 0.01$). Differences in lactate dehydrogenase, aspartate aminotransferase, and ATP levels did not reach statistical significance. Administration of desmopressin did not result in significant differences compared to the control group.
Conclusions: In conclusion, administration of furosemide during NMP triggered a clear response in perfusion characteristics and functional parameters, the extent of which may reflect relevant aspects of organ viability. Hence, furosemide administration during NMP could facilitate decision-making regarding suitability of renal grafts for transplantation.

Subtle association between TTV-load and tacrolimus exposure in kidney transplant recipients

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Background: Measuring immune function in kidney transplant recipients remains challenging given the precarious balance between over- and underimmunosuppression. This is primarily due to high inter- and intrapatient variability in pharmacokinetics and -dynamics of both tacrolimus (Tac) and mycophenolic acid (MPA) and their narrow therapeutic window. Torque teno virus (TTV), a non-pathogenic commensal virus, has been proposed as biomarker of immune function: higher loads may correspond to over-immunosuppression, and lower loads to under-immunosuppression. An inverse relation with TTV load and acute rejection has already been shown. This study evaluated the association of TTV loads and exposure to immunosuppressive drugs.
Methods: A cross-sectional cohort study was designed using a unique database of drug exposure data. Kidney transplant recipients (KTR) transplanted between 2005-2012 and started with Tac/MPA/-prednisolone were included. Patients without therapeutic drug monitoring, TTV load measurement or switches in immunosuppression were excluded, leaving 170 KTR for analysis on month 3 and 159 on month 6. Linear regression was used to study the association between TTV loads and Tac through (C0) levels, and Tac and MPA area-under-the-curve (AUC) data, measured on the day of, and 2 weeks before TTV load measurement.
Results: Linear regression showed an increase in predicted TTV load at month 3 with Tac C0 and AUC increase in the univariate analysis (C0: β=0.20 per 1 μg/L, p=0.01, R^2=0.04); AUC: β=0.18 per 20 mg*h/L, p=0.05, R^2=0.04), but not in the analysis adjusted for confounders (C0: β=0.16 per 1 μg/L, p=0.15, R^2=0.08); AUC: β=0.01 per 20 mg*h/L, p=0.17, R^2=0.08) for exposure samples taken on the same day as the TTV sample. Similar results were found when using samples taken 2 weeks before. For MPA no association was found. Analyses on month 6 showed similar results.
Conclusions: An association between tacrolimus exposure and TTV levels seems present, but subtle. The low R^2 values and absence of an association in the adjusted analyses indicate that most variation in TTV loads is not explained by drug exposure at the same day or 2 weeks before. The presence of an association with Tac exposure and absence of effect of MPA exposure provides insight into the immune response that controls TTV replication. Future study will examine different timeframes after transplantation and other covariates that might explain the high variation in TTV loads.

Histological heterogeneity in a kidney transplant: does one biopsy represent the whole kidney?

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Background: Biopsy is the most important tool to diagnose Interstitial Fibrosis and Tubular Atrophy (IFTA) in a kidney transplant. The assumption is that the outcome of this biopsy represents the whole kidney. However, there are indications that this might not be the case. Histological differences in the biopsies of varying regions of the same kidney, would imply that a renal biopsy is not representative of the whole kidney, thus making the diagnosis, prognosis and the subsequent treatment possibly not adequate. Evidence for sampling errors and histological differences in renal transplant biopsies in live studies are presently lacking. Therefore, we address the question if multiple biopsies from the same kidney show similar results with regard to IFTA.
Methods: From 2019 till 2021 17 patients had to undergo a transplantectomy. Of these transplantectomies four with still preserved kidney pathology were included in the analysis. From each transplantectomy biopsies were taken in six different regions of the kidney. IFTA was measured by two independent pathologists via the conventional method, and scored according to the Banff classification. The IFTA scores from each different region were compared in each kidney to see if there were variations in these scores.
Results: In each kidney biopsies showed differences in IFTA. For every kidney the range in IFTA was as follows: kidney 1: 50% (ci2) – 85% (ci3), kidney 2: 15% (ci1) – 30% (ci2) , kidney 3: 10% (ci1) – 40% (ci2), kidney 4: 45% (ci2) – 85% (ci3).
Conclusions: Our analysis shows that the level of IFTA differs within the same kidney. This might have clinical consequences as the amount of IFTA could affect decision on treatment of underlying medical problems like rejection. Our method of approaching the adequacy of kidney biopsies has not been performed earlier and gives insight in histological differences within the same kidney. The use of transplantectomy specimens is a limitation, because all kidneys showed extensive damage profiles (in fact only four were fit for analysis) and it is uncertain if the same differences will be seen in more subtle conditions as rejection in a still functioning kidney. More kidneys have to be analysed as a follow-up for this pilot.

Population pharmacokinetics of subcutaneous alemtuzumab in kidney transplantation

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Background: Alemtuzumab is a monoclonal antibody used as induction immunosuppressive therapy in kidney transplantation. It targets CD52 on lymphocytes, inducing profound immune cell depletion upon administration. Due to its off-label status in kidney transplantation, its pharmacokinetic (PK) characteristics are largely unknown and its fixed dosing algorithm originates from other populations. Substantial between-subject variability in lymphocyte recovery is observed after alemtuzumab induction, raising concerns about the current dosing strategy. We developed a population PK model for alemtuzumab in kidney transplant recipients and evaluated the potential of personalised alemtuzumab therapy.

Methods: 362 PK observations drawn at 0-165 days after transplantation were available from 61 kidney transplant recipients, who received 15 mg alemtuzumab subcutaneously before transplantation and 24h thereafter. The population PK of alemtuzumab were estimated using a nonlinear mixed-effects model. Body size, lymphocyte count, albumin, urine protein, and age were investigated as covariates, and evaluated for their potential to guide personalised alemtuzumab therapy. The final model was used to derive a CD52 saturation threshold and simulate alemtuzumab PK under various dosing regimens.

Results: The PK data were best described by a two-compartmental model with first-order absorption and parallel linear and time-varying nonlinear clearance. For the typical patient, alemtuzumab absorption was 0.093 day^{-1}, central and peripheral distribution volumes 6.52 L and 7.11 L, and linear and intercompartmental clearances 1.40 L/day and 0.311 L/day. The nonlinear clearance was maximal just after administration and diminished over the next two days. Between-subject variability was modelled on the linear clearance (37.5%) and central distribution volume (37.3%). Alemtuzumab PK varied with body size, displaying extended exposure to lytic concentrations (>0.1 mg/L; 44.5±9.91 *vs.* 39.7±8.81 days; 12.1% difference) and concentrations exceeding the model-derived CD52 saturation threshold (>0.4 mg/L; 20.9±6.00 *vs.* 16.6±5.92 days; 25.9% difference) in 60 kg *vs.* 100 kg patients. This variability could be reduced with lean bodyweight-adjusted dosing.

Conclusions: Alemtuzumab displays substantial PK variability in kidney transplant recipients, which may call for a personalised treatment strategy. Lean bodyweight-adjusted dosing poses an option for individualised dosing, but further evaluation of its potential clinical benefit is warranted.

Non-invasive, fast and accurate quantification of body composition in transplantation patients: The Future is Now!

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Background: Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength. Its presence has been associated with worse postoperative outcomes in various patient populations as well as overall physical disability and diminished quality of life. However, to date limited research has been conducted investigating its implications in transplantation patients. Various methods for determining body composition are currently clinically utilized, each with their own specificity and sensitivity. Unfortunately these methods are objective and invasive, limiting their clinical significance. Recent advancements in computed tomography (CT) and artificial intelligence (AI) have allowed for the development of a minimally invasive, accurate and fast new tool for the quantification of body composition.
Methods: SarcoMeas is an artificial intelligence program developed in our center which utilizes machine learning to rapidly identify, stratify and measure different body compartments according to their radiographic density (Hounsfield Units (HU)). For these measurements a cross-sectional CT slice at the vertebral level L3 is utilized for analysis. The radiodensity range for skeletal muscle has been determined by previous studies to be -29 to +150 HU. The quality and quantity of skeletal muscle is subsequently calculated and quantified in the form of a skeletal muscle index (SMI).
Results: Due to their comorbidity transplant candidates and recipients are generally considered to be at high risk for
developing sarcopenia and overall abnormal body composition. This new technique of body composition
quantification can have major implications in the transplant community. Our group has already validated the SarcoMeas program in a living kidney donor cohort and utilized it in a pilot study investigating the influence of CT defined sarcopenia on postoperative outcome in kidney transplant recipients. Currently we are analyzing the results from studies investigating the influence of CT defined sarcopenia on postoperative outcome in a larger kidney transplant cohort and in pancreas transplantation recipients.
Conclusions: The preoperative identification of sarcopenia in transplant patients can aid in clinical decision making as well as identify patients who would benefit most from preoperative interventions to increase muscle mass and quality such as physical activity coaching and/or prehabilitation.

A prior asymptomatic SARS-CoV-2 infection increases the magnitude of humoral and cellular responses in patients with chronic kidney disease, on dialysis, or living with a kidney transplant

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Background: COVID-19-related morbidity and mortality is high among kidney patients. Several studies recently suggested low humoral and cellular immune responses after two doses of mRNA-1273 (Moderna) in these patients. Vaccination strategies for these vulnerable patients do not consider a prior SARS-CoV-2 infection and thus they receive the same full vaccination regimen as SARS-CoV-2-naïve individuals. Here, we compare the functionality, magnitude, breadth and durability of the vaccine-induced immune response in kidney patients with or without prior asymptomatic SARS-CoV-2 infection up to 6 months post-vaccination, assessing both the humoral and cellular immune response.
Methods: Participants with an asymptomatic SARS-CoV-2 infection prior to vaccination were selected from a prospective controlled multicenter cohort study, including 6 controls, 6 chronic kidney disease (CKD) stages G4/5 (eGFR <30 mL/min/1.73m2), 9 dialysis and 3 kidney transplant patients. To assess the functionality and magnitude of the vaccine-induced immune response, we compared SARS-CoV-2 S1-specific IgG antibody levels (BAU/ml) in these 24 participants after receiving 1 and 2 doses of mRNA-1273 with that of naïve patients after receiving 2 doses. Further, to assess the breadth and durability of the SARS-CoV-2-specific immune response, we measured neutralizing antibody levels and SARS-CoV-2-specific T-cell responses to variants of concern (VOC) pre-vaccination, on day 28 and 6 months after vaccination.
Results: Patients with CKD, on dialysis or living with a kidney transplant with a prior asymptomatic infection, who received 1 dose of mRNA-1273, had higher vaccine-induced SARS-CoV-2-specific functional antibody levels compared to patients who were SARS-CoV-2 naïve and received 2 doses. In addition, these patients had higher levels of SARS-CoV-2-specific T-cell responses. The breadth and durability of the immune response to circulating VOC remains to be assessed.
Conclusions: This study shows an increased magnitude of humoral and cellular immune responses in kidney patients that had a prior asymptomatic SARS-CoV-2 infection. It is likely that kidney patients with hybrid immunity have functional antibodies and T-cells with increased potency and breadth, and will be able to control emerging SARS-CoV-2 variants better and longer.

Multicenter long-term evaluation of post-transplant lymphoproliferative disease in adult liver transplantation: risk factors and prevention by Epstein-Barr viral load monitoring strategy

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Background: Epstein-Barr virus (EBV) primo-infection or reactivation can occur after liver transplantation (LT) and can lead to post transplant lymphoproliferative disease (PTLD). In pediatric LT recipients an EBV-DNA viral load (EBV VL) monitoring strategy, including reduction of immunosuppression (IR), has led to a lower incidence of PTLD. For adult LT recipients, who have less primo-infection and more EBV reactivation than pediatric recipients, it is unknown whether this strategy is also effective, and risk factors may be different.
Objective: identify risk factors for developing PTLD and examine the impact of an EBV VL monitoring strategy on the incidence of PTLD in adult LT recipients.
Methods: Design: Cohort study.
Setting: Two university medical centers in the Netherlands.
Patients: Adult patients with first LT in Leiden 9/2003-1/2017 with EBV VL monitoring strategy formed the monitoring group (M), in Rotterdam without EBV VL monitoring strategy formed the contemporary control group (C), and those with first LT in Leiden 9/1992-9/2003 plus Rotterdam 1986-9/2003 formed the historic control group (H).
Measurements: Incidence of monomorphic PTLD (M-PTLD).
Results: M-PTLD incidence was 8/117 (6.8%) in H group, 10/606 (1.7%) in the C group and 0/322 patients in the EBV monitoring (M) group (M vs H: $p=0.0004$ with a confounder adjusted estimated incidence rate ratio (IRR) of 14.27, and M vs C: $p=0.023$ with an IRR of 6.50). PSC was a risk factor for PTLD in both the historic and contemporary cohorts ($p<0.01$).
Conclusions: In adult LT the indication PSC is an important risk factor for M-PTLD, while an EBV-DNA monitoring strategy can prevent M-PTLD.

The dynamics of trans-renal oxidative stress during living donor kidney transplantation

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Background: Mitochondrially produced reactive oxygen species(ROS) play a critical role in ischemia reperfusion injury (IRI) during kidney transplantation. We hypothesized that systemic free sulfhydryl groups (R-SH) decrease as a consequence of increased ROS formation during and early after transplantation and that a decrease in R-SH reflects kidney injury in living donor kidney transplantation (LDKT) recipients.
Methods: Systemic venous, arterial, renal venous and urinary samples were taken in donor and recipient up to day 9 post kidney transplantation. Systemic R-SH was measured colorimetrically. Linear mixed modelling and correlation analysis was performed.
Results: Post reperfusion arterial R-SH levels in recipients increased significantly over time($P=0.015$). Renal venous R-SH levels decreased significantly over time ($P=0.002$). This resulted in a significant decrease of delta R-SH (renal venous- arterial) over time ($P<0.001$). Systemic venous and urinary R-SH remained similar over time. However, urinary R-SH at day 9 post transplantation were significantly higher compared to pre-transplantation R-SH in the recipient ($P=0.036$).
Conclusions: The temporal character of R-SH in LDKT recipients is characterized by a trans-renal decrease of R-SH up to 30 minutes after reperfusion. Furthermore, the increase of arterial R-SH could suggest an effect in the recipient by increasing R-SH availability upon oxidative stress. In addition, our results suggest that the kidney itself influences systemic R-SH levels, as renal venous R-SH is higher than arterial R-SH at the start of reperfusion. Overall, these results suggest trans-renal oxidative stress as a consequence of IRI during the process of LDKT, with systemic and renal effects on R-SH levels in the recipient.

Tacrolimus withdrawal after mesenchymal stromal cell therapy is associated with donor-specific antibody formation in kidney transplant recipients

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Background: Immunosuppressive regimens in kidney transplantation are associated with increased risk for infections and malignancies. Although currently it is not possible to predict in which patients immunosuppression can be safely minimized, it has been previously shown that the degree of HLA class II eplet mismatch determines whether kidney transplant recipients (KTRs) tolerate lower tacrolimus through levels without formation of *de novo* donor-specific antibodies (dnDSA). Recently, the Triton study demonstrated that mesenchymal stromal cell (MSC) therapy is a safe and feasible method to facilitate tacrolimus withdrawal in KTRs. Here, we analyzed dnDSA development in MSC-treated KTRs and determined the association with HLA amino acid mismatch loads.
Methods: Patients in the control (n=29) and MSC group (n=29) of the Triton study were analyzed. Second-field HLA typing for 11 loci was performed for all donors and recipients. Post-transplant serum was screened for dnDSA using Luminex single antigen bead assay. The solvent-accessible amino acid mismatch (AA MM) load was determined with HLA-EMMA.
Results: In total, 5 out of 29 patients in the control group (17%) and 11 out of 29 patients in the MSC group (38%) developed dnDSA, of which the majority was directed against HLA-DQ (2 in the control group, 11 in the MSC group). The dnDSA in the MSC group were often of greater magnitude (higher mean fluorescent intensity) and persisted longer. Mean HLA-DQ AA MM loads in the two patient groups were not significantly different. In order to determine the association between AA MM load and dnDSA formation, HLA-DQ AA MM load was divided in 4 quartiles (Q1: <7, Q2: 7-13, Q3: 14-35, Q4: >35). In contrast to historical data showing a dose-dependent effect of HLA-DQ AA MM load, the incidence of dnDSA in the MSC group in Q1, Q2, Q3 and Q4 was 0%, 43%, 43% and 56% respectively. This illustrates that already at lower HLA AA MM loads, these patients are at risk for DSA formation after tacrolimus withdrawal, despite MSC treatment.
Conclusions: MSC-treated kidney transplant recipients are at increased risk for dnDSA formation after tacrolimus withdrawal. While previous studies have demonstrated a dose-dependent effect of HLA-DQ AA MM loads for the risk of dnDSA formation, the current results suggest that MSC-treated patients withdrawn from tacrolimus are at increased risk for dnDSA development already at relatively low HLA AA MM loads. Importantly, despite the increased dnDSA formation in MSC-treated patients, incidence of rejection was not increased and kidney function was stable. Further research is warranted to explore HLA AA MM load as a predictive biomarker to guide personalized immunosuppression in transplantation.

Impact of donor-specific antibodies in (highly-) immunized living donor kidney transplant recipients.

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Background: HLA-antibody screening is key in the pre-transplantation work-up of the transplant candidate. Due to the limited donor pool, donor-specific antibodies (DSA) might be accepted when a living donor is available. The impact of DSA in (highly-) immunized living donor kidney transplant recipients is not well characterized.
Methods: We performed a retrospective analysis of all consecutive DSA+ living donor kidney transplantations in our center between 2010-2019. Pretransplant CDC and either ELISA or Luminex screening were performed. If screening was positive, DSA were characterized with Luminex single antigen beads (One Lambda and/or Immucor) and defined as class I, class II or combined class I and II. For each DSA+ recipient (DSA+), 1 immunized without DSA (PRA+) and 2 non-immunized recipients (non-imm) were included (matching: recipient age, donor age, donor-recipient relation, pPRA and time of transplantation). Cox regression and Kaplan-Meier survival analysis were used to determine patient and graft survival. Rejection was defined as anti-rejection treatment either with or without biopsy.
Results: 71 HLA-incompatible living donor kidney transplant recipients were included, of whom 32.9% had class I, 27.1% class II and 40.0% combined class I and II DSA. Recipient age was 51, 53 and 53 median in DSA+, PRA+ and non-imm respectively. In DSA+ 39% were highly-immunized (pPRA ≥85%), as were 37% in PRA+. Retransplantation was 59% vs 44% vs 7% in DSA+ vs PRA+ and vs non-imm respectively (p=0.19 vs PRA+ and p=<0.001 vs non-imm). Mismatches on HLA-A and HLA-B did not differ, however DR mismatches were more frequent in DSA+ (43% 2 DR mismatches). Nineteen (26%) of DSA+ received depleting induction. Twelve of those 19 recipients were CDC+ and were desensitized with plasmapheresis. 66% of DSA+ patients received rejection treatment, versus 57% and 39% in PRA+ and non-imm respectively (p=0.87 and p=0.001). With a median follow-up of 5.9 years (IQR 3.6-8.6), patient survival was 85% and death-censored graft survival 57% in DSA+ (Kaplan-Meier). Death-censored graft survival was inferior in DSA+ as compared to PRA+ (HR 3.53 [95% CI 1.42-8.81]) and to non-imm (HR 4.70 [95% CI 2.27-9.70]). Death-censored graft survival of patients treated with depleting induction was not significantly different from DSA+ patients treated with basiliximab (HR 0.61 [0.23-1.59]).
Conclusions: (Highly) immunized patients with DSA have inferior death-censored graft survival after living donor kidney transplantation as compared to matched immunized, DSA-negative patients. The risk of these DSA should guide pre-operative counseling and postoperative surveillance. We are currently analyzing strength of DSA and flowcytometry results.

Clinically Relevant versus Irrelevant donor epitope specific HLA Antibodies in Predicting Kidney Transplantation Risk

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Background: Kidney transplantation is the best treatment for most end-stage renal failure patients. However, success rates are limited by rejection of the graft. In transplant rejection, patient antibodies against donor HLA play an important role, the so-called donor-specific HLA antibody (DSA). These DSA are currently detected with the single antigen bead (SAB) assay, but which of these DSA are clinically relevant is not fully understood yet. To determine the clinical relevance of DSA, the focus is shifted from molecular level to epitope level, a concept which is denoted as donor epitope specific HLA antibody (DESA). This study aims at identifying and including relevant DESA in a model to improve kidney transplantation risk prediction.
Methods: Dutch kidney transplants between 1995 to 2006 from the Netherlands Organ Transplant Registry (NOTR) are studied. The assignment of DESA is done using the SAB assay, most likely high-resolution typing, and an open-source registry of recognised epitopes. The relevant and irrelevant DESA are discerned using Kaplan-Meier analysis. The predictive power of relevant DESA is assessed in a Cox Proportional Hazard (CPH) model including non-immunological variables
Results: Hypothesis-based methods, in which parameters like DESA distance to cell membrane, quantity, and density were considered, did not show a strong association to graft rejection. Therefore, we have followed a hypothesis-free approach, where a cohort of deceased donors with DESA were analysed using Kaplan-Meier method. The analysis shows that the presence of certain DESA is associated with a higher risk (twice as high) of kidney rejection within 3-month after transplantation, compared to presence of DSA in a similar period. The results also show a higher immunological risk in the test dataset of living donors. The CPH model including relevant and irrelevant DESA considerably outperforms other methods in literature without relevant immunological variables.
Conclusions: A decision-support tool is developed to predict the 1-year risk of kidney rejection using both immunological as well as non-immunological variables. Relevant & irrelevant DESA, show a considerable predictive power in the CPH model developed on the cohort of deceased donors with DESA. In future works, we will consider the association of combination of DESA and risk of kidney transplant rejection.

CIAT: a major contribution to the number of transplantations in highly immunized patients and incompatible pair recipients compared to other available transplant programs

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Background: A number of alternative, both living and deceased donor kidney transplant programs have been developed for incompatible pairs and difficult to match patients. The National kidney exchange program (KEP) is the only computer based and nationally operating program. All other programs function locally and are interrelated but unstructured. Despite all these programs, there are still many long waiting (LW) and highly immunized patients (HI) waitlisted. Computerised Integration of Alternative Transplantation (CIAT) programs was developed to increase the chances of HI and LW kidney transplant candidates. CIAT integrates AB0-desensitisation, HLA-desensitisation, donor-exchange, altruistic and domino-paired donation. Strict criteria were defined for selected HI (sHI) and LW patients. sHI patients are given priority and AB0-incompatible (AB0i) and/or HLA-incompatible matching (HLAi) is allowed. LW candidates can opt for an AB0i match.
Methods: A pilot was established in our center between 2017-2021 to gain logistic experience, to test the algorithm and to optimize the program. Participation in CIAT as LW or sHI was discussed and decided by a professional committee. CIAT results were assessed in comparison with other available deceased and living donor kidney transplant programs.
Results: 105 incompatible couplesparticipated. 35% were transplanted via CIAT, 24% received a direct kidney transplantation (compatible donor or after AB0 and/or HLA desensitisation), 20% were delisted or still waiting, 11% received a deceased donor kidney, 10% a kidney via national KEP. There were 47 sHI patients, 60% was not transplanted. The majority of those transplanted, received the kidney via the CIAT program (17%), while 15% received an AM-deceased donor kidney, 6% were direct transplantations via HLA desensitisation and 2% via national KEP. There were 55 LW patients of whom 50% received a kidney via the deceased donor program, 24% via the CIAT program, 24% is delisted or still waiting, 1% received a compatible direct living donor kidney.
Conclusions: CIAT is a major addition to current kidney transplant programs for difficult to match patients. CIAT enabled substantially more kidney transplantations in highly-immunized patients than the national KEP. LW patients were primarily transplanted with a deceased donor, and secondly via CIAT. Compared to all other programs available for these specific groups, most HI patients and incompatible couples were transplanted via CIAT.

PROCARE 2.0: Towards clinical prediction of kidney graft survival through immunological profiling

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Background: Since 2014, nephrologists and immunologists from all 7 university medical centers in the Netherlands have joined forces in PROCARE: The PROfiling Consortium of Antibody Repertoire and Effector functions. The main aim of the PROCARE projects is to perform a comprehensive analysis of immunological risk factors for kidney graft loss. Ultimately, the goal is to provide clinically useful predictions of prognosis already before transplantation, which could also be used to inform organ allocation. The PROCARE 1.0 project included all Dutch kidney transplantations from 1995-2005 and was completed in 2018. PROCARE 2.0 was started in September 2020, to validate the results from PROCARE 1.0, and to assess the clinical relevance of novel developments in immunology research.
Methods: PROCARE 2.0 comprises a retrospective and a prospective study. The retrospective study will span a further 10 years of data (2006-2016), with at least 5 years of follow-up. Clinical data from all kidney transplantations in this timeframe are included via the Dutch Organ Transplant Registry (NOTR), supplemented with high- to intermediate-resolution HLA data and Luminex HLA antibody data from all Dutch tissue typing laboratories. The prospective study will collect blood samples and clinical data from 150 patients at high-risk of antibody-mediated rejection.
Results: Clinical data from 9.674 transplantations have been included in the retrospective study. Preliminary analyses show that several factors that were associated with graft loss in the PROCARE 1.0 cohort have changed substantially in the PROCARE 2.0 cohort. These include donor type (living donor transplantations and transplantations after cardiac death are more frequent), immune-suppressive medication (e.g., induction therapy with anti-IL-2R antibodies has become commonplace), and donor/recipient age (which have both increased). These (changes in) clinical risk factors may confound the relationship between graft loss and immunological risk factors (e.g., presence of donor-specific HLA antibodies). High- to intermediate-resolution HLA data and Luminex HLA antibody data are currently being extracted.
Conclusions: We present the current state of the PROCARE 2.0 project, one of the largest Dutch collaborations in the field of kidney transplantation. The comprehensive database that is put together in this project can serve to provide actionable clinical insights and patient-level risk predictions using state-of-the-art immunological tools.

Clinical and molecular profiling to develop a prediction model for the response to alemtuzumab therapy for severe or glucocorticoid-resistant kidney transplant rejection

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Background: Alemtuzumab is an effective drug for the treatment of severe or glucocorticoid-resistant acute kidney transplant rejection (AR). Patient-specific predictions on treatment response are however, urgently needed, given the severe side effects of alemtuzumab. This study developed a multidimensional prediction model with the aim of generating clinical useful prognostic scores for the response to alemtuzumab.
Methods: Clinical and histological characteristics were collected from patients who were treated with alemtuzumab for AR. In addition, gene expression profiling of AR biopsy tissues was performed using the NanoString® platform. LASSO logistic regression modelling was used to construct the ALEMtuzumab for Acute Rejection (ALEMAR) prognostic score. Response to alemtuzumab was defined as patient and allograft survival and at least once an eGFR above 30 mL/min/1.73m^2 during the first 6 months after treatment.
Results: One-hundred-and-fifteen patients were included, of which 84 (73%) had a response to alemtuzumab. The ALEMAR-score accurately predicted the chance of low (<25%), intermediate (25-40%) and high risk (40-100%) of non-response. Internal validation confirmed the high discriminating capacity of the model. In addition, gene expression analysis identified 13 differentially expressed genes between responders and non-responders. Pathway scoring highlighted that B lymphocyte function was different between the two groups. The combination of the ALEMAR-score and selected genes resulted in improved predictions of treatment response.
Conclusions: The present prediction model may assist clinicians when making therapeutic decisions for patients suffering from AR.

High alemtuzumab exposure is associated with delayed lymphocyte recovery in kidney transplant recipients

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Background: While alemtuzumab is increasingly being used as an induction therapy in kidney transplantation, little is known about the relation between alemtuzumab exposure, lymphocyte recovery and clinical outcomes in kidney transplant recipients (KTRs). Recently, a population pharmacokinetic model was developed based on alemtuzumab plasma concentrations of KTRs in the Triton Study, which allows for estimation of individual alemtuzumab pharmacokinetics. We hypothesized that alemtuzumab exposure would demonstrate substantial interpatient variability and correlate with lymphocyte recovery rate and infection incidence post-transplantation (post-Tx).
Methods: KTRs in the control arm of the Triton Study (n=29) were included in this analysis. All patients received alemtuzumab induction (2x 15 mg subcutaneously), steroids, tacrolimus and everolimus. As previous studies have suggested that alemtuzumab has lympholytic capacity at concentrations exceeding 0.1 mg/L, the time above this threshold concentration (TATC) and the maximum concentration (C_{max}) were predicted using a validated population pharmacokinetic model. Immune monitoring of lymphocyte subsets was performed at baseline and at week 6, 12, 24, 52 and 104 post-Tx. CD4 T cell recovery was defined as > 50,000 CD4 T cells/ml peripheral blood as counts below this limit have been associated with a higher risk of viral reactivation.
Results: The predicted TATC and C_{max} demonstrated considerable interpatient variability ranging from 29.9-64.0 days (median: 39.7) and 0.54 to 1.39 mg/L (median: 0.80) respectively. KTRs with a TATC > 66th percentile (42.4 days) were categorized as 'high exposure' and patients below this threshold as 'low exposure'. Median absolute CD4 T cell numbers at week 6 (118 vs 443, P=0.0096) and week 12 (1519 vs 7762, P=0.003) were lower in KTRs with high exposure than in patients with low exposure. Similar trends were observed for CD8 T cells, regulatory T cells and to a lesser degree for B cells. In order to predict the timepoint that patients reached CD4 T cell recovery more accurately, the time to CD4 T cell recovery for every patient was predicted using a basic, empirical nonlinear mixed effects model. Kaplan Meier analysis demonstrated that KTRs with high exposure reached CD4 T cell recovery at later timepoints than patients with lower exposure (P=0.003). Regardless of differences in lymphocyte recovery rate, there was no statistically significant difference in the cumulative incidences of BK-virus, CMV, EBV or *de novo* donor-specific antibody formation between the two groups.
Conclusions: Alemtuzumab exposure demonstrates extensive interpatient variability and impacts lymphocyte recovery rate early after transplantation.

PIRCHE-II score is independently associated with the incidence of antibody-mediated rejection in a long-term follow-up cohort of kidney transplant recipients

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Background: Chronic-antibody mediated rejection is the major cause of kidney graft loss at long-term follow-up. To date, the presence of donor-specific anti-HLA antibodies is the most prominent risk factor for antibody-mediated rejection both shortly after transplantation and at longer follow-up. The number of donor-derived Predicted Indirectly ReCognizable HLA Epitopes presented by recipient HLA class II (PIRCHE-II) as calculated by a computer algorithm is associated with development of donor-specific anti-HLA antibodies after transplantation and graft survival. Currently, there is a paucity of data relating the PIRCHE-II score directly to the risk for ABMR after transplantation.
Methods: The clinical data of a cohort of kidney recipients transplanted between 1995-2005 (n= 734) were collected with a follow-up to January 2021. A diagnosis of ABMR was made in all cases by a kidney biopsy on indication. As part of the PROCARE I study, the pre-transplantation anti-HLA DSA were retrospectively assessed (pretransplant DSApos or DSAneg). The control group for the ABMR cases (ABMRpos) consisted of recipients with at least a follow-up of 15 years and no diagnosis of ABMR within that period (ABMRneg, n=277). The PIRCHE-II peptides and their weights were calculated based on serological typing data using the PIRCHE-II algorithm version 3.3.30.
Results: Eighty-nine cases of ABMR were recorded and available for PRICHE-II analysis with an average follow-up of 10.2 years. The mean time to ABMR diagnosis was 6.6 years. Clinical and demographic parameters for the ABMRpos and ABMRneg groups were similar, except for a significant higher % of pre-transplantation DSA in the ABMRpos group (35% vs 19%, $p<0.01$). The overall PIRCHE-II score was significantly higher in the ABMRpos group (61 vs 52, $p=0.03$), a difference which was observed for both the HLA class I- and HLA class II-derived epitope mismatch load. Logistic regression analysis identified both pretransplant DSA (HR 1.96) and PIRCHE-II (HR 1.8 for above median high score vs below median score) as independent factors associated with the incidence of ABMR. In addition, the highest tertile of the PIRCHE-II score was associated with a shorter time to graft loss after the diagnosis of ABMR (mean 2.6 years vs 5.0 years), but only in the pre-transplant DSAneg subgroup.
Conclusions: The PIRCHE-II score is an independent risk factor for the incidence of ABMR within a cohort of kidney transplant recipients with a long-term follow up.

Electronic nose for distinguishing chronic lung allograft dysfunction phenotypes

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Background: Chronic lung allograft dysfunction (CLAD) increases risk of death of lung transplant recipients (LTR). Although the main CLAD phenotypes bronchiolitis obliterans syndrome (BOS) and restrictive allograft syndrome (RAS) differ in spirometric and radiological characteristics, establishing the final diagnosis can be challenging. Yet, differentiation between BOS and RAS is crucial, since prognosis of the phenotypes considerably differs.
Timely diagnosis of CLAD and CLAD phenotypes remains problematic due to a lack of accurate markers of CLAD. Promising evidence suggests that electronic nose (eNose) technology has 86% accuracy for the detection of CLAD and may even identify CLAD phenotype. Hence, we aimed to assess diagnostic accuracy of exhaled breath analysis using an eNose to distinguish between CLAD phenotypes.
Methods: In this cross-sectional study, exhaled breath of consecutive LTR with ISHLT criteria based CLAD was collected using an eNose (SpiroNose). Patients with mixed or undefined phenotype were excluded (n = 13). Statistical analyses were conducted using partial least square discriminant analysis and receiver operating characteristics (AUC) analysis to assess differences in breathprint between CLAD phenotypes.
Results: A total of 25 LTR with CLAD were included during outpatient follow-up. 56% were male, median age was 63 (range 32 – 77) years, time after LTx was 9.7 (2.5 – 18.8) years, and time till onset of CLAD was 5.8 (1.7 – 18.8) years. Based on ISHLT criteria, 20 LTR were diagnosed with BOS, and 5 with RAS. The eNose accurately discriminated between BOS and RAS with an AUC of 0.94 (CI 0.85-1.00), a sensitivity of 100%, specificity of 90%, and an accuracy of 92%.
Conclusions: The BOS and RAS phenotype differ in breathprint. Exhaled breath analysis using an eNose is a promising tool to distinguish between CLAD phenotypes. Validation of results is needed in a larger dataset, as well as assessment whether this technique allows earlier diagnosis of CLAD and its phenotype.

Prolonged preservation by hypothermic machine perfusion facilitates logistics in liver transplantation: a European observational cohort study

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Background: A short period (1-2 hours) of hypothermic oxygenated machine perfusion (HOPE) after static cold storage is safe and reduces ischemia-reperfusion injury-related complications after liver transplantation. Machine perfusion time is occasionally prolonged for logistical reasons, but it is unknown if prolonged HOPE is safe and compromises outcomes.
Methods: We conducted a multicenter, observational cohort study of patients transplanted with a liver preserved by prolonged (≥4 hours) HOPE. Postoperative biochemistry, outcomes, complications, and survival were evaluated.
Results: The cohort included 93 recipients from 12 European transplant centers between 2014-2021. The most common reason to prolong HOPE was the lack of an available operating room to start the transplant procedure. Grafts underwent HOPE for a median (range) of 4:42h (4:00-8:35h) with a total preservation time of 10:50h (5:50h–20:50h). Postoperative peak ALT was 675 IU/L (interquartile range 419-1378 IU/L). The incidence of postoperative complications was low, and 1-year graft and patient survival were 94%, and 88%, respectively.
Conclusions: To conclude, good outcomes are achieved after transplantation of donor livers preserved with prolonged (median 4:42 hours) HOPE, leading to a total preservation time of almost 21 hours. These results suggest that simple, end-ischemic HOPE may be utilized for safe extension of the preservation time to ease transplantation logistics.

Factors influencing access to Kidney transplantation (FIAT): An integrative multiphasic stakeholders' perspective

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Background: Despite the fact that various barriers to optimal access to transplantation described in literature, there is no research combining perspectives of all stakeholders in renal care. The aim of this project is to qualitatively explore multiple factors that influence access to kidney transplantation in the Netherlands.
Methods: Stakeholders involved in renal care are interviewed (individual and group) about their perceptions, opinions and attitudes regarding access to transplantation. The topic list for the interviews contains clinical, psychological, ethical, social, economic and policy aspects. The study method is based on grounded theory.
Results: A total of 117 participants were interviewed, namely: patients (21), donors (10), social workers (25), nephrologists (22), surgeons (5), nurses (6), policy officers (24) and representatives of insurance companies (4).The following six major barriers are typical for the themes that emerged: 1. Psychological: psychosocial stress relates to delay kidney transplantation; 2. Policy-based: health care providers experience a lack of or unclarity regarding treatment guidelines; 3. Medical: no consensus on criteria for acceptance for transplantation (e.g. age, BMI, comorbidity). Equal patients are treated differently depending on the local policy. 4. Ethical: lack of insufficient use of programs/interventions that could help patients reach equal access to information and care versus patients' self-management/deployment of their social network to overcome disadvantages; 5. Social: lack of an effective social network or lack of skills to activate social support system; 6. Economical: differences in purchasing agreements and following reimbursements for dialysis and transplantation could provide an economic incentive for choosing one or the other therapy. Underlying subthemes, facilitating factors and stakeholders' quotes will be presented.
Conclusions: According to stakeholders, access to transplantation rely heavily on well-informed patients, donors and health professionals. Despite the existence of national clinical, psychosocial and financial guidelines, participants report ambiguity about their existence. Decision making by patients and donors is hampered by an experienced lack of good, understandable, equal and accessible information about the different treatment options. Financial incentives can influence access as they are not always aimed at encouraging early referral for kidney transplantation.

Early endocrine function after total pancreatectomy with islet autotransplantation

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Background: For patients with chronic pancreatitis, total pancreatectomy may prove to be a last resort to alleviate pain and improve quality of life. To (partially) preserve pancreatic endocrine function, pancreatic islets can be isolated from the resected pancreas and transplanted intrahepatically. This leads to more stable glycemic control with fewer hypoglycemic events and a lower risk for vascular complications. Total pancreatectomy with islet autotransplantation (TPIAT) is performed by few centers in Europe. Here, we report on endocrine function after TPIAT in 8 patients.
Methods: Patients were referred to our center for TPIAT. After pancreatectomy, the resected pancreas was perfused with enzyme stock solution, transported to the Good Manufacturing Practice facility and digested via combined mechanical and enzymatic digestion. Tissue volume reduction was performed if necessary by gradient separation of the islets from the exocrine tissue. The islet cell preparation was infused into the liver after percutaneous transhepatic portal catheterization. A mixed meal tolerance test (MMTT) was administered at baseline and 3 months postoperatively to assess glucose-stimulated beta cell function. Data were analyzed in GraphPad Prism and the two timepoints were compared with Wilcoxon matched-pairs signed rank test.
Results: In this analysis, 8 female patients were included. All patients underwent TPIAT for chronic pancreatitis. The etiology of the pancreatitis was identified as idiopathic (n=4), genetic (n=2), alcohol abuse (n=1) and pancreas divisum (n=1). The median age was 44.5 years (IQR 30.3-54.5). Three patients were diagnosed with diabetes prior to TPIAT. One patient was treated with metformin only, 1 patient with metformin and an insulin pump and 1 patient with a combination of short-acting and long-acting insulin. Patients received 2770 ± 759 islet equivalents per kilogram bodyweight. Three months after TPIAT, all patients used insulin. The median insulin dosage was 0.28 IU·kg^{-1}·day^{-1} (0.20-0.42). HbA1c increased from median 39.4 (34.7-42.4) at baseline to 50.4 (44.8-66.5) mmol·mol^{-1} ($p < 0.01$) at 3 months post-TPIAT. AUC C-peptide during 120 minutes MMTT decreased from median 120.9 (84.9-207.9) to 63.4 (25.3-94.0) nmol·120min·L^{-1} ($p < 0.05$).
Conclusions: Partial pancreatic endocrine function can be retained with TPIAT. However, there is an increase in HbA1c, a decrease in AUC C-peptide and a necessity to start or increase insulin therapy. This warrants further research into factors influencing islet yield and endocrine outcome. For that reason, we are starting a cohort study on TPIAT focused on long-term endocrine function, pain scores, quality of life and pancreatic exocrine insufficiency.

Development and determinants of health-related quality of life in elderly kidney transplant recipients

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Background: Although survival benefit is limited with increasing age, kidney transplantation is nowadays regarded as the optimal treatment for end-stage kidney disease even in elderly patients. However, little is known regarding (determinants of) health-related quality of life (HRQoL), and changes in HRQoL in elderly kidney transplant recipients (KTR).
Methods: We used data from KTR ≥65 years old at the time of kidney transplantation, enrolled in the ongoing prospective TransplantLines Biobank and Cohort Study. Data on HRQoL were assessed using SF-36 mental and physical component scores (MCS and PCS). Side effects of immunosuppressive drugs were assessed using MTSOSD-59R questionnaires. In a subgroup with available data on HRQoL before transplantation, we investigated HRQoL trajectories.
Results: We included 111 KTR (mean age 70 ± 4 years, 39% pre-emptive and 45% living kidney transplant procedures). At 12 months after transplantation, mean eGFR was 48 ± 16 ml/min/1.73m^2, mean MCS was 51.2 ± 7.6, and mean PCS was 52.0 ± 7.3.
Female sex (P = 0.018, St. β -0.223), low education level (P = 0.037, St. β -0.246), number of comorbidities (P = 0.034, St. β -0.201), an eGFR < 30 ml/min/1.73m^2 (P = 0.049, St. β -0.187), the occurrence of rejection (P = 0.005, St. β -0.264), and any hospitalization within the first year (P = 0.047, St. β -0.189) were all inversely associated with MCS.
Prosperity (P = 0.018, St. β -0.253), post-transplant diabetes mellitus (P = 0.008, St. β -0.250), and dialysis before transplantation (P = 0.010, St. β -0.223) were all inversely associated with PCS.
The number of side-effects of immunosuppressive drugs was strongly associated with both MCS (P <0.001, St. β -0.405), and PCS (P <0.001, St. β -0.503). In 43 KTR with available data both before and after transplantation, PCS increased significantly after transplantation (from 47.8 ± 8.2 to 52.3 ± 6.8; $P_{\text{paired t-test}}$= 0.001; Cohen's D 0.54), while MCS did not significantly improve (from 49.0 ± 8.6 to 51.2 ± 7.6; $P_{\text{paired t-test}}$ = 0.095; Cohen's D 0.26).
Conclusions: HRQoL in elderly kidney transplant recipients is good, and, in particular physical component scores, improve after kidney transplantation. Medication-related side-effects have a strong association with worse HRQoL among elderly KTR.

Histological score of regulated necrosis executor phosphorylated MLKL is associated with increased risk for early allograft dysfunction after liver transplantation

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Background: Early allograft dysfunction (EAD) following liver transplantation (LT) remains a major threat to the survival of liver grafts and recipients. Necroptosis is a type of regulated necrosis that has been proven to contribute to hepatic ischemia-reperfusion injury (IRI) in animal models. However, the clinical relevance of necroptosis in human LT remains largely unexplored. In this study, we aimed to assess if necroptosis occurs during hepatic IRI, both in a rodent LT model and in human LT biopsies, and if necroptosis is associated with the development of post-transplant EAD.
Methods: We conducted a retrospective cohort study of 64 LT recipients. Human graft liver biopsies were obtained at the end of the back table procedure (B1) and ~1 hour after reperfusion (B3). Expression of phosphorylated mixed lineage kinase-like (pMLKL) was assessed by immunohistochemistry and presented as an H-score (scale 0 to 300) based on the percentage of cytoplasmic positive cells and the intensity of labeling. The pMLKL-index for each graft liver was calculated by dividing the pMLKL score at B3 by that at B1. To characterize the pMLKL-positive cells, immunostaining was performed on consecutive sections. A similar analysis was done on liver tissue collected from rats 24 hours after LT and sham-operated rats.
Results: Expression of pMLKL is exclusively visible in the portal triad in both human and rat liver biopsies that underwent IRI. The pMLKL score was significantly elevated in rat biopsies compared to the sham (1.78 vs. 0.18, $p<0.01$). Immunohistochemistry on serial sections identified most pMLKL-positive cells as Elastin and Fibulin2 double-positive portal fibroblasts. In human LT, the pMLKL score at B3 significantly increased in recipients with EAD ($p<0.01$). Notably, the pMLKL score at B3 was significantly higher than B1 in EAD patients rather than non-EAD patients (1.88 vs. 0.70, $p<0.01$). ROC curve revealed a high predictive value of pMLKL score at B3 (AUC 0.70) and pMLKL index (AUC 0.82) for EAD. The pMLKL index significantly associated with serum ALT (rho=0.458, $p<0.001$), AST (rho=0.417, $p<0.01$), LDH (rho=0.381, $p<0. 01$) within 24 hours after LT. Univariate and logistic regression analysis revealed that pMLKL index (HR=1.25, 95% CI 1.03-1.51) and LDH (HR=1.00, 95% CI 1.00-1.00) were independent predictors of EAD development.
Conclusions: The expression of the pMLKL in the portal triad increased significantly after reperfusion in both human and rat LT. The pMLKL index is an independent predictor for the development of post-transplant EAD. The pMLKL-positive cells share similar features with portal fibroblast, potentially suggesting an unexplored role of portal fibroblast necroptosis in hepatic IRI.

Employment Status and Work Functioning among Kidney Transplant Recipients: Results of the TransplantLines Biobank and Cohort Study

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Background: Reliable employment figures of stable kidney transplant recipients in Europe are lacking. Additionally, little is known about work functioning of employed kidney transplant recipients and work functioning trajectories before and after transplantation.
Methods: Data of the ongoing TransplantLines Biobank and Cohort Study were used. Work and health-related work functioning were assessed with the Work Role Functioning Questionnaire 2.0 (WRFQ 2.0), and compared with healthy controls.
Results: We included 668 kidney transplant recipients of working age (59% male, age 51±11 years), at a median of 3 [IQR: 2 to 10] years after transplantation, and 246 healthy controls (43% male, age 53±9 years). Employment rates were lower among kidney transplant recipients compared to healthy controls (56% vs. 79%). If employed, functioning at work was slightly lower compared to employed healthy controls (WRFQ total score: 92 [80 to 98] *vs*. 94 [86 to 99], p=0.026). Backward linear regression analyses revealed that plasma albumin (standardized beta (st. β) 0.12, 95%CI 0.02 to 0.23) was positively associated with work functioning among kidney transplant recipients. Muscle weakness (st. β -0.15, 95%CI -0.26 to -0.04), depressive feelings (st. β -0.13, 95%CI -0.24 to -0.01), concentration/memory problems (st. β -0.20, 95%CI -0.31 to -0.08), and severe fatigue (st. β -0.19, 95%CI -0.30 to 0.08) were negatively associated with work functioning among kidney transplant recipients. Subgroup analyses showed that work functioning improved after transplantation among employed patients with end-stage kidney disease (WRFQ total score before *vs*. 12 months after transplantation: 83 [71 to 93] vs. 92 [88 to 98], p=0.002).
Conclusions: Work functioning is only slightly lower than healthy controls and seemed to be improved in patients with end-stage kidney disease after successful kidney transplantation. Nevertheless, only 56% of the kidney transplant recipients of working age were employed compared to 79% of the healthy controls, highlighting that more effort is needed to increase the employment rate in this population.

The risks of endoscopic retrograde cholangiopancreatography after liver transplantation

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Background: Biliary complications (BC), such as strictures and bile leakage, are common after liver transplantation (LT). Endoscopic retrograde cholangiopancreatography (ERCP) is the preferred method to treat. However, ERCP is not risk-free and may impose greater risk in the LT population, mainly because of immunosuppressive therapy in this patient population. Post-ERCP pancreatitis (PEP) is the most common and most feared complication with an estimated prevalence of 3.5% and a mortality rate of 3.0% in the general population. Little is known about the risk and severity of PEP and possible risk factors for PEP in LT recipients. The aim of this study was therefore to define frequency and severity of PEP and to identify possible risk factors in LT recipients.
Methods: In this retrospective cohort we included all patients ≥ 18 years who underwent one or more ERCP procedures after LT between September 2014 and October 2021 in our center. Frequency and severity of PEP, defined according to the revised Atlanta criteria until 30 days after ERCP were identified from the electronic patient system. Possible risk factors for PEP were determined from literature, collected from the electronic patient system and analysed by univariable and multivariable logistic regression analysis.
Results: We included 166 patients, in whom 198 LTs were performed. A total of 745 ERCPs after LT were performed. 710 ERCPs were performed in patients with a duct-to-duct anastomosis (N= 154). PEP occurred after 14 (2.0%) ERCPs. This consisted of ten cases of mild PEP and four cases of severe PEP, with subsequent mortality in three (21.4%). Univariable logistic regression identified sphincterotomy (OR, 7.35; 95% CI, 3.07-17.61; P < 0.01), difficult cannulation (OR, 7.95; 95% CI, 3.25-19.44; P < 0.01), wire cannulation of the pancreatic duct (PD) (OR, 7.39; 95% CI, 3.11-17.59; P < 0.01), and contrast injection in the PD (OR, 7.56; 95% CI, 2.92-19.59; P < 0.01) as possible risk factors for PEP. Multivariable logistic regression identified sphincterotomy (OR, 7.35; 95% CI, 3.07-17.61; P = 0.02) and wire cannulation of the PD (OR, 2.96; 95% CI, 1.01- 8.64; P = 0.05) to be significant risk factors for PEP.
Conclusions: The complication rate of PEP after LT in this study was shown to be low (2.0%) and was shown to be lower compared with patients without a history of LT. However, the mortality rate of 21.4% is much higher. Possible risk factors for PEP were sphincterotomy and wire cannulation of PD during ERCP.

Home monitoring with the SElf Care after REnal Transplantation (SECRET) kit in the COVID-19 pandemic

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Background: In recent years, many healthcare institutions have introduced home monitoring, which has been accelerated by the COVID-19 pandemic. We introduced a home monitoring program for kidney transplant recipients with COVID-19 to provide high quality care to this vulnerable group and reduce the health care burden.
Methods: All kidney transplant recipients with a positive PCR test for SARS-CoV2 were eligible for home monitoring. Our SECRET kit contains CE-certified devices; a blood pressure monitor, pulse oximeter and a thermometer. Measurements were entered into the Luscii® app. The Luscii app is CE-certified as a Class IIa medical device and integrated in to our electronic health record. We developed a custom-made program, with alarms generating a message to the recipient to call out for medical assistance 24/7. Alarms were set for a temperature ≥38C, oxygen saturation ≤93% and blood pressures of ≥180/110 mmHg or ≤100/50 mmHg and if no measurements were done for >24 hours. On top of that we proactively contacted recipients in case of frequent alarms or if digitally requested by the recipient.
Results: A total of 41 recipients were included from March 21st till October 14th 2021, 56% women, with an average age of 49 years (range 22-82). Of those 41, 30 used the Luscii app, while 8 could or did not (3 included before the app was online). During an average usage of 12 days (range 2-34) recipients performed 75 measurements (range 8-260) and generated 7 alarms (range 0-41). About half of the recipients (n=21) were safely monitored at home, while the other half had to visit the Emergency Department, where the majority was admitted (n=18, median 8 days, range 3-45). Our home monitoring program prevented 2 Emergency Department visits and 2 hospitalizations. It also led to 12 Emergency Department visits, mainly because of early detection of hypoxia (9/12 recipients) and to 2 re-admissions after early discharge. Eight recipients evaluated our home monitoring program, scoring an average of 4.5 out of 5 points. Most recipients stated that home monitoring contributed to feeling more secure about their illness.
Conclusions: Home monitoring of kidney transplant recipients with COVID using medical devices and the Luscii app is feasible, well appreciated and provides high quality medical care at home. It likely detects disease progression at earlier stages and prevents hospital admissions, thereby making more efficient use of scarce health care facilities.