NEDERLANDSE TRANSPLANTATIE VERENIGING

Online Bootcongres 2021

Wetenschappelijke voorjaarsvergadering

Nederlandse Transplantatie Vereniging

3 en 4 maart 2021

georganiseerd in samenwerking met

Radboudumc

Radboudumc

Inhoudsopgave

Welkom op het eerste Online Bootcongres!

Beste congres-deelnemer,

Het is me een eer om je namens de lokale organisatiecommissie van harte welkom te heten op het *eerste* online Bootcongres. Ondanks de veranderde omstandigheden denken we een gevarieerd en interessant programma te hebben samengesteld. Niet in de laatste plaats doordat er een ruim aanbod was van ingezonden abstracts van hoog niveau.

We starten het programma met een lezing over complotdenken, iets wat in deze periode heel actueel is. In plenaire sessies hebben we verder ruimte gemaakt voor de als best beoordeelde abstracts, de in 2019 in het Radboudumc uitgevoerde dubbele hand-armtransplantatie, diverse prijsuitreikingen, en uiteraard ook COVID-19.

Iedere dag is er een blok met drie parallelsessie met uitgenodigde sprekers over een breed palet van onderwerpen, variërend van basale immunologie tot diverse aspecten van orgaandonatie. De abstractpresentaties vinden plaats in *virtual classrooms* met circa 15 deelnemers om op die manier toch interessante discussies mogelijk te maken. Na alle serieuze kost zullen we het congres op luchtige wijze afsluiten.

Hoewel directe ontmoetingen tijdens deze editie van het Bootcongres niet mogelijk zijn, vertrouwen we er op dat jullie de wegen om digitaal met elkaar in contact te komen inmiddels kennen en gebruiken. Desalniettemin gaan we er graag vanuit dat dit voorlopig ook weer het *laatste* (volledige) online Bootcongres is.

We wensen jullie een leerzaam en genoeglijk congres!

Namens de lokale organisatiecommissie,
Luuk Hilbrands, Radboudumc

Organisatiecommissie Bootcongres 2021

Vanuit het Radboudumc
Rianne van Zoggel
Marjo van Helden
Jeroen Langereis
Arnold van der Meer
Hans Koenen
Michiel Warlé
Paul Poyck
Michel van der Jagt
Frank d'Ancona
Hans Langenhuijsen
Xiaoye Zhu
Janneke Mulder
Simone Willems
Alec van Veenendaal
Marlies Cornelissen
Rutger Maas
Raphaël Duivenvoorden
Marije Baas
Luuk Hilbrands

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

Vanuit het secretariaat NTV te Haarlem
Marie José van Gijtenbeek
Emma Bocxe
Jeanine van Aalst

Accreditatie is aangevraagd bij de volgende verenigingen:

Nederlandse Vereniging voor Heelkunde	12
Nederlandse Vereniging voor Immunologie	10
Nederlandse Internisten Vereniging	8
Nederlandse Vereniging voor Kindergeneeskunde	11
Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose	12
Nederlandse Vereniging van Maag-Darm-Leverartsen	8
Nederlandse Vereniging voor Thoraxchirurgie	12
Nederlandse Vereniging voor Urologie	

V&VN, kwaliteitsregister algemeen

V&VN, kwaliteitsregister, deskundigheidsgebied Dialyse

V&VN, verpleegkundig specialisten register

Nederlandse Associatie van Physician Assistants 12

Bijeenkomsten tijdens Bootcongres

Woensdag 3 maart 2021

Ledenvergadering Nederlandse Transplantatie Vereniging 17.00-18.00 uur

Schematisch overzicht programma - Woensdag 3 maart 2021

09.00 – 10.45	**Plenair I** *Voorzitters: Marlies Reinders en Luuk Hilbrands* Bizarre theorieën, normale denkers: waarom complotdenkers zo gek nog niet zijn *Dr. Harmen Ghijsen, Universitair docent filosofie van cognitie en taal, Radboud Universiteit* **Best abstracts** **Prijsuitreikingen** NTV wetenschapsprijs Gauke Kootstraprijs 2021, gevolgd door voordracht			
10.45 – 11.15	Pauze - Powerd by Young Professionals			
11.15 – 12.45	**Classroom 1** Preservation / perfusion Abstractsessie	**Classroom 2** Kidney transplantation – clinical Abstractsessie	**Classroom 3** Preservation injury / repair Abstractsessie	**Classroom 4** Pharmacokinetics and living kidney donation Abstractsessie
12.45 – 13.15	Pauze			
13.15 – 14.45	**Parallel I - Casus** *Voorzitters: Anne Breek* "Donatie, nooit vanzelfsprekend"	**Parallel 2 - Immunologie** *Voorzitters: Raphaël Duivenvoorden en Hans Koenen* Cellular immune therapy in transplantation *Prof. dr. Giovanna Lombardi, professor of Human Transplant Immunology, Kings College London* Innate allorecognition *Dr. Martin Oberbarnscheidt, Assistant Professor of Surgery, University of Pittsburgh, Thomas E. Starzl Transplantation Institute* Abstracts	**Parallel 3 – Beter gezien en gehoord** *Voorzitters: Coby Annema en Marjo van Helden* Frailty in de context van orgaantransplantatie – *Dr. Angele Kerckhoffs, internist ouderengeneeskunde-nefroloog, Jeroen Bosch Ziekenhuis* Transitie in de context van orgaantransplantatie – *Dr. AnneLoes van Staa, Lector Transities in Zorg, Hogeschool Rotterdam* Abstracts	

14.45 – 15.15	Pauze - Meet the Expert sessies
15.15 – 16.45	**Plenair 2** *Voorzitters: Marije Baas en Martin Hoogduijn* NTV Onderwijs Innovatieprijs LWTV Innovatie-Kwaliteitsprijs 2021, gevolgd door presentatie winnaar 2020 Dubbele hand-arm transplantatie *Team o.l.v. Prof. dr. Steven Hovius, plastisch chirurg, Radboudumc, Nijmegen*
17.00	Ledenvergadering via Teams, aanmelding niet vereist

Schematisch overzicht programma - Donderdag 4 maart 2021

09.00 – 10.45	**Plenair 3 – COVID19** *Voorzitters: Raphaël Duivenvoorden en Niels van der Kaaij* COVID-19 – de actualiteit - *Dr. Jan-Stephan Sanders, nefroloog, Universitair Medisch Centrum Groningen* Individuele gevoeligheid voor SARS-CoV-2 – *Dr. Frank van de Veerdonk, internist-infectioloog, Radboudumc* Abstracts **Prijsuitreikingen** Astellas Transplantatie Research Prijs 2021 Chiesi prijs 2021 – Beste Idee in Transplantatie Novartis Transplantation Awards 2021		
10.45 – 11.15	Pauze - Powerd by Young Professionals: Throwback Thursday		
11.15 – 12.45	**Parallel 4 – HLA immunisatie en allocatie** *Voorzitters: Arnold van der Meer en Jeroen Langereis* CIAT: een nieuw en veelbelovend cross-over programma *Dr. Joke Roodnat, internist-nefroloog en Dr. Marry de Klerk, coördinator cross-over programma, Erasmus MC, Rotterdam* Abstracts	**Parallel 5 – Informatieuitwisseling op afstand** *Voorzitters: Marlies Cornelissen en Rutger Maas* Monitoring op afstand binnen het ziekenhuis *Dr. Bas Bredie, internist, Radboudumc, Nijmegen* Monitoring op afstand buiten het ziekenhuis *Dr. Jolt Roukema, kinderarts-pulmonoloog, Radboudumc, Nijmegen* Abstracts	**Parallel 6 -** **Het belang van (anoniem) contact** *Voorzitters: Marjo van Helden en Paul Poyck* Contact tussen nierpatiënt en nabestaanden postmortale donor *Willem Hordijk, orgaandonatie coordinator, Radboudumc, Sabine Hopman en Gerben van den Bosch, medisch maatschappelijk werkers, Radboudumc, Janneke Vervelde, verpleegkundig specialist, LUMC.* Contact tussen nierpatiënt en gerichte altruïst *Gerben van den Bosch, Radboudumc*
12.45 – 13.15	Pauze		
13.15 – 14.45	**Classroom 5** Preservation / perfusion Abstractsessie	**Classroom 6** Rejection Abstractsessie	**Classroom 7** Clinical – Surgical Abstractsessie
14.45	Plenaire afsluiting in theatrale stijl		

Plenair 1 – Openingssessie

Voorzitters: *Prof. dr. Luuk, Hilbrands, voorzitter LOC, internist-nefroloog, Radboudumc*
Prof. dr. Marlies Reinders, voorzitter NTV, internist-nefroloog, Erasmus MC

09.00 Bizarre theorieën, normale denkers: waarom complotdenkers zo gek nog niet zijn
Dr. *Harmen Ghijsen, Universitair docent filosofie van cognitie en taal, Radboud Universiteit*

Best abstracts
Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

09.30 Nierkeuze.nl: A web based application to support the decision process for kidney replacement therapy based on outcome data (p. 28)
S.P. Berger[2], H. Peters Sengers[1], AW Gomes Neto[2], HGK Scholten-Gerben[2], H. Bart[3], M ten Dam[4], L Heuveling[4], A. Hemke[5], C. Konijn[5], J.H de Ruiter[6] [1]Center for Experimental and Molecular Medicine, Amsterdam UMC, Amsterdam, The Netherlands. [2]Interne Geneeskunde-Nefrologie, UMCG, Groningen, The Netherlands. [3]Nierpatiënten Vereniging Nederland, Bussum, The Netherlands. [4]Nefrovisie, Utrecht, The Netherlands. [5]Nederlandse Transplantatie Stichting, Leiden, The Netherlands. [6]Hanzehogeschool, Groningen, The Netherlands.

09.42 A Clinical Comparison of Two Different Oxygen Carriers For Combined Hypothermic and Normothermic Machine Perfusion of High-risk Donor Livers (p. 29)
O.B. van Leeuwen[1], Bodewes SB[1], M.P.D. Haring[1], I.M.A. Brüggenwirth[1], V.A. Lantinga[1], A.M. Thorne[1], A.P. van den Berg[2], M.T. de Boer[1], R.H.J. de Kleine[1], T. Lisman[1], Y. de Vries[2], V.E. de Meijer[1], R.J. Porte[1,] [1]Afd. Chirurgie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [2]Afd. Maag, darm, en leverziekten, Universitair Medisch Centrum Groningen, Groningen, Nederland.

09.54 Blockade of the IL-21 Pathway: A New Perspective for the Treatment of T and B cell Mediated Allogeneic Responses after Transplantation (p. 30)
C.C. Baan[1], K. de Leur[1], M.J. Hoogduijn[1], D.A. Hesselink[1], [1]Internal Medicine, Erasmus MC, Rotterdam, The Netherlands.

10.06 Tacrolimus monotherapy in immunologically low-risk kidney transplant recipients: follow-up of a randomized-controlled trial (p. 31)
A.E. de Weerd[1], M.J. Verschragen[1], J.A. van Gestel[1], D.L. Roelen[2], M. Dieterich[1], M.G.H. Betjes[1] [1]Nephrology and Kidney Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands. [2]HLA Laboratory, dept. of Immunology, Leiden University Medical Center, Leiden, The Netherlands.

Woensdag 3 maart 2021

10.18 NTV Wetenschapsprijs 2020
Uitgereikt door prof. dr. Marlies Reinders, voorzitter NTV

10.21 Gauke Kootstraprijs 2021
Uitreiking door prof. dr. Gauke Kootstra, naamgever van de prijs
Gevolgd door lezing prijswinnaar

10.45 Koffie- / theepauze

Koffie break - Powered by Young Professionals

10.45 Koffie- / theepauze met diverse gespreksonderwerpen in vier breakout sessies

Breakout 1:
- Transplantatiepatiënten en corona vaccinatie

Breakout 2:
- Digitale congressen, ook na coronacrisis

Breakout 3:
- Anonimiteit tussen donor en ontvanger moet opgeheven worden

Breakout 4:
- Direct deceased donation in Nederland

Classroom 1 Preservation / perfusion

Voorzitters: *Dr. Wojciech Polak, chirurg, Erasmuc MC*
Dr. Dorottya de Vries, chirurg, LUMC

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

11.15 Oxygenated versus non-oxygenated flush out and storage of DCD porcine livers - A proof of concept study (p. 32)
R.J. Porte[1], I.M.A. Brüggenwirth[1], W.S. van der Plas[1], O.B. van Leeuwen[1], A.M. Thorne[1], M. Rayar[2], V.E. de Meijer[1], [1]Chirurgie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [2]Chirurgie Hepatobiliaire et Digestive, Centre Hospitalier Universitaire de Rennes, Rennes, Frankrijk.

11.27 The effects of oxygen level during normothermic regional perfusion after circulatory death in a porcine model (p. 33)
N.M. Moeslund[1], Z..L. Zha Zhang[2], PR Ryhammer[3], L.I. Ilkjaer[4], M.P. Pedersen[5], S.T. Tsui[6], M.E. Erasmus[2], H.E. Eiskjaer[7], [1]Dept. of Cardiology - Research, Aarhus University, Aarhus N, Denemarken. [2]Dept. of cardiothoracic surgery, University Medical Center Groningen, Nederland. [3]Dept. of Anesthesiology, Regionshospitalet Silkeborg, Silkeborg, Denemarken. [4]Dept. of cardiothoracic surgery, Aarhus University Hospital, Aarhus, Denemarken. [5]Comparative Medicine Lab, Institute for Clinical Medicine, Aarhus University, Aarhus, Denemarken. [6]Dept. of cardiothoracic surgery, Royal Papworth Hospital NHS Foundation Trust, Cambridge, Verenigd Koninkrijk. [7]Dept. of Cardiology, Aarhus University Hospital, Aarhus, Denemarken.

11.39 The effect of different hematocrit levels during normothermic reperfusion of porcine DCD kidneys on renal function and metabolism (p. 34)
T.M. Huijink[1], L.A. van Furth[1], A. Lammerts[1], H. Maassen[1], S.P. Berger[2], H.G.D. Leuvenink[1], L.H. Venema[1], [1]Chirurgie, UMC Groningen, Groningen, Nederland. [2]Nefrologie, UMC Groningen, Groningen, Nederland.

11.51 Challenges using banked red blood cells for oxygen delivery during normothermic machine perfusion of donor kidneys (p. 35)
A.S. Arykbaeva[1], D.K. de Vries[1], J.B. Doppenberg[1], J. Lagerberg[2], D. de Korte[2], R.J. Ploeg[1], I.P.J. Alwayn[1], [1]Dept. artment of Surgery, LUMC Transplant Center, Leids Universitair Medisch Centrum, Leiden, Nederland. [2]Dept. of Blood Cell Research, Sanquin Research Laboratory, Amsterdam, Nederland.

12.03 Rescue of declined extended criteria DCD livers using in-situ normothermic regional perfusion (NRP) (p. 36)
I.J. Schurink[1], F.H.C. de Goeij[1], F.E.M. van der Leemkolk[2], L.J.M. Habets[2], C.A.A. van Dun[3], I.P.J. Alwayn[2], W.G. Polak[1], V.A.L. Huurman[2], J. de Jonge[1], [1]Dept. of Surgery, Erasmus MC, Rotterdam, The Netherlands. [2]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [3]Organ Donation Coordinator, Erasmus MC, Rotterdam, The Netherlands.

12.15 Outcome of kidney transplantation after in-situ normothermic regional perfusion (NRP) of extended criteria donors is comparable to matched controls (p. 37)
L.J.M. Habets[1], F.E.M. van de Leemkolk[2], I.J. Schurink[3], F.H.C. de Goeij[3], C.C.A. van Dun[4], L. Guo[5], M.J. Heemskerk[6], A.P.J. de Vries[7], J. de Jonge[3], V.A.L. Huurman[2], [1]Division of Transplant Surgery, Dept. of Surgery, Leiden University Medical Center, Leiden, Nederland. [2]Division of Transplant Surgery, Dept. of Surgery, LUMC, Leiden, Nederland. [3]Division of Transplant Surgery, Dept. of Surgery, Erasmus Medical Center, Rotterdam, Nederland. [4]Dept. of Surgery, Erasmus Medical Center, Rotterdam, Nederland. [5]Ministry of Health, Welfare and Sport, Ministry of Health, Welfare and Sport, The Hague, Nederland. [6]Dutch Transplant Foundation, Dutch Transplant Foundation, Leiden, Nederland. [7]Division of Nephrology, Dept. of Internal Medicine, LUMC, Leiden, Nederland.

Classroom 2 Kidney transplantation / clinical

Voorzitters: *Dr. Maarten Christiaans, internist-nefroloog, MUMC*
Dr. Xiaoye Zhu, uroloog, Radboudumc

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

11.15 Combining existing models and recent data into an up-to-date prediction model for evaluating kidneys from older deceased donors: development and external validation study (p. 38)
C.L. Ramspek[1], M El Moumni[2], E. Wali[1], M.B.A. Heemskerk[3], R.A. Pol[4], M.J. Crop[5], N.E. Jansen[3], A. Hoitsma[3], F.W. Dekker[1], M van Diepen[1], C. Moers[4], [1]Klinische Epidemiologie, LUMC, Leiden, Nederland. [2]Trauma chirurgie, UMCG, Groningen, Nederland. [3]-, Nederlandse transplantatie stichting, Leiden, Nederland. [4]Chirurgie, UMCG, Groningen, Nederland. [5]Interne geneeskunde, UMCG, Groningen, Nederland.

11.27 Donation after Circulatory Death kidney transplantation has equal long-term graft and patient survival as Donation after Brain Death: a systematic review and meta-analysis (p. 39)
E Rijkse[1], S Ceuppens[1], H Qi[2], JNM IJzermans[1], DA Hesselink[1], RC Minnee[1], [1]Heelkunde, Erasmus MC, Rotterdam, Nederland. [2]Biostatistics, Erasmus MC, Rotterdam, Nederland.

11.39 Donor factors only marginally impact short-term outcomes in kidney transplantation. Results from nationwide paired-outcome analyses (p. 40)
M.J.C. de Kok[1], A.F.M. Schaapherder[1], M. Kaisar[2], L. Mumford[3], M. Robb[3], R. Johnson[3], F.J. Bemelman[4], J. van de Wetering[5], A.D. van Zuilen[6], M.H.L. Christiaans[7], M.C. Baas[8], A.S. Nurmohamed[4], S.P. Berger[9], E. Bastiaannet[10], A.P.J. de Vries[11], E. Sharples[2], R.J. Ploeg[1], J.H.N. Lindeman[1], [1]Dept. of Surgery and Leiden Transplant Center, Leiden University Medical Center, Leiden, Nederland. [2]Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, Verenigd Koninkrijk. [3]Statistics and Clinical Studies, NHS Blood and Transplant, Bristol, Verenigd Koninkrijk. [4]Dept. of Internal Medicine (Nephrology), Amsterdam UMC, Amsterdam, Nederland.[5]Dept. of Internal Medicine (Nephrology), Erasmus University Medical Center,

Rotterdam, Nederland.[6]Dept. of Internal Medicine (Nephrology), University Medical Center Utrecht, Utrecht, Nederland.[7]Dept. of Internal Medicine (Nephrology), Maastricht University Medical Center, Maastricht, Nederland. [8]Dept. of Internal Medicine (Nephrology), Radboud University Medical Center, Nijmegen, Nederland.[9]Dept. of Internal Medicine (Nephrology), University Medical Center Groningen, Groningen, Nederland.[10]Dept. of Surgery, Leiden University Medical Center, Leiden, Nederland.[11]Division of Nephrology, Dept. of Internal Medicine and Leiden Transplant Ce, Leiden University Medical Center, Leiden, Nederland.

11.51 Counselling on Conceiving: Considerations of Professionals in Transplantation (p. 41)
M. Gosselink[2], M.C. van Buren[1], E.K. Massey[1], J. van de Wetering[1], A.T. Lely[2], [1]Nefrologie & Niertransplantatie, Erasmus MC, Rotterdam, Nederland. [2]Dept. of Obstetrics, Wilhelmina Children's Hospital Birth Center, University Medical Center Utrecht, Utrecht, Nederland.

12.03 Circulation and hemodynamics in living donation of kidney transplantation in children The child-kitc study: magnetic resonance - arterial spin labeling perfusion imaging in pediatric ktx (p. 42)
E.L. Stille[1], M. Voet[2], E.A.M. Cornelissen[3], A. Nusmeier[4], W.M. Klein[5], J. Lemson[4], J.I. Malagon[2], J.J. Futterer[5], [1]Radiologie en Nucleaire Geneeskunde, Radboudumc, Nijmegen, Nederland. [2]Anesthesiologie, Radboudumc, Nijmegen, Nederland. [3]Kindergeneeskunde, Radboudumc, Nijmegen, Nederland. [4]Intensive care, Radboudumc, Nijmegen, Nederland. [5]Radiologie en Nucleaire geneeskunde, Radboudumc, Nijmegen, Nederland.

12.15 Systematic screening for diabetes and pre-diabetes post-heart transplantation
S. Roest[1], M.M. Goedendorp-Sluimer[1], J.J. Köbben[2], J.J. Brugts[1], A.A. Constantinescu[1], K. (p. 43)
Caliskan[1], A.A.M. Zandbergen[2], O.C. Manintveld[1], [1]Cardiology, Thorax Centre, Erasmus MC, University Medical Centre Rotterdam, Rotterdam, The Netherlands. [2]Internal Medicine, Erasmus MC, University Medical Centre Rotterdam, Rotterdam, The Netherlands.

12.27 Risk factors for early graft failure after solitary pancreas transplantation in the modern era: a single-center, retrospective study (p. 44)
A.P.M. van Enckevort[1], M. Mallat[2], M. Nijhoff[2], E.J.P. de Koning[2], P. van der Boog[2], D. Roelen[3], A.G. Baranski[1], I.P.J. Alwayn[1], A.E. Braat[1], A.P.J. de Vries[2], V.A.L. Huurman[1], [1]Transplantatiechirurgie, Leids Universitair Medisch Centrum, Leiden, Nederland. [2]Interne Geneeskunde, Leids Universitair Medisch Centrum, Leiden, Nederland. [3]Immunologie, Leids Universitair Medisch Centrum, Leiden, Nederland.

Classroom 3 Preservation injury / repair

Voorzitters: *Prof. dr. Luc van der Laan, onderzoeker, Erasmus MC*
Prof. dr. Henri Leuvenink, onderzoeker, UMCG

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

11.15 Kidney organoids are capable of forming Wilms-like tumors, but not teratomas (p. 45)
A.S Shankar[1], Z. Du[1], W. Cao[2], H. Tejeda Mora[1], T.P.P. Van den Bosch[3], S.S. Korevaar[1], E.M.J. Bindels[4], B. Eussen[5], A. de Klein[5], Q. Pan[2], L. Oudijk[3], M.C. Clahsen-van Groningen[3], E.J. Hoorn[1], C.C. Baan[1], J. Gribnau[6], M.J. Hoogduijn[1], [1]Dept. of Internal Medicine, Division of Nephrology and Transplantation, Erasmus MC, University Medical Center, Rotterdam, Nederland. [2]Dept. of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, Nederland. [3]Dept. of Pathology, Erasmus MC, University Medical Center, Rotterdam, Nederland. [4]Dept. of Hematology, Erasmus MC, University Medical Center, Rotterdam, Nederland. [5]Dept. of Clinical Genetics, Erasmus MC, University Medical Center, Rotterdam, Nederland. [6]Dept. of Developmental Biology, Erasmus MC, University Medical Center, Rotterdam, Nederland.

11.27 Efficient recellularization of human vascular grafts with patient derived endothelial cells (p. 46)
H. Tejeda Mora[1], J. Willemse[2], M.M.A. Verstegen[2], J. de Jonge[2], R.C. Minnee[2], M.W.F. van der Hoogen[1], C.C. Baan[1], M.J. Hoogduijn[1], L.J.W. van der Laan[2], [1]Internal Medicine, Nephrology and Transplantation, Erasmus MC, Rotterdam, Nederland. [2]Surgery, Erasmus MC, Rotterdam, Nederland.

11.39 Complement C3 deposition on ischemia-reperfusion injured endothelial cells is induced by anti-ARHGDIB monoclonal antibodies (p. 47)
T. Kardol-Hoefnagel[1], A.M. Ehlers[2], A.D. van Zuilen[3], H.D. Luijk[4], H.G. Otten[1], [1]Center for Translational Immunology, UMC Utrecht, Utrecht, The Netherlands. [2]Center for Translational Immunology; and Dept. of Dermatology, UMC Utrecht, Utrecht, The Netherlands. [3]Dept. of Nephrology, UMC Utrecht, Utrecht, The Netherlands. [4]Dept. of Respiratory Medicine, UMC Utrecht, Utrecht, The Netherlands.

11.51 The small bowel is protected by the presence of luminal preservation solution during cold storage in a brain-dead rat model (p. 48)
G. Trentadue[1], L Vecchio[2], G Kats-Ugurlu[3], JW Haveman[4], KN Faber[5], M Rumbo[6], H Leuvenink[4], G Dijkstra[7], [1]Gastroenterology and Hepatology, Universiteit Medisch Centrum Groningen, Groningen, Nederland. [2]Laboratorio de Trasplante de Organos y Tejidos, La Plata National University, La Plata, Argentinië. [3]Pathology and Medical Biology, Universitair Medisch Centrum Groningen, Groningen, Nederland. [4]Surgery, Universitair Medisch Centrum Groningen, Groningen, Nederland. [5]Laboratory Medicine, Gastroenterology and Hepatology, Universitair Medisch Centrum Groningen, Groningen, Nederland. [6]Instituto de Estudios Inmunológicos y Fisiopatológicos, La Plata National University, La Plata, Argentinië. [7]Gastroenterology and Hepatology, Universitair Medisch Centrum Groningen, Groningen, Nederland.

12.03 Anti-fibrotic effects of Membrane Particles from mesenchymal stromal cells in renal ischemia reperfusion injury mouse model (p. 49)
A. Merino[1], Z. Du[1], A. Shankar[1], V. Palomares[2], S.S. Korevaar[1], D. Reijerkerk[1], C.C. Baan[1], M.E.J. Reinders[1], M.J. Hoogduijn[1], [1]Internal medicine, Erasmus MC, Rotterdam, Nederland. [2]Oral and Maxillofacial Surgery, Erasmus MC, Rotterdam, The Netherlands.

12.15 Mesenchymal stromal cell derived membrane particles are internalized by macrophages and endothelial cells and exhibit mixed pro- and anti-inflammatory effects (p. 50)
F. Da Costa Goncalves[1], S.S. Korevaar[1], C.C. Baan[1], M.E.J. Reinders[1], A. Merino[1], M.J. Hoogduijn[1], [1]Inwendige Geneeskunde, Erasmus MC, Rotterdam, Nederland.

12.27 Treating circulatory death donor kidneys with anti-fibrotic drugs using ex vivo precision cut kidney slices (p. 51)
L.L. van Leeuwen[1], M.J.R. Ruigrok[2], P. Olinga[2], H.G.D. Leuvenink[1], [1]Chirurgie, UMCG, Groningen, Nederland. [2]Pharmaceutical Technology and Biopharmacy, University of Groningen, Groningen, Nederland.

Classroom 4 Pharmacokinetics and living kidney donation

Voorzitters: *Dr. Aiko de Vries, internist-nefroloog, LUMC*
Dr. Arjan van Zuilen, internist-nefroloog, UMCU

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

11.15 Normothermic Machine perfusion of explanted livers in patients undergoing liver transplantation to study hepatic pharmacokinetic processes (p. 52)
L.J. Stevens[1], J. Dubbeld[1], J.B. Doppenberg[1], B. van Hoek[2], C.A.J. Knibbe[3], W.H.J. Vaes[4], E. van de Steeg[4], I.P.J. Alwayn[1], [1]Heelkunde, LUMC, Leiden, The Netherlands. [2]MDL, LUMC, Leiden, The Netherlands. [3]Division of Systems Biomedicine and Pharmacology, LACDR, Leiden, Nederland. [4]Metabolic Health Research, TNO, Leiden, Nederland.

11.27 Avoiding tacrolimus under- and overexposure with a dosing algorithm for renal transplant recipients: a single arm prospective intervention trial (p. 53)
M.I. Francke[1], L.M. Andrews[2], H.L. Le[2], J. van de Wetering[1], M.C. Clahsen-van Groningen[3], T. van Gelder[4], R.H.N. van Schaik[5], B. van der Holt[6], B.C.M. de Winter[2], D.A. Hesselink[1], [1]Internal medicine, nephrology and transplantation, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands. [2]Hospital pharmacy, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. [3]Pathology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. [4]Clinical Pharmacology and Toxicology, Leiden University Medical Center, Leiden, The Netherlands. [5]Clinical Chemistry, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. [6]Hematology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands.

11.39 Combination of low-dose sirolimus and extended-release tacrolimus versus standard dose extended-release tacrolimus in de novo liver transplant recipients comparing long-term renal function; 24-month results from a multi-center randomized, open label, controlled study (p. 54)

M.B. Mulder[1], S. Darwish Murad[2], K.P. De Jong[3], A.P. Van den Berg[4], B Van Hoek[5], I.P.J. Alwayn[6], N.S. Erler[7], W.G. Polak[8], B.C.M. De Winter[1], C.M. Den Hoed[2], H.J. Metselaar[2], [1]Ziekenhuisapotheek, Erasmus MC, Rotterdam, Nederland. [2]Gastroenterologie en hepatologie, Erasmus MC, Rotterdam, Nederland. [3]Chirurgie, UMCG, Groningen, Nederland. [4]Gastroenterologie en hepatologie, UMCG, Groningen, Nederland. [5]Gastroenterologie en hepatologie, LUMC, Leiden, Nederland. [6]Chirurgie, LUMC, Leiden, Nederland. [7]Biostatistiek, Erasmus MC, Rotterdam, Nederland. [8]Chirurgie, Erasmus MC, Rotterdam, Nederland.

11.51 Intra-patient variability in tacrolimus pharmacokinetics in kidney transplant patients treated with different tacrolimus formulations (p. 55)

K.L.W. Bunthof[1], L. Al-Hassany[2], G. Nakshbandi[2], D.A. Hesselink[3], R.H. van Schaik[4], M.A.G.J. ten Dam[5], M.C. Baas[1], L.B. Hilbrands[1], T. van Gelder[2], [1]Nierziekten, Radboudumc, Nijmegen, Nederland. [2]Farmacie, Erasmus MC, Rotterdam, Nederland. [3]Nefrologie en transplantatie, inwendige geneeskunde, Erasmus MC, Rotterdam, Nederland. [4]Klinische chemie, Erasmusmc, Rotterdam, Nederland. [5]Interne geneeskunde, Erasmus MC, Rotterdam, Nederland.

12.03 The risk of post-donation kidney function impairment for prospective living kidney donors with persistent isolated microscopic hematuria (p. 56)

J. van der Weijden[1], M. van Londen[1], I.M. Nolte[2], M.H. de Borst[1], S.P. Berger[1], [1]Nefrologie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [2]Epidemiologie, Universitair Medisch Centrum Groningen, Groningen, Nederland.

12.15 Recurrence of IgA After Kidney Transplantation in Adults (p. 57)

A. Uffing[1], S.P. Berger[1], TANGO Consortium[2], [1]Interne Geneeskunde - Nefrologie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [2]Nefrologie, Brigham and Women's Hospital, Boston, Verenigde Staten.

12.27 Impact of measured versus estimated GFR on living kidney donor selection: A multicenter cohort study (p. 58)

J. van der Weijden[1], M. van Londen[1], J.I. Roodnat[2], M.L. Kho[2], J. van de Wetering[2], I.M. Dooper[3], H.J. Kloke[3], S.J.L. Bakker[1], G. Navis[1], I.M. Nolte[4], M.H. de Borst[1], S.P. Berger[1], [1]Nefrologie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [2]Nefrologie en transplantatie, Erasmus Medisch Centrum Rotterdam, Rotterdam, Nederland. [3]Nefrologie, Radboud Universitair Medisch Centrum Nijmegen, Nijmegen, Nederland. [4]Epidemiologie, Universitair Medisch Centrum Groningen, Groningen, Nederland.

12.45 Lunchpauze

Parallel 1 **Donatie, nooit vanzelfsprekend**

Voorzitters: *Anne Breek, transplantatie coördinator, UMCG*

13.15 Voorbereidende handelingen voor orgaandonatie? Ja natuurlijk! Intuberen? Zeker ook. Maar wat als een patiënt in een eerdere, curatieve setting heeft aangegeven niet meer gereanimeerd en geïntubeerd te willen worden? Mag deze wens in het donatietraject dan genegeerd worden? Mag je intuberen? Want is die afgesproken behandelbeperking nu nog wel van toepassing?

Maar er is meer. Uit het medisch dossier blijkt dat de patiënt mogelijk wilsonbekwaam is. Hoe en bij wie moet je dit verifiëren? Welke (medische) gegevens mogen wij, ODC's, eigenlijk op- en uitvragen? Valt dit onder collegiaal overleg? Hoe verhoudt 'veilig doneren' zich tot de privacy van de patiënt?

Mooie vragen, ethische dilemma's, op basis van waargebeurde casussen. Aan de hand van een interactieve sessie, ondersteund door filmpjes en interviews met de betrokkenen, gaan we hier met een panel deskundigen dieper op in.

Panelleden:
Dr. Hugo Touw, anesthesioloog- intensivist, Radboudumc
Ger Palmboom, klinisch ethicus bureau "Zwart|Wit, morele reflectie in de zorg"
Lydia Dijkhuizen, juridisch beleidsadviseur, NTS
Dr. Tineke Wind, orgaandonatiecoördinator Maastricht UMC

Parallel 2 Immunologie

Voorzitters: *Dr. Raphaël Duivenvoorden, internist-nefroloog, Radboudumc*
Dr. Hans Koenen, onderzoeker, Radboudumc

13.15 Cellular immune therapy in transplantation
Prof. dr. Giovanna Lombardi, Professor of Human Transplant Immunology, Kings College London

13.40 Innate allorecognition
Dr. Martin Oberbarnscheidt, Assistant Professor of Surgery, University of Pittsburgh, Thomas E. Starzl Transplantation Institute

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

14.05 Antibody mediated rejection in kidney transplantation: What is the role of complement activation? (p. 59)
S.P. Berger[4], G Tiller[1], R.G.M. Lammerts[1], J Karijosemito[1], A Diepstra[2], A Meter[1], MAJ Seelen[1], M.C. van den Heuvel[2], B.G. Hepkema[3], J van den Born[1], [1]Interne Geneeskunde/Nefrologie, UMCG, Groningen, The Netherlands. [2]Pathologie, UMCG, Groningen, The Netherlands. [3]Laboratoriumgeneeskunde, UMCG, Groningen, The Netherlands. [4]Interne Geneeskunde-Nefrologie, UMCG, Groningen, The Netherlands.

14.17 The assesment of pre-transplant alloreactive T cells is a valuable addition in predicting patients at risk for acute rejecion (p. 60)
A Mendoza Rojas[1], T van Gelder[2], P de Kuiper[1], D Reijerkerk[1], M.C. Clahsen-van Groningen[3], D.A. Hesselink[1], C.C. Baan[1], N.M. van Besouw[1], [1]Dept. of Internal Medicine. Nephrology & Transplantation, Erasmus Medical Center, Rotterdam, Nederland. [2]Dept. of Clinical Pharmacy & Toxicology, Leiden Universitity Medical Center, Leiden, Nederland. [3]Dept. of Internal Medicine. Pathology, Erasmus Medical Center, Rotterdam, Nederland.

14.29 Characterization of the immunogenicity of iPSC-derived kidney organoids (p. 61)
A.S Shankar[1], V. Palomares Cabeza[2], H. Tejeda Mora[3], Z. Du[3], S.S. Korevaar[3], T.P.P. Van den Bosch[4], E.M.J. Bindels[5], M.C. Clahsen-van Groningen[4], J. Gribnau[6], E.J. Hoorn[3], C.C. Baan[3], M.J. Hoogduijn[3], [1]Dept. of Internal Medicine, Division of Nephrology and Transplantation, Erasmus MC, University Medical Center, Rotterdam, Nederland. [2]Dept. of Oral and Maxillofacial Surgery, Erasmus MC, University Medical Center, Rotterdam, Nederland. [3]Dept. of Internal Medicine, Division of Nephrology and Transplantation, Erasmus MC, University Medical Center, Rotterdam, Nederland. [4]Dept. of Pathology, Erasmus MC, University Medical Center, Rotterdam, Nederland. [5]Dept. of Hematology, Erasmus MC, University Medical Center, Rotterdam, Nederland. [6]Dept. of Developmental Biology, Erasmus MC, University Medical Center, Rotterdam, Nederland.

Parallel 3	**Beter gezien en gehoord**
Voorzitters:	*Dr. Coby Annema, verpleegkundig onderzoeker, UMCG* *Marjo van Helden, verpleegkundig specialist, Radboudumc*
13.15	Frailty in de context van orgaantransplantatie *Dr. Angele Kerckhoffs, internist ouderengeneeskunde-nefroloog, Jeroen Bosch Ziekenhuis, Den Bosch*
13.40	Transitie in de context van orgaantransplantatie *Dr. AnneLoes van Staa, Lector Transities in Zorg, Hogeschool Rotterdam* *Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.*
14.05	Patient reported outcomes in kidney transplantation recipients, a cross-sectional overview (p. 62) *D.M.J. Veltkamp[1], Y. Wang[2], W.M. Michels[1], Y. Meuleman[2], F.W. Dekker[2], P.J.M. van der Boog[1], A.P.J. de Vries[1], [1]Nefrologie & Transplantatie Centrum, LUMC, Leiden, Nederland. [2]Epidemiologie, LUMC, Leiden, Nederland.*
14.17	Medication adherence and fear of rejection in tacrolimus treated kidney transplant recipients with and without mycophenolate mofetil: randomized controlled trial (p. 63) *R. van Zanten[1], A.E. de Weerd[1], M.G.H. Betjes[1], R. Zietse[1], M.J. Boer - Verschragen[1], E.K. Massey[1], [1]Interne geneeskunde - Nefrologie en Transplantatie, Erasmus MC, Rotterdam, Nederland.*
14.45	Theepauze

Pauze : Meet the Expert: Parallel 2 - Immunologie

Praat na tijdens een Meet the Expert sessie met de volgende sprekers:.

Prof. dr. Giovanna Lombardi, Professor of Human Transplant Immunology, Kings College London
Dr. Martin Oberbarnscheidt, Assistant Professor of Surgery, University of Pittsburgh, Thomas E. Starzl Transplantation Institute

Pauze: Meet the Expert Parallel 3 - Beter gezien en gehoord

Praat na tijdens een Meet the Expert sessie met de volgende sprekers:.

Dr. Angele Kerckhoffs, internist ouderengeneeskunde-nefroloog, Jeroen Bosch Ziekenhuis, Den Bosch
Dr. AnneLoes van Staa, Lector Transities in Zorg, Hogeschool Rotterdam

Woensdag 3 maart 2021

Plenair 2

Voorzitters: *Dr. Marije Baas, internist-nefroloog, Radboudumc*
Dr. Martin Hoogduijn, universitair docent, Erasmus MC

Prijsuitreiking

15.15 NTV Onderwijs Innovatieprijs

15.17 LWTV Innovatie-Kwaliteitsprijs 2021
Uitgereikt door Marjo van Helden, voorzitter LWTV

Presentatie winnaar LWTV Innovatie-Kwaliteitsprijs 2020
AanZET studie; zelfmanagement na transplantatie
Regina van Zanten, promovendus, Erasmus MC

15.30 Dubbele hand-arm transplantatie
Team o.l.v. Prof. dr. Steven Hovius, plastisch chirurg, Radboudumc, Nijmegen

Algemene ledenvergadering NTV

17.00 Aanvang ALV
Leden ontvangen separaat een uitnodiging met link naar de ledenvergadering.

Plenair 3 – COVID19

Voorzitters: *Dr. Raphaël Duivenvoorden, internist-nefroloog, Radboudumc*
Dr. Niels van der Kaaij, cardiothoracaal chirurg, UMCU

09.00 COVID-19 – de actualiteit
Dr. Jan-Stephan Sanders, nefroloog, Universitair Medisch Centrum Groningen

09.25 Individuele gevoeligheid voor SARS-CoV-2
Dr. Frank van de Veerdonk, internist-infectioloog, Radboudumc

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

09.50 Impact of COVID-19 self-quarantine measures on behaviour, stress, anxiety and glycaemic control in patients with β-cell replacement therapy (p. 64)
C.P. Landstra[1], M.M. Ruissen[1], M.F. Nijhoff[1], B.E.P.B. Ballieux[2], A.P.J. de Vries[1], E.J.P. de Koning[1], [1]Interne Geneeskunde, Leids Universitair Medisch Centrum, Leiden, Nederland. [2]Klinische Chemie en Laboratoriumgeneeskunde, Leids Universitair Medisch Centrum, Leiden, Nederland.

10.02 Impact of the COVID-19 pandemic on daily lives, emotions and behaviours of kidney transplant recipients (p. 65)
R. van Zanten[1], D.M. Peelen[1], M. Laging[1], R. Kraaijeveld[1], A.M.A. Peeters[1], C.C. Baan[1], M. Tielen[1], M.W.F. van den Hoogen[1], E.K. Massey[1], [1]Interne geneeskunde - Nefrologie en Transplantatie, Erasmus MC, Rotterdam, Nederland.

10.14 Astellas Transplantatie Research Prijs 2021
Uitgereikt door Vincent Sloos, sales director a.i., Astellas Pharma

Voordracht winnaar prijs 2020:
What's on your liver? Real-time liver function testing during normothermic regional perfusion
Ivo Schurink, student, Erasmus MC

10.21 Chiesi-prijs Beste Idee in Transplantatie 2021
Uitgereikt door Niels van Dijk, Chiesi

10.27 Novartis Transplantation Awards 2021
Uitgereikt door Dr. Arjan van Zuilen, internist-nefroloog UMCU en voorzitter Novartis Transplant Advisory Board

10.45 Pauze

Parallel 4 HLA immunisatie en allocatie

Voorzitters: *Dr. Jeroen Langereis, medisch immunoloog i.o., Radboudumc*
Dr. Arnold van der Meer, transplantatie immunoloog, Radboudumc

11.15 CIAT*: een nieuw en veelbelovend cross-over programma
*Computerised Integration of Alternative kidney Transplantation programs (p. 66)
Dr. Joke Roodnat, internist-nefroloog, Erasmus MC, Rotterdam
Dr. Marry de Klerk, coördinator cross-over programma, Erasmus MC, Rotterdam

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

11.55 The national desensitization program for HLA-incompatible living-donor kidney transplantation: an underused option for unsuccesful HLA-incompatible couple (p. 67)
A.E. de Weerd[1], D.L. Roelen[2], M.M.L. Kho[1], J.I. Roodnat[1], M.G.H. Betjes[1], J. van de Wetering[1], [1]Nephrology and Kidney Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands. [2]HLA Laboratory, dept. of Immunology, Leiden University Medical Center, Leiden, The Netherlands.

12.07 Discrimination between Relevant vs Irrelevant HLA antibodies in Kidney Transplantation (p. 68)
D. Senejohnny[1], H. Otten[2], [1]CTI, UMC Utrecht, Utrecht, Nederland. [2]Central Diagnostic Laboratory (CDL) / Center of Translational Immunology (CTI), UMC Utrecht, Utrecht, Nederland.

12.19 HLA Class I and HLA-DR antibody-verified eplet mismatch load is an independent determinant for graft failure in renal transplantation (p. 69)
S. Bezstarosti[1], G.W. Haasnoot[1], H. Mohammadhassanzadeh[2], A. Madbouly[3], R. Sapir-Pichhadze[2], J.W. de Fijter[4], M.E.J. Reinders[5], S. Heidt[1], [1]Dept. of Immunology, Leiden University Medical Center, Leiden, Nederland. [2]Centre for Outcomes Research and Evaluation, McGill University Health Centre, Montreal, Canada. [3]Bioinformatics, National Marrow Donor Program, Minneapolis, Verenigde Staten. [4]Dept. of Nephrology, Leiden University Medical Center, Leiden, Nederland. [5]Dept. of Internal Medicine, Erasmus University Medical Center, Rotterdam, Nederland.

12.31 A preliminary kidney transplant cohort study to define the most immunogenic HLA-DQ amino acid mismatches using HLA-EMMA (p. 70)
C.S.M. Kramer[1], G.W. Haasnoot[1], E.G. Kamburova[2], B.W. Wisse[2], B.G. Hepkema[3], C.E. Voorter[4], C. Ranzijn[5], N.M. Lardy[5], H.G. Otten[2], D.L. Roelen[1], F.H.J. Claas[1], S. Heidt[1], [1]Dept. of Immunology, Leiden University Medical Center, Leiden, The Netherlands. [2]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands. [3]Dept. of Laboratory Medicine, University Medical Center Groningen, Groningen, The Netherlands. [4]Dept. of Transplantation Immunology, Maastricht Medical Center, Maastricht, The Netherlands. [5]Dept. of Immunogenetics, Sanquin Diagnostic Services, Amsterdam, The Netherlands.

12.45 Pauze

Parallel 5 **Informatieuitwisseling op afstand**

Voorzitters: *Dr. Marlies Cornelissen, kinderarts-nefroloog, Radboudumc*
Dr. Rutger Maas, internist-nefroloog, Radboudumc

11.15 Remote monitoring in het ziekenhuis
Dr. Bas Bredie, internist, Radboudumc, Nijmegen

11.35 Monitoring op afstand buiten het ziekenhuis
Dr. Jolt Roukema, kinderarts-pulmonoloog, Radboudumc, Nijmegen

11.55 Topics, Delivery Modes, and Social-Epistemological Dimensions of Web-Based Information for Patients Undergoing Renal Transplant and Living Donors During the COVID-19 Pandemic: Content Analysis (p. 71)
C.W. van Klaveren[1], P.G.M. de Jong[2], R.A. Hendriks[2], F. Luk[1], A.P.J. de Vries[1], P.J.M. van der Boog[1], M.E.J. Reinders[3], [1]Nephrology and Transplant Center, Leiden University Medical Center, Leiden, Nederland. [2]Center for Innovation in Medical Education, Leiden University Medical Center, Leiden, The Netherlands. [3]Nephrology and Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands.

12.07 Digitale flowvolumemeting na longtransplantatie, toepassing van een innovatie (p. 72)
S.H Smit[1], E.A.M. Verschuuren[1], C.T. Gan[1], [1]Longziekten en Tuberculose, UMCG, Groningen, Nederland.

12.19 Simultaneous LC-MS/MS quantification of creatinine, iohexol and five immunosuppressants in volumetric microsamples for remote renal transplant recipient monitoring (p. 73)
T.C. Zwart[1], E Metscher[1], S.R.M. Gokoel[2], P.J.M. van der Boog[2], J.W. de Fijter[3], H.J. Guchelaar[4], J.J. Swen[4], A.P.J. de Vries[3], D.J.A.R. Moes[4], [1]Klinische Farmacie en Toxicologie, Leids Universitair Medisch Centrum, Leiden, Nederland. [2]Interne Geneeskunde (Nefrologie), Leids Universitair Medisch Centrum, Leiden, Nederland. [3]Interne Geneeskunde (Nefrologie) & LUMC Transplantatie Centrum, Leids Universitair Medisch Centrum, Leiden, Nederland. [4]Klinische Farmacie en Toxicologie & Leiden Network for Personalised Therapeutics, Leids Universitair Medisch Centrum, Leiden, Nederland.

12.31 The clinical validation of a dried blood spot method for simultaneous tacrolimus and creatinine measurement (p. 74)
M.I. Francke[1], S. Bouarfa[2], B. van Domburg[2], D. van de Velde[2], M.E. Hellemons[3], O.C. Manintveld[4], S.M. Last-Koopmans[5], M.B. Mulder[2], D.A. Hesselink[1], B.C.M. de Winter[2], [1]Internal medicine, nephrology and transplantation, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands. [2]Hospital pharmacy, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. [3]Pulmonary medicine, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. [4]Cardiology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. [5]Hematology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands.

12.45 Pauze

Parallel 6	**Het belang van (anoniem) contact**

Voorzitters: *Marjo van Helden, verpleegkundig specialist, Radboudumc*
Dr. Paul Poyck, vaatchirurg, Radboudumc

11.15 "Het belang van anoniem contact"
Interactieve workshop over het schrijven van brieven van nierpatiënten aan nabestaanden van overleden donoren.
Willem Hordijk, orgaandonatie coordinator, Radboudumc, Nijmegen
Sabine Hopman, medisch maatschappelijk werker, Radboudumc, Nijmegen
Gerben van den Bosch, medisch maatschappelijk werker, Radboudumc, Nijmegen
Janneke Vervelde, verpleegkundig specialist, Leids Universitair Medisch Centrum

11.50 "Op zoek naar de juiste donor"
Presentatie en interactieve workshop over handleiding transplantatie met een gerichte altruïst
Gerben van den Bosch, medisch maatschappelijk werker, Radboudumc, Nijmegen

12.45 Pauze

Classroom 5 Preservation / perfusion

Voorzitters: *Dr. Jeroen de Jonge, chirurg, Erasmus MC*
Dr. Volkert Huurman, chirurg, LUMC

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

13.15 Clamping of cerebral circulation may improve left ventricular contractility after normorthermic regional perfusion after anoxic circulatory death in a porcine model (p. 75)
N.M. Moeslund[1], Z..L.. Zha Zhang[2], F.F.D. Dalsgaard[1], S.B. Bay[3], P.R. Ryhammer[4], L.I. Ilkjaer[5], M.P. Pedersen[6], M.E. Erasmus[2], H.E. Eiskjaer[7], [1]Dept. of Cardiology - Research, Aarhus University, Aarhus, Denemarken. [2]Dept. of cardiothoracic surgery, University Medical Centrer Groningen, Groningen, Nederland. [3]Comparative Medicine Lab, Institute for Clinical Medicine, Aarhus University, Aarhus N, Denemarken. [4]Dept. of Anesthesiology, Regionshospitalet Silkeborg, Silkeborg, Denemarken. [5]Dept. of cardiothoracic surgery, Aarhus University Hospital, Aarhus, Denemarken. [6]Comparative Medicine Lab, Institute for Clinical Medicine, Aarhus University, Aarhus, Denemarken. [7]Dept. of Cardiology, Aarhus University Hospital, Aarhus, Denemarken.

13.27 Case reports of ex situ heart perfusion in hearts donated following euthanasia (p. 76)
V. van Suylen[1], E.M. Bunnik[2], J.A.M. Hagenaars[3], I.A. Ertugrul[1], J.A.M Bollen[4], M.A. Mariani[1], M.E. Erasmus[1], [1]Cardiothoracale Chirurgie, UMC Groningen, Groningen, Nederland. [2]Medische Ethiek, Filosofie en Geschiedenis van de Geneeskunde, Erasmus MC, Rotterdam, Nederland. [3]Chirurgie, Erasmus MC, Rotterdam, Nederland. [4]Anesthesiologie, Radboudumc, Nijmegen, Nederland.

13.39 Prolonged normothermic machine perfusion of discarded human donor kidneys (p. 77)
A.S. Arykbaeva[1], D.K. De Vries[1], J.B. Doppenberg[1], V.A. Lantinga[2], L. Van Leeuwen[2], T.L. Hamelink[2], V.A.L. Huurman[1], R.C. Minnee[3], C. Moers[2], R.A. Pol[2], H.G.D. Leuvenink[2], R.J. Ploeg[1], I.P.J. Alwayn[1], [1]Dept. of Surgery, LUMC Transplant Center, Leids Universitair Medisch Centrum, Leiden, Nederland. [2]Dept. of Surgery, Universitair Medisch Centrum Groningen, Groningen, Nederland. [3]Dept. of Surgery, Erasmus Medisch Centrum, Rotterdam, Nederland.

13.51 Magnetic resonance imaging to assess renal flow distribution during ex vivo normothermic machine perfusion in porcine and discarded human kidneys (p. 78)
R Schutter[1], VA Lantinga[1], TL Hamelink[1], HGD Leuvenink[1], RJH Borra[2], C Moers[1], [1]Surgery, University Medical Center Groningen, Groningen, The Netherlands. [2]Radiology, University Medical Center Groningen, Groningen, The Netherlands.

14.03 Complement is activated during normothermic machine perfusion of porcine and discarded human kidneys (p. 79)
N.M. Jager[1], L.H. Venema[2], L. van Leeuwen[2], A. Arykbaeva[3], C. Moers[2], R. Pol[2], I. Alwayn[3], S.E. Pischke[4], H.G.D. Leuvenink[5], [1]Surgery, University Medical Center Groningen, Groningen, Nederland. [2]Surgery, Organ Donation and Transplantation, University Medical Center Groningen, Groningen, The Netherlands. [3]Surgery, Leiden University Medical Center, Leiden, The Netherlands. [4]Immunology and Clinic for Emergencies and Critical Care, Oslo University Hospital, Oslo, Noorwegen. [5]Organ Donation and Transplantation, University Medical Center Groningen, Groningen, The* Netherlands.

14.15 Validation of flavin mononucleotide (FMN) to monitor the quality of donor kidneys during hypothermic machine perfusion -with or without oxygen- in kidney transplantation (p. 80)
F.E.M. van de Leemkolk[1], L. Lo Faro[2], S. Saheed[2], J. Mulvey[2], V.A.L. Huurman[1], I.P.J. Alwayn[1], H. Putter[3], J.H.N. Lindeman[1], R.J. Ploeg[2], [1]Dept. of Surgery, Leiden University Medical Center, Leiden, The Netherlands. [2]Nuffield Dept. of Surgical Sciences, University of Oxford, Oxford, Verenigd Koninkrijk. [3]Dept. of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands.

Classroom 6 Rejection

Voorzitters: *Dr. Azam Nurmohamed, internist-nefroloog, Amsterdam UMC*
Dr. Jan-Stephan Sanders, internist-nefroloog, UMCG

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

13.15 Torque teno virus load kinetics as predictor for both allograft rejection, polyomavirus and cytomegalovirus infection in kidney transplantation; a cohort joint modelling study (p. 81)
AL van Rijn[1], HF Wunderink[2], IA Sidorov[1], CS de Brouwer[1], ACM Kroes[1], JW de Fijter[3], H Putter[4], APJ de Vries[3], JI Rotmans[3], MCW Feltkamp[1], [1]Medische Microbiologie, Leids Universitair Medisch Centrum, Leiden, Nederland. [2]Medische Microbiologie, Universitair Medisch Centrum Utrecht, Utrecht, Nederland. [3]Interne Geneeskunde, Leids Universitair Medisch Centrum, Leiden, Nederland. [4]Medische Statistiek, Leids Universitair Medisch Centrum, Leiden, Nederland.

13.27 Clinical and molecular profiling can help in predicting the response to alemtuzumab treatment in kidney transplant recipients with severe or glucocorticoid-resistant acute rejection (p. 82)
D.M. Peelen[1], M van de Zwan[1], M.C. Clahsen-van Groningen[2], D.A.M. Mustafa[2], C.C. Baan[1], D.A. Hesselink[1], [1]Interne geneeskunde-Nefrologie & Transplantatie, Erasmus MC, Rotterdam, Nederland. [2]Pathologie, Erasmus MC, Rotterdam, Nederland.

13.39 Evaluation study of protocol kidney transplant biopsies: the presence of subclinical rejection and its relationship to graft outcome (p. 83)
M.I.D. Pheifer[1], A.D. van Zuilen[1], B.J. Petri[2], T.Q. Nguyen[3], [1]Nephrology, University Medical Centre Utrecht, Utrecht, The Netherlands. [2]Dept. of Surgery, University Medical Centre Utrecht, Utrecht, The Netherlands. [3]Dept. of Pathology, University Medical Centre Utrecht, Utrecht, The Netherlands.

13.51 A single nucleotide polymorphism within the FCGR3A 158 F/V gene is associated with decreased survival of renal allografts with chronic active antibody-mediated rejection (p. 84)
N.H.R. Litjens[1], A.M.A. Peeters[1], J. Kal-van Gestel[1], M. Klepper[1], M.G.H. Betjes[1], [1]Inwendige Geneeskunde, Nefrologie en Transplantatie, Erasmus MC, Universitair Medisch Centrum, Rotterdam, Nederland.

14.03 Tocilizumab for the treatment of chronic-active antibody-mediated rejection: a case series (p. 85)
A.E. de Weerd[1], H. de Jong[2], M.M.L. Kho[1], J.I. Roodnat[1], M.G.H. Betjes[1] [1]Nephrology and Kidney Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands. [2]Pediatrics, dept. of Nephrology, Erasmus Medical Center, Rotterdam, The Netherlands.

14.15 Chronic allograft enteropathy treated with vedolizumab (p. 86)
G. Trentadue[1], G. Kats-Ugurlu[2], T. Blokzijl[3], J.W. Haveman[4], K.N. Faber[5], G. Dijkstra[1], [1]Gastroenterology and Hepatology, Universiteit Medisch Centrum Groningen, Groningen, Nederland. [2]Pathology and Medical Biology, Universitair Medisch Centrum Groningen, Groningen, Nederland. [3]Laboratory Medicine, Universitair Medisch Centrum Groningen, Groningen, Nederland. [4]Surgery, Universitair Medisch Centrum Groningen, Groningen, Nederland. [5]Laboratory Medicine, Gastroenterology and Hepatology, Universitair Medisch Centrum Groningen, Groningen, Nederland.

Classroom 7 Clinical - Surgical

Voorzitters: *Dr. Frank d'Ancona, uroloog, Radboudumc*
Michel van der Jagt, chirurg, Radboudumc

Voordrachten in het Engels, 8 minuten presentatie en 4 minuten discussie.

13.15 The non-muscle splitting mini-open donor nephrectomy is a safe alternative in the laparoscopic era of live kidney donation (p. 87)
L.J.M. Habets[1],V.A.L. Huurman[3], D. van der Helm[2], K. Ramdhani[3], A. Haasnoot[3], R.E. Dam[3], A.P.J. de Vries[2], A.E. Braat[3], J. Dubbeld[3], H.D. Lam[3], W.N. Nijboer[3], D.K. de Vries[3], I.P.J. Alwayn[3], A.G. Baranski[3], A.F.M. Schaapherder[3], [1]Division of Transplant Surgery, Dept. of Surgery, Leiden University Medical Center, Leiden, Nederland. [2]Division of Nephrology, Dept. of Internal Medicine, LUMC, Leiden, Nederland. [3]Division of Transplant Surgery, Dept. of Surgery, LUMC, Leiden, Nederland.

13.27 External ureteric stent or internal double J stent placement in renal transplantation: effect on the occurrence of urinary tract infections and urologic complications? (p. 88)
S.J.M. Middelkoop[1], I.T. Hazenberg[1], A.A.E. De Joode[1], J.D. Rabbeljee[1], R.A. Pol[2], J.S.F. Sanders[1], C.A. Stegeman[1], [1]Dept. of Internal Medicine, Division of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. [2]Dept. of Surgery, Division of Transplantation Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

13.39 Magnetic ureteral JJ stents in cadaveric kidney transplantation: initial results (p. 89)
J.L.Z. van der Kam [1], F.J. Bemelman[2], M.M. Idu[3], J.R. Oddens[4], [1]Urologie, Amsterdam UMC, locatie AMC, Amsterdam, Nederland. [2]Nefrologie, Amsterdam UMC, locatie AMC, Amsterdam, Nederland. [3]Vaatchirurgie, Amsterdam UMc, Amsterdam, Nederland. [4]Urologie, Amserdam UMC, locatie AMC, Amsterdam, Nederland.

13.51 Antithrombotic Management by European Kidney Transplant Professionals – A survey study (p. 90)
T.A.J. van den Berg[1], F.J.M.F. Dor[2], J.A. Lisman[1], S.J.L. Bakker[3], R.A. Pol[1], [1]Chirurgie, Universitair Medisch Centrum Groningen (UMCG), Groningen, Nederland. [2]Surgery & Cancer, Imperial College, London, Verenigd Koninkrijk. [3]Interne Geneeskunde - Nefrologie, Universitair Medisch Centrum Groningen (UMCG), Groningen, Nederland.

14.03 Donor lung clots and emboli: frequency, composition and estimated age (p. 91)
J.S. Bergtop[1], Z.L. Zhang[2], W. Timens[3], T. Lisman[4], M.E. Erasmus[2], C. van de Wauwer[2], L.H. Venema[4], C.T. Gan[1], E.A.M. Verschuuren[1], [1]Dept. of Pulmonary diseases and tuberculosis University Medical Centre Gron, Universitair medisch centrum Groningen, the Netherlands., Groningen, Nederland. [2]Dept. of Cardio-thoracic surgery, Universitair medisch centrum Groningen, the Netherlands., Groningen, Nederland. [3]Dept. of Pathology, Universitair medisch centrum Groningen, the Netherlands., Groningen, Nederland. [4]Surgical Research Laboratory, Dept. of Surgery, Universitair medisch centrum Groningen, the Netherlands., Groningen, Nederland.

14.15 Clinical experience with bariatric surgery prior to liver transplantation (p. 92)
T. Stilma[1], M. Kaijser[2], H. Blokzijl[3], L. de Heide[4], R.H.J. de Kleine[5], P. van Putten[6], F. Voogd[6], V.E. de Meijer[5], F.G.I. van Vilsteren[3], [1]MDL UMCG en Bariatrische chirurgie MCL, UMCG en MCL, Groningen, Nederland. [2]Centrum Obesitas Noord-Nederland / Chirurgie, Medisch Centrum Leeuwarden, Leeuwarden, Nederland. [3]MDL, Universitair Medisch Centrum Groningen, Groningen, Nederland. [4]Interne geneeskunde / Centrum Obesitas Noord-Nederland, Medisch Centrum Leeuwarden, Leeuwarden, Nederland. [5]HPB-chirurgie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [6]MDL, Medisch Centrum Leeuwarden, Leeuwarden, Nederland.

14.27 Modifying the RETREAT score to predict recurrence of hepatocellular carcinoma after liver transplantation: a focus on PIVKA-II, tumor differentiation grade and tacrolimus trough levels (p. 93)
M.J.C. Devillers[1], M.C.B. van Hooff[1], M.J. Sonneveld[1], P.A. Boonstra[1], M. Doukas[1], R.A. De Man[1], C.M. Den Hoed[1], [1]Maag-, Darm- en Leverziekten, Erasmus MC, Rotterdam, Nederland.

Plenair 4 Afsluiting

Voorzitter *Prof. dr. Luuk Hilbrands, voorzitter LOC*

14.45 Afsluiting in theatrale stijl

Nierkeuze.nl: A web based application to support the decision process for kidney replacement therapy based on outcome data

S.P. Berger[2], H. Peters Sengers[1], AW Gomes Neto[2], HGK Scholten-Gerben[2], H. Bart[3], M ten Dam[4], L Heuveling[4], A. Hemke[5], C. Konijn[5], J.H de Ruiter[6] [1]Center for Experimental and Molecular Medicine, Amsterdam UMC, Amsterdam, The Netherlands. [2]Interne Geneeskunde-Nefrologie, UMCG, Groningen, The Netherlands. [3]Nierpatiënten Vereniging Nederland, Bussum, The Netherlands. [4]Nefrovisie, Utrecht, The Netherlands. [5]Nederlandse Transplantatie Stichting, Leiden, The Netherlands. [6]Hanzehogeschool, Groningen, The Netherlands.

Background: The decision process for kidney replacement therapy is complex, ranging from peritoneal and hemodialysis to transplantation with a kidney from a living or deceased donor including the option to accept an elderly deceased donor in the case of eligible elderly recipients. We aim to develop and implement a personalized data driven decision support tool incorporating basic patient characteristics and treatment options.
Methods: Consecutive Dutch patients above 18 years of age with end-stage-renal-disease (ESRD) who were registered for a first transplantation and started renal replacement therapy between 2000 and 2019 were included from the national registry databases RENINE and NOTR. In a subset of patients, SF 12 quality of life data was obtained from RENINE for waitlisted dialysis patients and from the local database for transplant patients. Several algorithms were developed for various treatment options according to factors that are known at ESRD (i.e. age, sex, blood group, underlying kidney disease). Quantile regression analysis was used to predict waiting time and components of the SF-12 quality of life survey. Multistate survival analysis was used to predict patient survival, with transplantation handled as intermediate event. Cox regression was used to predict death-censored graft survival. This is currently being implemented in a web application in collaboration with an ICT company with testing and input from patients and kidney professionals.
Results: We analyzed data from 14.953 renal transplant candidates who were wait-listed and started renal replacement therapy. Of these candidates, 6346 received a living donor transplant and 5100 received a deceased donor transplant. Of the deceased donation group, 813 kidneys were allocated by the Eurotransplant senior program. SF12 quality of life of 513 waitlisted patients on dialysis was compared with 1042 transplanted patients. The most recent version of the decision tool will be presented with an overview of the first experiences in the local implementation in the renal failure clinic.
Conclusions The decision process for renal replacement therapy should include solid information incorporating both qualitative and quantitative data that is tailored to the individual patient and presented in an accessible form. The nierkeuze.nl decision tool will help to inform patients and potential living donors by making outcome data available in a personalized fashion.

A Clinical Comparison of Two Different Oxygen Carriers For Combined Hypothermic and Normothermic Machine Perfusion of High-risk Donor Livers

O.B. van Leeuwen[1], Bodewes SB[1], M.P.D. Haring[1], I.M.A. Brüggenwirth[1], V.A. Lantinga[1], A.M. Thorne[1], A.P. van den Berg[2], M.T. de Boer[1], R.H.J. de Kleine[1], T. Lisman[1], Y. de Vries[2], V.E. de Meijer[1], R.J. Porte[1], [1]Afd. Chirurgie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [2]Afd. Maag, darm, en leverziekten, Universitair Medisch Centrum Groningen, Groningen, Nederland.

Background: Ex-situ normothermic machine perfusion (NMP) is increasingly used for pretransplant viability assessment of high-risk donor livers. A short period of hypothermic oxygenated machine perfusion (HMP) prior to NMP reduces ischemia-reperfusion injury during NMP. Excellent results have been reported after combined HMP and NMP, using a single perfusion solution containing an hemoglobin-based oxygen carrier (HBOC). We aimed to determine whether similar results can be obtained with a perfusion solution containing red blood cells (RBC) instead of HBOC.
Methods: In a prospective observational cohort study, sequential HMP and NMP was applied in 49 nationwide discarded donor livers in the Netherlands (2017-2020). The first 18 procedures were part of a prospective clinical trial with a HBOC-based perfusion solution for both HMP and NMP (www.trialregister.nl; NTR5972). The subsequent 31 procedures were performed using Belzer Machine Perfusion Solution (MPS) for HMP, followed by an RBC-based perfusion solution for NMP. A post-hoc comparison was performed with all regular (non-perfused) donation after circulatory death (DCD) livers transplanted in our center between 2010-2020 (n=73). Continuous variables were presented as median with interquartile range (IQR) and compared with MannWhitney test. Categorical variables were compared using Chi-squared test. One-year graft and patient survival were analyzed using Kaplan-Meier method with log rank test.
Results: Donor baseline characteristics were similar between the HBOC (n=18) and RBC (n=31) group. All but two livers were derived from DCD donors, with a median donor risk index of 2.83 (IQR 2.51 -3.09) and median donor age of 63 years (IQR 53-71). After viability assessment during NMP, 12 livers in the HBOC-group were transplanted versus 17 in the RBC-group (utilization rate 67% versus 55%, P=0.42). One-year graft and patient survival were 92% and 100% in the HBOC-group versus 94% and 100% in the RBC-group, resp. (P=0.96 and P=1.00). Post-transplant cholangiopathy occurred in one patient (3%). A post-hoc comparison of all transplanted HMP-NMP livers (n=29) with a contemporary comparator cohort of regular DCD liver transplants (n=73) revealed similar one-year graft survival rates (93% versus 80%, p=0.13) and a lower rate of posttransplant cholangiopathy after HMP-NMP (3% versus 27%, p<0.01).
Conclusions: Ex-situ machine perfusion using sequential HMP-NMP for resuscitation and viability assessment of high-risk human donor livers results in excellent transplant outcomes, irrespective of the type of oxygen carrier used.

Blockade of the IL-21 Pathway: A New Perspective for the Treatment of T and B cell Mediated Allogeneic Responses after Transplantation

C.C. Baan[1], K. de Leur[1], M.J. Hoogduijn[1], D.A. Hesselink[1], [1]Internal Medicine, Erasmus MC, Rotterdam, The Netherlands.

Background: IL-21 is a T cell growth factor for and secreted by Th17 and T follicular helper (Tfh)-cells. This cytokine has pleiotropic effects on a broad range of immune cells. It regulates CD8+ T cell expansion and their effector functions, and is crucial for T cell-dependent B cell differentiation of antigen-activated B cells into antibody-producing plasma cells. However, little is known about IL21 mediated T and B cell responses in alloreactivity after transplantation.
Methods: First, we explored the actions of IL-21 in alloreactive T cell proliferation and cytotoxicity in mixed lymphocyte reactions. Second, to test the role of IL-21 producing Tfh cells in the regulation of B cells in an alloantigen-driven setting, we performed co-culture experiments of transplant recipient Tfh cells and B cells that were stimulated with donor antigen. Third, the effect of an aIL-21R blocking antibody on the early phase of allograft rejection was studied in a humanized skin transplantation model in mice reconstituted with human T and B cells.
Results: Alloactivated T and B cells highly express IL-21R. In the presence of IL-21, a marked increased proliferative response of alloactivated T cells was found. Also, the expanded CD8+ T cells had significant cytolytic functions, while blockade of the IL-21 route by an aIL-21R antagonist inhibited the proliferation of alloactivated T-cells. Next, we determined the role of IL-21 in T cell dependent B cell responses. Donor antigen stimulation of the co-cultured Tfh – B cell initiated expression of the activation markers ICOS and PD-1 on Tfh cells with a shift toward a mixed Tfh2 and Tfh17 phenotype. The alloantigen activated memory B cells underwent class switch recombination and differentiated toward IgM- and IgG-producing plasma blasts. Anti-IL-21R antagonists significantly inhibited B cell differentiation. Finally, in the humanized mouse skin transplant model, in mice treated with the aIL-21R antagonist reduced signs of alloreactivity were measured including significantly less CD4+ and CD8+ T and B cell infiltration and less expression of inflammatory markers Keratin 17 and Ki67.
Conclusions: These findings suggest that 1) IL-21 is crucial for both T cell and B cell-dependent allogeneic immune responses, and 2) treatment with IL-21R antagonists may ameliorate these anti-donor responses after transplantation.

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

A.E. de Weerd[1], M.J. Verschragen[1], J.A. van Gestel[1], D.L. Roelen[2], M. Dieterich[1], M.G.H. Betjes[1] [1]Nephrology and Kidney Transplantation, Erasmus Medical Center, Rotterdam, The Netherlands. [2]HLA Laboratory, dept. of Immunology, Leiden University Medical Center, Leiden, The Netherlands.

Background: Malignancy and infection are major causes of death with a functioning kidney graft and therefore contribute significantly to overall graft loss. To diminish these complications, it is key to lower the immune suppression when possible. For this reason we have performed a randomized-controlled trial to evaluate the safety of tacrolimus monotherapy in immunologically low-risk kidney transplant recipients [NTR4672, www.trialregister.nl].
Methods: Inclusion criteria were HLA mismatches 3 or lower, peakPRA 4% or lower, and the absence of an immunological disease. After a run-in period of six months after transplantation, recipients were randomized if the following critera were met: eGFR >30 ml/min, proteinuria <50 mg/mmol, no BPAR after three months, and no lymphocyte depleting therapy. Recipients were randomized to either receive standard TAC/MMF or to taper and discontinue MMF at month 9 (TACmono). Advagraf target trough levels were 5-8 ug/L in both groups.
Results: Between March 2015 and October 2018, 79 recipients were randomized to either TACmono (n=38) or TAC/MMF (n=41). Mean recipient age was 59, 37% were ≥65 years of age and 59% received a living donor transplant. After randomization and at a median follow-up of 45 months, 3 TACmono and 4 TAC/MMF recipients experienced BPAR. One graft loss occurred in the TACmono group (month 35, chronic prostatitis and borderline rejection), and 2 in the TAC/MMF group (mixed Banff IIA/ antibody-mediated rejection due to non-adherence at month 28, and one Banff IIA vascular rejection at month 35). Three TACmono recipients died of respectively stomach carcinoma, pulmonary carcinoma and sepsis due to diabetic ulcers 19, 22 and 32 months after transplantation. Three TAC/MMF recipients died of respectively pneumonia, sudden cardiac death and liver cirrhosis 35, 42 and 48 months after transplantation. Kidney function did not differ with eGFR 57.6 (SEM 3.6) versus 52.2 (SEM 2.5, p 0.22) ml/min, and proteinuria 19.8 (SEM 2.6) versus 17.2 (SEM 2.9, p 0.51) mg/mmol in respectively TACmono vs TAC/MMF at last follow-up. Luminex screening did not detect any HLA-antibodies in both groups 15 months after transplantation. Tacrolimus trough levels were 6.5 and 6.3 ug/L in TACmono vs TAC/MMF at month 15.
Conclusions: Tacrolimus monotherapy does not increase the risk of rejection or graft loss in immunologically low-risk kidney transplant recipients. Weaning to tacrolimus monotherapy between six and nine months after transplantation, can be considered a safe strategy.

Oxygenated versus non-oxygenated flush out and storage of DCD porcine livers - A proof of concept study

R.J. Porte[1], I.M.A. Brüggenwirth[1], W.S. van der Plas[1], O.B. van Leeuwen[1], A.M. Thorne[1], M. Rayar[2], V.E. de Meijer[1], [1]Chirurgie, Universitair Medisch Centrum Groningen, Groningen, Nederland. [2]Chirurgie Hepatobiliaire et Digestive, Centre Hospitalier Universitaire de Rennes, Rennes, Frankrijk.

Background: In donation after circulatory death (DCD) donor procedures, hepatic adenosine triphosphate (ATP) levels are rapidly depleted due to warm ischemia sustained during the agonal phase, the time between cardiac arrest and flush out, and hepatectomy. ATP levels are further depleted during static cold storage (SCS). This study sought to investigate a simple and cheap approach to prevent ATP depletion and subsequent ischemia-reperfusion injury using a porcine liver reperfusion model.
Methods: After 30 min warm ischemia, porcine livers were flushed via the portal vein with cold (◦4C) non-oxygenated University of Wisconsin (UW) solution by gravity (n=6, control) or with cold oxygenated UW using a pressure-controlled perfusion device with the pressure set to 5 mmHg (n=6, OxyFlush). Livers were then subjected to 4 hr SCS in non-oxygenated (control) or oxygenated (OxyFlush) UW, followed by 4 hr normothermic reperfusion using autologous whole blood. ATP levels were compared and hepatobiliary function and injury was assessed.
Results: Hepatic ATP depletion was slightly less in the OxyFlush group compared to the control group (median of 0.26 µmol/g protein at the end of SCS corrected for baseline vs. -0.68 µmol/g protein, P = 0.045). After 4 hr normothermic reperfusion, ATP levels were similar in both groups. All livers produced bile and cleared lactate, and there were no differences between the groups. Grafts in the OxyFlush group had lower blood glucose levels throughout the reperfusion period, which was significant after 3 hr (P = 0.045). Bile composition, a marker for biliary function, was not different between the groups in terms of pH, glucose and bicarbonate levels. Alanine aminotransferase and lactate dehydrogenase levels in the SCS solution and during reperfusion were not different between the groups.
Conclusions: Oxygenated flush out and storage of DCD porcine livers slightly improves ATP preservation, but this does not seem sufficient to mitigate ischemia-reperfusion injury.

The effects of oxygen level during normothermic regional perfusion after circulatory death in a porcine model

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Background: Heart transplantation from circulatory dead donors is emerging. In situ thoracoabdominal regional perfusion is a method to perfuse and evaluate the hearts after circulatory death. There are conflicting results regarding oxygenation during resuscitation from cardiac arrest and speculations that high oxygenation may increase reactive oxygen species formation. The purpose of this study was to investigate the impact of high versus low oxygenation during normothermic regional perfusion (NRP) after anoxic circulatory death on donor heart contractility in a porcine model.
Methods: The animals were anaesthetized, pressure-volume catheters were placed in both ventricles and a pulmonary artery catheter was inserted percutaneously. Through a midline sternotomy, the heparinized animals were cannulated for extracorporeal circulation. Baseline data were obtained. Mechanical ventilation was withdrawn. After 15 minutes of warm ischemia, the aortic arch vessels and infrarenal aorta were clamped before NRP was commenced using a standard heart-lung machine. The animals were randomized to receive either FiO2 of 1.0 (HOX) or 0.21 (LOX) with a gradual increase to 0.40 during NRP. The NRP flow-protocol includes early volume loading of the right ventricle and gradual wean over 35 minutes. Dobutamine and norepinephrine infusions were started during NRP for haemodynamic support. The animals were observed for 180 minutes after NRP with repeated measurements of cardiac function and biochemistry.
Results: 15 of 19 animals were successfully weaned from NRP; 8/9 in the HOX and 7/10 in the LOX group, ($p = 0.58$). All weaned animals displayed acceptable cardiac function during the observation period and sustained a mean arterial pressure >60 mmHg with low filling pressures and cardiac index >2.5 L/min/m^2. The preload independent end-systolic pressure-volume relationship as an index of contractility was preserved in both groups. The HOX RV contractility was higher than the LOX group ($p=0.035$), and not significantly in the LV ($p=0.37$) (Fig. 1). Biochemistry showed lower lactate levels in the HOX group. There was no difference in norepinephrine requirement between groups.
Conclusions: There were minimal haemodynamic and biochemical differences between the groups as all weaned animals demonstrated acceptable cardiac function. The high oxygenation group showed marginally better cardiac performance and lower lactate concentrations.

The effect of different hematocrit levels during normothermic reperfusion of porcine DCD kidneys on renal function and metabolism

T.M. Huijink[1], L.A. van Furth[1], A. Lammerts[1], H. Maassen[1], S.P. Berger[2], H.G.D. Leuvenink[1], L.H. Venema[1], [1]Chirurgie, UMC Groningen, Groningen, Nederland. [2]Nefrologie, UMC Groningen, Groningen, Nederland.

Background: Normothermic machine perfusion (NMP) is a relatively new technique for pre-transplant preservation, assessment and conditioning of marginal donor kidneys. An adequate oxygen supply during NMP is required to maintain renal metabolism. The optimal conditions in terms of sufficient oxygen supply during NMP are not established yet. This study aims to evaluate the effects of different hematocrit levels on oxygen consumption, renal sodium handling and energy production during ex vivo kidney NMP.
Methods: Porcine kidneys obtained from an abattoir were subjected to 35 minutes of warm ischemia. Thereafter, the kidneys were preserved with oxygenated hypothermic machine perfusion for 3 hours. Subsequently, they were reperfused for 4 hours in a normothermic, pressure-controlled, set up with an autologous blood-based solution containing either 12% (2 mmol/L; n=6), 24% (4,5 mmol/L; n=6) or 36% hematocrit (7 mmol/L; n=6). Oxygen consumption, fractional sodium excretion and creatinine clearance were measured. Adenosine triphosphate (ATP), lactate dehydrogenase (LDH) and aspartate aminotransferase (ASAT) analysis were performed.
Results: Total oxygen consumption was highest in the 36% hematocrit group and significantly higher compared to the 12% hematocrit group (p=0.001). However, no differences in kidney function by means of creatinine clearance or fractional sodium excretion levels were observed. Other metabolic parameters, among ATP levels, metabolic coupling, lactate and pH were similar in all three groups. Furthermore, no differences in injury markers such as LDH and ASAT were seen.
Conclusions: Low hematocrit levels during NMP are associated with lower total oxygen consumption by the kidney. However, no signs of (mitochondrial) malfunction or additional injury are seen in the low hematocrit group, indicating either reduction in metabolic rate or higher efficiency. The increased oxygen consumption in the 36% group did not result in improved function, indicating that other oxygen consuming processes are responsible for the higher consumption. Whether low hematocrit levels are associated with renal injury needs further evaluation.

Challenges using banked red blood cells for oxygen delivery during normothermic machine perfusion of donor kidneys

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Background: Ex situ normothermic machine perfusion (NMP) is a new opportunity to assess high risk deceased donor kidney grafts and to facilitate prolonged organ preservation. Successful implementation of organ perfusion critically relies on adequate nutrient and oxygen delivery. For the latter, banked red blood cells (BRBCs) are often used as an oxygen carrier in the perfusate. Clinical studies imply reversible loss of function with gradual recovery following transfusion. Despite the increasing interest in NMP, comparatively little attention has been paid to the functional aspects of BRBCs. Therefore, the aim of this study was to assess oxygen delivery during prolonged renal NMP using BRBCs.
Methods: Discarded deceased donor kidneys (n=24) were perfused in a closed system at 37°C for 6hrs with a BRBC-based perfusion solution with RBCs stored for 2-30 days. Sequential arteriovenous perfusate samples were collected which allowed measurements of free hemoglobulin (fHb), a sign of hemolysis, and blood gas analyses at each hour after start of perfusion.
Results: Striking is the observation of a large and significant arterio-venous pO2 difference in perfusate during 6hrs perfusion (hourly average: paO2 73.8±6.8 kPa vs. pvO2 20.7±8.6 kPa, p<0.05). Yet, while under physiologic conditions the hemoglobin saturation drops to ~80% in venous outflow [1], Hb saturation did not drop significantly after passing the kidney on NMP (hourly average: saO2 99.0±0.7% vs. svO2 95.6±4.8%, p=0.06). NMP conditions were further associated with significant hemolysis: mean Hb in perfusate was 5.3±0.4 mmol/l at 0h and 4.5 mmol/l after 6 hours. fHb increased steadily from 7.3±3.0 µmol/L to 49.1±20.2 µmol/L. Additionally, we observe a significant increase in lactate throughout the perfusion (t=0hr 5.1±0.6 mmol vs. t=6hrs 16.0±2.8 mmol).
Conclusions: During storage, RBCs undergo changes that affect both quality and function, such as decreased adenosine triphosphate (ATP) and 2,3-diphosphoglycerate (2,3-DPG) levels and accumulation of released lactate and K^+[2]. Although the latter was easily overcome by washing RBCs with an autologous cell salvage system, we postulate that the BRBCs used in the perfusate are not functioning optimally to deliver oxygen. This is reflected by the proportionally large amount of O2 that was delivered to the kidney by diffusion from unbound O2, whereas the HbO2 did not contribute as much as would have been expected. Both the freeHb and lactate produced by the RBCs can become a strain for prolonged NMP. Our future studies will focus on rejuvenating RBCs to improve their oxygen transport and diminish hemolysis.

Rescue of declined extended criteria DCD livers using in-situ normothermic regional perfusion (NRP)

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Background: In donation after circulatory death (DCD), the combination of donor risks, such as high age or high BMI, with the uncontrolled organ injury during the agonal phase makes the quality of these organs unpredictable. To prevent primary graft dysfunction and late biliary complications, livers from DCD are often declined. Normothermic regional perfusion (NRP) is an oxygenated normothermic perfusion technique, in which the abdominal compartment of the donor is perfused. Macroscopic appearance and liver enzyme levels are used to determine "transplantability". Our aim was to investigate if DCD liver grafts, declined by all three Dutch liver transplant centers according to normal acceptance criteria, could be functionally evaluated with NRP and successfully transplanted. Methods: Between 01-10-2018 and 01-11-2020, NRP was offered to a subgroup of DCD donors outside regular liver acceptance criteria. After the donor agonal phase, in the operation room the abdominal compartment of the donor was connected to an extra corporeal membrane circuit and perfused for two hours. Liver grafts were accepted for transplantation when ALT levels did not exceed the level of 200U/l, glucose was produced, lactate decreased during perfusion and macroscopic appearance of the graft was good. Continuous variables are presented as median with interquartile range. Results: In total 35 potential DCD grafts were offered for NRP, one donor had a premature cardiac arrest. Of the 34 donors after withdrawal of life support treatment, 22 cases had circulatory arrest and NRP was started. 13 liver grafts were transplanted resulting in an organ utilization rate of 59%. Reasons for decline after NRP were high ALT levels (N=5), unsuccessful perfusion (N=3) and presence of malignancy in the donor (N=1). The main differences during NRP between the transplanted grafts and the non-transplanted grafts were ALT levels (51 (34-56) U/l vs. 236 (77-397 U/l; p=0.017)) and glucose levels in perfusate (11.3 (9.7-12.8) mmol/l vs. 18.9 (14-22.1 mmol/l; p=0.006)). All 13 transplanted grafts showed immediate function post-transplantation. The median Intensive care and hospital stay was 2 (1-3) days and 12 (11-18) days. Both patient and graft survival at 6 months after transplantation was 100%.
Conclusions: Implementation of NRP for DCD liver grafts was successful. Functional assessment criteria proved safe to evaluate liver function during NRP and allowed to transplant 13 declined livers successfully.

Outcome of kidney transplantation after in-situ normothermic regional perfusion (NRP) of extended criteria donors is comparable to matched controls

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Background: Normothermic regional perfusion (NRP) is an increasingly used preservation method in donation after circulatory death (DCD). Immediate restoration of oxygenated normothermic perfusion in the donor abdomen by an extracorporeal membrane circuit offers potential advantages for improvement of organ quality and assessment of suitability for transplant. Whereas the potential benefit of NRP for liver transplantation has become increasingly clear in the literature, the effect on extended criteria donor kidney transplantation is not yet clarified. This study aimed to study outcome and safety of NRP in extended criteria donors compared to matched controls.
Methods: In 2018, NRP was introduced in a subgroup of extended criteria DCD donors in the Western part of the Netherlands. In the operation room the abdominal compartment of the donor was connected to an extra corporeal membrane circuit and perfused for two hours; after procurement, standard hypothermic machine perfusion of the kidneys was performed. Outcome of kidney transplants from these donors was compared to outcome of a matched group of donors from other parts of the Netherlands, not receiving NRP, using the same criteria on age (>60 yrs) and initial organ acceptance.
Results: NRP was performed in a total of 21 donors. 4 kidneys were declined during or after the NRP procedure. Follow up data was available of all 38 kidneys, transplanted in 37 recipients due to one case of en-bloc transplantation. 131 standard DCD kidney recipients were included in the control cohort. Donor characteristics were comparable between the groups except for a lower BMI (22.8 ± 3.0 vs. 25.6 ± 3.6, p=0.002) and longer 1st warm ischemia time in NRP donors due to the cannulation process (23.8 vs. 16.9 minutes, p=<0.001). PNF rate was comparable (8.1 vs. 8.4%, p=0.572). Rejection rates were also comparable (29.7 vs. 20.6%, p=0.087). A trend was observed towards a higher rate of DGF in NRP recipients (48.6 vs. 32.8%, p=0.121). 6 month graft survival was comparable between NRP and non-NRP donors (81 vs. 82%, p=0.77).
Conclusions: NRP donation in extended criteria DCD donors led to results comparable to a matched control group. Survival rates are in the expected range for this donor type. A trend towards higher DGF rate was observed after NRP, which may be explained by higher first WIT or by incomplete reporting of DGF in control data. In conclusion, NRP can be executed in this donor population without significant effect on kidney transplant outcome while offering the possibility of increased utilization of other abdominal organs.

Combining existing models and recent data into an up-to-date prediction model for evaluating kidneys from older deceased donors: development and external validation study.

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Background: With a rising demand for kidney transplantation, reliable pre-transplant assessment of organ quality becomes top priority. In clinical practice, physicians are regularly in doubt whether suboptimal kidney offers from older donors should be accepted. Multiple models that predict kidney graft survival prior to transplantation are available. These models have predominantly been developed on US data and include young donors for which the decision to accept or decline is of little concern. The aim of the current study was to externally validate existing prediction models in a European population of older deceased donors, as well as develop and externally validate a new adverse outcome (AO) prediction tool.
Methods: Recipients of kidney grafts from deceased donors ≥50 years were included from the Dutch and United States organ transplant registry (NOTR and OPTN database) from 2006-2018. Firstly, seven existing graft survival models were validated in these cohorts. Subsequently, new AO models were developed. The predicted AO was a composite of graft failure, death or CKD stage 4+ within 1 year after transplantation, modelled using logistic regression. Candidate predictors were selected based on existing literature and predictor ranking by an expert panel of 10 nephrologists. Three logistic regression models were developed: a full, backward selection and expert opinion model. The AO models were internally, temporally and externally validated by assessing discrimination and calibration.
Results: The NOTR development cohort contained 2510 patients and 823 events. The temporal validation NOTR had 837 patients with 230 events and the external validation OPTN 31987 patients with 6758 events. The existing 7 models showed poor discrimination with a mean C-statistic of 0.57 (standard deviation 0.02). Discrimination of our AO models was moderate in external validation with C-statistics of 0.63, 0.62 and 0.62 for the full, backward selection and expert opinion model, respectively. The AO models' calibration was highly accurate.
Conclusions: Existing kidney graft survival models performed poorly in a population of older deceased donors. To improve upon existing models a broader outcome definition and the newest methodological recommendations were employed in the development and external validation of novel AO models. Though the adverse outcome models had a moderate discrimination, they were more accurate than existing models and may assist clinicians in deciding whether to accept a kidney from an older deceased donor.

Donation after Circulatory Death kidney transplantation has equal long-term graft and patient survival as Donation after Brain Death: a systematic review and meta-analysis

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Background: Donation after circulatory death (DCD) kidney transplantation has been introduced to address organ shortage. However, DCD kidneys are not accepted worldwide due to concerns about their quality. To investigate whether these concerns are justified, outcomes after DCD kidney transplantation compared to donation after brain death (DBD) kidney transplantation were investigated by performing a systematic review and meta-analysis. The primary outcome was graft survival. Secondary outcomes were the risk of primary non-function (PNF), delayed graft function (DGF), biopsy-proven acute rejection (BPAR) within 3 months after transplant, 1-year estimated Glomerular Filtration Rate (eGFR), patient survival, and risk of urologic complications.
Methods: EMBASE, Medline (OVID), Cochrane, Web of Science and Google Scholar (200 top ranked) databases were searched for studies published until September 15th, 2020. Studies comparing DCD to DBD for any of the outcomes of interest were included. Exclusion criteria were: studies using normothermic machine perfusion or regional perfusion and studies exclusively reporting on pediatric/dual kidney transplants. The quality of individual studies was assessed using the Newcastle-Ottawa scale.
Results: 1808 original studies were found, 50 studies were finally included . The risk of 1-year all-cause graft loss was increased in DCD recipients compared to DBD recipients (risk ratio (RR) 1.13 (95%-confidence interval (CI) 1.08 to 1.19)), while 5-year and 10-year risk of all-cause graft loss was similar (RR 1.03 (95%-CI 0.97 to 1.10) and RR 1.03 (95%-CI 0.94 to 1.13), respectively). The risk of 1-year death-censored graft loss was higher in DCD recipients (RR 1.10 (95%-CI 1.04 to 1.16), while the 5-year (RR 0.99 (95%-CI 0.95 to 1.02) and 10-year risk (RR 1.02 (95%-CI 0.92 to 1.13) were similar. DCD recipients had a higher risk of PNF (RR 1.52 (95%-CI 1.19 to 1.94)) and DGF (RR 2.02 (95%-CI 1.88 to 2.16)). The risk of BPAR was not significantly different (RR 1.09 (95%-CI 0.96 to 1.23)). One-year eGFR was similar with a mean difference of -1.58 (95%-CI -4.08 to 0.91). One-year mortality risk was increased in DCD recipients (RR 1.10 (95%-CI 1.01 to 1.21), while the 5-year and 10-year mortality risk were similar to DBD. The risks of ureter leakage and stenosis were not significantly different.
Conclusions: DCD kidney transplant recipients have similar long-term graft and patient survival as DBD recipients, despite a higher risk of PNF, DGF and a 10% higher risk of mortality in the first year. These results should encourage implementation of DCD programs worldwide to increase the donor pool.

Donor factors only marginally impact short-term outcomes in kidney transplantation. Results from nationwide paired-outcome analyses.

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Background: In an era of pressing donor shortages and progressive reliance on extended criteria donors, there is an increased dependency on donor characteristics-based algorithms in the allocation process. Yet, it is consistently concluded that the performance characteristics of the algorithms are moderate at max. While this may reflect incomplete imputation of relevant donor aspects, it may also indicate that donor factors impact transplant outcomes to a limited degree. In this study we therefore aim to evaluate the impact of donor factors on kidney transplantation outcomes.
Methods: An instrumental variable analysis based on registry data for all kidney donor pairs separately transplanted into two recipients was performed. This study included the national registry data for all donor pairs transplanted in the Netherlands (1990-2018, 2187 pairs) and the United Kingdom (2000-2018, 10,175 pairs). The focus of the study was on early graft loss (EGL, i.e. all death-censored graft losses occurring within 90-days of transplantation) as this represents the most unambiguous short-term outcome measure.
Results: Overall EGL rates for the Dutch and UK cohorts were 7.9% and 6.6%, and the incidences of congruent EGL 1,2 and 1.1% respectively, these incidences were 2.3 and 2.9-fold higher than the anticipated arithmetical (stochastic) incidences. Although these data confirm an impact of donor-factors on incident EGL, the large majority of EGLs (>80%) were non-concordant. An impact of donor factors was further explored by comparing outcomes for functional grafts for which the contralateral graft was lost due to EGL with symmetrically functional grafts. Survival analysis showed similar recipient survival, but marginally impaired graft survival (Exp(B) 1.160 (95% CI: 1.002-1.343), P<0.046) for grafts in the asymmetrical outcome group. One- and 5-years eGFRs were respectively slightly impaired (OR: 1.017 (1.010-1.025), P<0.0001) and equal (1.000 (0.994-1.007)).
Conclusions: This analysis implies that donor factors of grafts accepted for transplantation minimally impact transplant outcome. A strong focus on donor characteristics or donor risk indices of grafts deemed acceptable for transplantation may result in an unjustified decline or discard of viable organs.

Counselling on Conceiving: Considerations of Professionals in Transplantation

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Background: Pregnancy after kidney transplantation (KT) conveys higher risks of adverse pregnancy outcomes (APO). In the Netherlands approximately 10 women are pregnant after KT each year. Guidelines and consensus statements sketch ideal circumstances for pregnancy after KT. Little is known about pre-pregnancy counselling after KT in the Netherlands, especially in less ideal situations. The PARTOUT (Pregnancy After Renal Transplantation OUTcomes) network aims to improve (pre) pregnancy care after KT and therefore wanted to gain understanding of the current status on pre-pregnancy counselling in the Netherlands.
Methods: A cross-sectional survey on pre-pregnancy counselling after KT was conducted between March and July 2020. This web-based survey consisted of socio-demographic and general questions on counselling, and 5 clinical vignettes were presented. These vignettes were based on known risk factors for APO after KT such as proteinuria, hypertension and poor kidney function. The survey was distributed by email from the PARTOUT network to nephrologists and gynecologists in the Netherlands. Positive versus negative attitudes towards pregnancy after KT were examined per vignette, including factors influencing this attitude and estimation of outcomes.
Results: 46 professionals participated: 16 (35%) gynecologists and 30 (65%) nephrologists. 25 (54%) participants work in an academic hospital. Participants had median experience in KT of 10 years. One third of the participants had no experience in treating pregnant KT recipients. 61% of the participants felt a very large responsibility for the decision to become pregnant after KT. 100% consensus on a positive pregnancy advice was only achieved in the vignette with good kidney function, good blood pressure and no proteinuria. In the vignettes where only one of these three risk factors were present, the advice on pregnancy was mixed, although the majority was positive. In general nephrologists had a more negative attitude towards pregnancy than gynecologists.
Conclusions: Generally, pregnancy after KT is positively reviewed, even in less ideal situations. Most important factors influencing advice were pre-pregnancy kidney function, proteinuria and blood pressure. Although pregnancy after KT is rare, it is important that woman after KT receive good quality counselling. Therefore, expert opinion consensus statements to inform specialists are needed. Furthermore, referral to teams with experience could improve care in these high- risk pregnancies.

Circulation and hemodynamics in living donation of kidney transplantation in children - The child-kitc study: magnetic resonance - arterial spin labeling perfusion imaging in pediatric ktx

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Background: In pediatric kidney transplantation, adequate perfusion of an adult-sized renal graft demands significant hemodynamic changes in young recipients. (Relative) hypoperfusion can shorten graft survival by loss of kidney mass and function, especially in cases of donor-recipient size mismatch. In order to adequately perfuse the transplanted adult-sized kidney, young recipients are hypothesized to develop a supraphysiological hemodynamic state, preventing long term ischemic tissue damage. Our primary objective is to enhance knowledge and insight in hemodynamic response after pediatric kidney transplantation with a living, adult donor. By combining Magnetic Resonance – Arterial Spin Labeling (MR-ASL) and transabdominal ultrasound (US), our secondary objective is to investigate the reliability of non-invasive imaging techniques in monitoring donor kidney perfusion after transplantation.
Methods: Twenty children (including donors) with a maximum age of 15 and a maximum body weight of 40 kg will be included in this prospective clinical pilot study with a follow-up of 12 months. Peri-operative hemodynamic monitoring includes blood pressure and invasive cardiac output measurements. We measured volume of the renal graft (MR), whole organ kidney perfusion (MR-ASL) and afferent blood flow (US and MR) before, during and 6 months after transplantation. We present the first three patients with complete series of imaging in follow up.
Results: MR-ASL perfusion imaging yields good quality images and reproducible perfusion values. Renal graft volumetrics and flow measurements using US and MR are corresponding, and in line with our hypotheses. All transplanted kidneys showed a considerable decrease in perfusion as compared to pre-operative baseline measurements in donors (mean: 407 ml/min vs. 161 ml/min), and a subsequent compensatory increase after 6 months (mean: 161 ml/min vs. 233 ml/min). No regional perfusion deficits were detected.
Conclusions: In pediatric kidney transplantation with an adult living donor, whole organ renal graft perfusion showed a considerable decrease after transplantation. At 6 months, graft perfusion recovered partially, demonstrating a significant increase in kidney perfusion as compared to post-operative measurements. Complementing current monitoring techniques, MR-ASL proves to be a feasible non-invasive peri-operative imaging technique, yielding reproducible perfusion values and good quality images.

Systematic screening for diabetes and pre-diabetes post-heart transplantation

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Background: Post-transplant diabetes mellitus (PTDM) is a frequent complication post-heart transplantation (HT). Moreover, PTDM has been associated with cardiovascular adverse events long-term post-HT. The golden standard to diagnose PTDM is an oral glucose tolerance test (OGTT). Studies investigating the incidence of PTDM long-term post-HT are missing. The aim was to investigate the prevalence of unknown PTDM long-term post-HT.
Methods: Data were prospectively collected from all adult HT patients who had an OGTT between August 2018 and October 2020. Patients with known DM, an active infection or active treatment of a malignancy were excluded as well as patients who did not want to undergo an OGTT. Either the patient came sober to the outpatient clinic for a regular appointment or visited the general practitioner when the distance to the hospital was too far. A fasting glucose was determined after which the patient was administered 75 grams of glucose in a 200 mL solution as advised by the American Diabetes Association. After two hours, glucose was measured again. Furthermore, glycated hemoglobin (HbA1c) was determined. Definitions of PTDM, pre-diabetes and no diabetes were used according to the American Diabetes Association guidelines. Diabetes range tests were repeated after six weeks with another OGTT to confirm PTDM.
Results: Out of 251 patients, 148 patients were tested excluding 71 patients with known DM and 32 patients not able or willing to undergo an OGTT. Median age at OGTT was 54.5 [IQR 42.4-64.8] years and 60 (41%) were female. Main reason for HT was non-ischemic cardiomyopathy (n=118, 80%). Median time from HT until OGTT was 8.6 [IQR 4.8-14.4] years. Steroids were used in 90 (61%) patients and 134 (91%) patients used tacrolimus at the time of OGTT. In total, OGTT demonstrated new PTDM in 21 (14%) patients, pre-diabetes in 41 (28%) patients and no diabetes in 86 (58%) patients.
Conclusions: PTDM as well as pre-diabetes are frequently seen long-term post-HT. As such, systematic screening by OGTT is warranted for timely intervention as this may improve the long-term outcome.

Risk factors for early graft failure after solitary pancreas transplantation in the modern era: a single-center, retrospective study

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Background: Solitary pancreas transplantation (SPT, either pancreas after kidney (PAK) or pancreas transplant alone (PTA)) is performed less often than simultaneous pancreas kidney transplantation (SPK), and early graft loss is observed more frequently. Only very limited information exists on risk factors for early graft failure specific for SPT, especially in the modern era of improved immunosuppression and increased use of high-risk donor organs.
Methods: A single-center retrospective analysis was performed on all SPT since the introduction of modern induction immunosuppression (2000-2019). Short term outcome of SPT was compared to SPK. Multivariate regression analysis in the SPT group was performed to identify risk factors for pancreas graft failure in the first three months after transplantation.
Results: In total 50 SPT (40 PAK, 10 PTA) were analyzed and compared to 318 SPK. Three-month patient and death-censored graft survival was 100% and 70.0% in SPT and 98.1% and 92.1% in SPK, respectively (p=0.33 and p<0.001). Reasons for early graft loss in SPT transplants were thrombosis (80%), rejection (6.7%) and bleeding (6.7%). No association with immunologic factors was observed. Multivariate analysis in the SPT group showed that donor BMI (HR 1.43, p=0.02) and enteric drainage (HR 6.3, p=0.04) were associated with early graft loss.
Conclusions: SPT is associated with a higher risk for early graft loss than SPK. Possible risk factors include donor BMI and type of exocrine drainage. Early graft loss in SPT is mainly caused by thrombosis of the pancreas graft. Therefore, specific perioperative protocols for SPT should be developed with the aim of reducing pancreas graft thrombosis to improve outcome. The current analysis needs to be confirmed in larger multicenter analyses.

Kidney organoids are capable of forming Wilms-like tumors, but not teratomas

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Background: Human kidney organoids represent an early stage of nephrogenesis and have been shown to successfully vascularize and mature further in *in vivo* models. However, there are concerns regarding the long-term safety and stability of iPSC-derivatives. Specifically, the potential for tumorigenic transformation may impede the road to safe clinical application.
Methods: Therefore, we set out to analyze the tumorigenic risk of human iPSC-derived kidney organoids (n=4).
Results: Residual undifferentiated iPSCs are prone to form tumors but we detected no iPSC in differentiated kidney organoids as analyzed by gene expression analysis, single cell sequencing and immunohistochemistry. This was supported by the observation that kidney organoids lacked the ability to form teratoma, in contrast to undifferentiated iPSCs. However, upon long-term subcutaneous implantation of whole organoids in immunodeficient IL2Ry$^{-/-}$RAG2$^{-/-}$ mice we observed the capacity of kidney organoids to form tumors in 4 out of 44 implantations. Clusters within the tumors displayed mitotic activity as indicated by the high proportion of Ki-67+ cells. Furthermore, there was a resemblance to Wilms tumor, a common pediatric renal cancer, as they contained WT1+CD56+ immature blastemal cells. No genetic changes could be found that contributed to the occurrence of tumorigenic cells within the kidney organoids.
Conclusions: Therefore, we suggest that the lack of environmental cues may have caused an arrest in terminal differentiation and incomplete mesenchymal–epithelial transition of kidney organoid cells, resulting in the formation of Wilms-like tumor. Our results indicate that safe implementation of kidney organoids as a therapeutic option should be preceded by analysis of tumorigenic risk of kidney organoids.

Efficient recellularization of human vascular grafts with patient derived endothelial cells

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Background: In transplant surgery, the endothelial lining is the first barrier between the donor and recipient. Damaged endothelium reveals extracellular membrane (ECM) molecules that can start of thrombosis, aggravate inflammation and cause rejection. Endothelial repair strategies may improve transplant outcomes. Re-endothelialization of acellular blood vessels using kidney-vein endothelial cells (EC) was used to establish a research platform for endothelial repair strategies.
Methods: Human common iliac veins (CIV) (n=19) from deceased healthy donors were decellularized by submersion in Triton X-100 (4%) and ammonia (1%), and used as a scaffold for vascular endothelialization and functional analysis. The detergents were refreshed every 30 minutes for 10 times. Subsequently, CIV were treated with 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 at concentrations of $2 \cdot 10^5$, $4 \cdot 10^5$ or $1 \cdot 10^6$ cells/cm^2 under static conditions. The re-endothelialised veins were analysed using confocal microscopy for EC confluency. Restoration of the EC barrier was analyzed using trans-endothelial electrical resistance (TEER) and FITC-Dextran diffusion assays.
Results: The CIV were fully decellularized, demonstrated by the complete removal of cellular components as shown by HE and DAPI stained slides, 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 (0.23±0.14 µg/mg wet weight). Confocal microscopy showed the formation of a confluent monolayer of cells as soon as 24 hours after seeding for the highest EC concentration. Repopulated CIV scaffolds remained fully confluent for up to 28 days. After 10 days, the $4 \cdot 10^5$ or $1 \cdot 10^6$ cells/cm^2 concentrations had TEER measurements above background of 5.0±2.9 Ω·cm^2 and 15.1±12.2 Ω·cm^2 respectively (n=4) indicating the maintenance of the barrier function. Vascular remodelling and proliferation associated genes (VEGFA, TEK, VCAM1, ICAM) showed a higher mRNA expression in EC on CIV scaffolds (p<0.05) compared to EC grown on plastic dishes.
Conclusions: We developed an efficient procedure to decellularize human CIV and generated functional and long-term stable re-endothelialized veins using patient derived kidney-vein EC. This research platform will enable the study of re-endothelialization mechanisms.

Complement C3 deposition on ischemia-reperfusion injured endothelial cells is induced by anti-ARHGDIB monoclonal antibodies

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Background: Antibodies against Rho GDP-dissociation inhibitor 2 (ARHGDIB) have been associated with inferior graft survival in kidney transplant recipients. However, it remains unclear if these antibodies are involved in the pathogenesis of graft loss. In the present study, we investigated the ability of anti-ARHGDIB antibodies to bind their cytoplasmic target upon ischemia reperfusion injury and if so, whether antibody binding results in complement activation.
Methods: The role of ischemia reperfusion in exposure of ARHGDIB to the cell surface of endothelial cells was studied in a hypoxia-reperfusion model. In this model, primary kidney and lung endothelial cells were exposed to 1% O2 at 4°C in a hypoxia chamber followed by reperfusion at normoxic conditions at 37°C. Cells were stained for ARHGDIB, annexin V and fixable viability dye. Complement activation upon antibody binding was assessed with in-house produced monoclonal human antibodies to ARHGDIB or to peanut allergen Ara h 2 (control antibody) supplemented to serum, followed by staining for C3 and C5b-9. Data were collected with IS100 ImageStream system and analyzed using ImageStream Data Analysis and Exploration Software.
Results: Cells incubated at low oxygen concentrations followed by reperfusion showed increased apoptosis compared with cells incubated at normal oxygen concentrations. Furthermore, these injured cells showed increased expression of ARHGDIB on their cell surface. Binding of anti-ARHGDIB antibodies resulted in a 5-10% increase in the amount of C3 positive cells compared with the control. We confirmed that antibodies co-localized with C3 deposition by a co-localization assay.
Conclusions: The present study showed that antibodies against ARHGDIB are not solely a biomarker, but also play a pathogenic role in graft loss after kidney transplantation as shown by their ability to fix complement on ischemia-reperfusion injured endothelial cells. Complement activation by other non-HLA antibodies may also play a role in graft loss. It would be interesting to research this further, and to investigate whether graft loss caused by complement-fixing non-HLA antibodies can be prevented by, for example, complement inhibitors.

The small bowel is protected by the presence of luminal preservation solution during cold storage in a brain-dead rat model

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Background: Small bowel (SB) transplantation is performed a handful of times a year, and graft survival rates are disappointing. Thus, animal models are needed to understand the mechanisms occurring before, during and after the procedure. The SB, donated after brain death (DBD), is viable for up to 10 hours of storage, shorter than other abdominal organs which are preserved in the same way. There have also been no developments in the way the graft is treated, stored and transported. The protective effects of luminal perfusion (LP) with an ice-cold solution have been consistent in previous studies in small and large animals, but none of these models include DBD. The aim of our study is to investigate whether the beneficial effects of LP occur also in a DBD model.
Methods: Wistar rats (N=9) underwent brain death induction by inflation of a balloon at 1 ml/hr for 30 minutes and kept stable for 2 hours. Donor vessels were then perfused with University of Wisconsin solution (UW) and the SB explantated. The bowel was then divided into three pieces for cold storage (CS). One segment was kept empty (control), and the rest were filled with 0.06 ml/cm of either UW (UW/UW) or polyethylene glycol 3350 (UW/PEG). All segments were then tied shut and stored in ice-cold UW. Analysis time points were procurement (t=0) and after 4 and 8 hours of CS (t=4, t=8 respectively). Samples were evaluated by histopathological scoring of preservation injury (IPI; median [range]; Kruskall-Wallis and Dunn's statistics, p < 0.05 for significance), percentage of absent epithelial lining and presence of oedema. More analyses are to be performed.
Results: Basal score at t=0 shows a median value of 2 [0-3]. IPI results from control samples were 4 [2-5] (t=4) and 2 [2-6] (t=8). UW/UW at t=4 had less damage, 2 [2-3, p < 0.005) and all other samples showed a tendency to lower damage but no statistical significance. 50% of the epithelial lining is detached from t=4 in control, while in UW/UW is 30%. Increasing amounts of oedema beneath the epithelial layer in the UW/UW reflects the largely conserved mucosal surface in comparison to other groups.
Conclusions: Luminal perfusion of the small bowel is protective of the mucosa in the brain-dead rat. The LP solution with the best effect is UW for up to 4 hours of static cold storage. These results show less effect of LP than previously described, when using non-DBD models. More attention should be paid to the effect of DBD in the grafts viability on further studies.

Anti-fibrotic effects of Membrane Particles from mesenchymal stromal cells in renal ischemia reperfusion injury mouse model

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Background: Membrane particles (MP) are nanovesicles artificially generated by extrusion of the mesenchymal stromal cell (MSC) membranes. MP were designed to circumvent the risks of MSC therapy such as a poor biodistribution due to their large size and unknown mechanistic behaviour after infusion, while keeping the reparative and immunomodulatory properties of MSC. We have demonstrated earlier that MP have immunomodulatory properties, endothelial regenerative capacity, and antifibrotic effect on lung fibroblasts *in vitro*. In this study, the aim is to demonstrate the efficacy of MP as an antifibrotic treatment on a renal ischemia reperfusion injury (IRI) mouse model.
Methods: Unilateral ischemia injury was performed by clamping the right kidney of the mice for 37 minutes. The MP were intravenously infused 3-5 hours after ischemia. Animals were sacrificed and the kidney harvested 3 days after renal IRI. Four groups of mice were analysed: Sham, IRI, IRI+MP derived from 1 million of MSC, and IRI+MP derived from half million of MSC. Gene expression of proinflammatory cytokines was measured in the kidneys such as IL6, and TNFα; kidney injury marker KIM-1, infiltration of monocytes and lymphocytes (F4/80, CD3); and profibrotic markers such as TGFβ, PAI-1, fibronectin, tenascin C, collagen I, and III.
Results: We found no difference between IRI mice treated with MP and IRI untreated mice respect to the proinflammatory markers IL6, TNFα, injury marker KIM-1 or infiltration of monocytes and lymphocytes. IRI induced an upregulation of the gene expression of profibrotic markers such as TGFβ and PAI-1, and proteins from the extracellular matrix, such as fibronectin, tenascin C, collagen I, and III. Interestingly, both doses of MP significantly decreased the expression of the TGFb, PAI-1 and the main extracellular matrix proteins involved in fibrogenesis.
Conclusions: Our findings show that MP may have an early antifibrotic effects on renal IRI.

Mesenchymal stromal cell derived membrane particles are internalized by macrophages and endothelial cells and exhibit mixed pro- and anti-inflammatory effects

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Background: Mesenchymal stromal cells (MSC) are a promising therapy for immune modulation and regeneration in organ transplantation. However, MSC are large and become trapped in the lungs after intravenous infusion, where they have a short survival time. To steer MSC therapy beyond the lungs and improve their mechanism of action, we generated nm-sized particles from MSC membranes (membrane particles, MP), which we demonstrated earlier to interact with various cell types and exhibit immunomodulatory and repair properties.
Methods: We investigated the mode of interaction of MP with macrophages and human umbilical vein endothelial cells (HUVEC) under control and inflammatory conditions (in the presence of TNFα).
Results: We found that macrophages and HUVEC take up MP in a dose, time, and temperature-dependent manner. Specific inhibitors for endocytotic pathways revealed that MP internalization depended on heparan sulfate proteoglycan-, dynamin-, and clathrin-mediated endocytosis but did not involve caveolin-mediated endocytosis. MP uptake also involved the actin cytoskeleton and phosphoinositide 3-kinase, which are implicated in macropinocytosis and phagocytosis. Anti-inflammatory M2 macrophages took up more MP than pro-inflammatory M1 macrophages. Moreover, MP induced a mixed anti- and pro-inflammatory gene expression profile in macrophages by increasing IL10 and TGFβ mRNA, but also TNFα and IL1β. In HUVEC challenged with inflammatory stimuli, MP reduced HLA and co-stimulatory molecules expression, and elevated VE-cadherin protein expression, which is involved in endothelial cell barrier function.
Conclusions: Our findings on the mechanisms of uptake of MP under different conditions help the development of target-cell specific MP therapy to modulate immune and endothelial cell responses in transplant organs.

Treating circulatory death donor kidneys with anti-fibrotic drugs using ex vivo precision cut kidney slices

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Background: Chronic kidney disease is characterized by a gradual loss of kidney function, often requiring a kidney transplant for survival. As waiting lists keep growing, suboptimal kidneys such as circulatory death donor (DCD) kidneys are increasingly used to enlarge the donor pool. Unfortunately, these kidneys undergo ischemia/reperfusion injury (IRI), frequently leading to renal fibrosis and failure. Transforming growth factor beta 1 (TGF-β1) and matrix metalloproteases have been identified as central mediators of fibrosis, and inhibition of these targets could attenuate fibrosis in DCD kidneys. We therefore studied whether galunisertib, doxycycline, taurine, and febuxostat alleviated fibrosis in precision-cut kidney slices (PCKS) prepared from porcine DCD kidneys.
Methods: PCKS were prepared from porcine kidneys that were exposed to 30 minutes of warm ischemia followed by 3 hours of oxygenated hypothermic machine perfusion. We subsequently incubated PCKS for 48 hours at 37 °C with either galunisertib (10 μM), doxycycline (113 μM), taurine (80 mM), or febuxostat (16 μM). ATP levels were measured to assess the viability of PCKS and real-time polymerase chain reaction (qPCR) was used to investigate expression of fibrosis-related genes. To further elucidate the antifibrotic effects of galunisertib, we cultured PCKS with TGF-β1 to promote fibrosis.
Results: ATP levels remained stable regardless of the treatment, demonstrating that PCKS were viable for up to 48 hours. We first screened the effects of the compounds in the absence of TGF-β1. Significant effects were only observed for galunisertib, which lowered the expression of α-SMA, and FN2. Doxycycline, taurine and febuxostat did not affect expression of fibrosis-related genes significantly. We then investigated the effects of galunisertib in fibrotic PCKS that were cultured with TGF-β1. TGF-β1 promoted fibrosis in PCKS as shown by a significantly increased expression of TGF-β1, FN1, PAI-1, HSP47, and COL1A2 after 48 hours of incubation. Galunisertib, however, clearly attenuated the expression of all tested fibrosis-related genes.
Conclusions: The combination of machine perfusion and precision cut kidney slices provide a suitable way for assessing anti-fibrotic effects of pharmaceutical interventions in a transplant setting. We convincingly demonstrated that galunisertib exhibited strong antifibrotic effects in PCKS cultured with and without TGF-β1. Galunisertib therefore appears to be a promising antifibrotic compound for further research in a preclinical model, and may ultimately be implemented during machine perfusion in a clinical setting as treatment to prevent or to attenuate fibrosis in DCD kidneys.

Normothermic Machine perfusion of explanted livers in patients undergoing liver transplantation to study hepatic pharmacokinetic processes

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Background: The prediction of hepatic clearance and biliary excretion is of high importance to assess the pharmacokinetics of drugs. This is particularly important in patients with hepatic diseases where altered liver function can result in an altered pharmacokinetic profile of the administered drugs. We therefore aim to develop a physiologically relevant human pre-clinical model to investigate drug pharmacokinetics 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: Patients waitlisted for liver transplantation were given the opportunity to participate in this study. During liver transplantation, the portal vein and the hepatic artery of the explanted liver were immediately flushed with a cold histidine-tryptophan-ketoglutarate (HTK) 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 a set temperature of 37°C. Livers underwent NMP for 6 hours and blood gas analyses were performed hourly. After acclimatization period of 120 min, a bolus of a drug cocktail was applied to study drug pharmacokinetics. Samples from the perfusate and bile were taken at prespecified times.
Results: Five explanted livers in patients undergoing liver transplantation were included in this study. The underlying disease processes of these livers were Primary Biliary Cirrhosis (PBC), Non-alcoholic Steatohepatitis (NASH), 2x Alcoholic Liver Disease, and Hepatocellular carcinoma in the context of Hepatitis B viral disease (HBV+HCC).Major differences were observed in the portal flow between the livers. The ALD livers showed the lowest portal flow of 250 ml/min while the HBV liver generated a portal flow of 1500 mL/min. Arterial flow was stable and no major differences were observed (288±35 mL/min). All livers except PBC produced >30 mL bile throughout the duration of the experiment with a biliary pH >7.75 and low biliary glucose levels(<3 mmol/L). A relation was shown between the MELD score of the patient and the perfusate lactate levels. Lactate remained low(<10 mmol/L) in perfused livers of patients with a low lab MELD score (6-9) while livers of patients with a higher lab MELD score (14-23), perfusate lactate strongly increased (>25mmol/L) after 4 hours of perfusion. The same effect was observed for perfusate AST levels. Bilirubin showed to extensively build up in the plasma during perfusion of the PBC liver, while other livers showed low and stable plasma bilirubin levels. Drug cocktail measurements in plasma and bile samples are currently performed.
Conclusions: Here we demonstrate for the first time stable NMP of explanted livers of patients undergoing liver transplantation to study hepatic clearance, biliary excretion and DDI under specific disease circumstances.

Avoiding tacrolimus under- and overexposure with a dosing algorithm for renal transplant recipients: a single arm prospective intervention trial

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Background: Bodyweight-based tacrolimus dosing followed by therapeutic drug monitoring is standard clinical care after renal transplantation. However, after transplantation, a meagre 38% of patients is on target at first steady state and it can take up to three weeks to reach the target tacrolimus pre-dose concentration (C_0). Tacrolimus under- and overexposure is associated with an increased risk of rejection and drug-related toxicity, respectively. To minimize sub- and supra-therapeutic tacrolimus exposure in the immediate post-transplant phase, a previously-developed dosing algorithm to predict an individual's tacrolimus starting dose was tested prospectively.
Methods: In this single-arm, prospective, therapeutic intervention trial, 60 *de novo* kidney transplant recipients received a tacrolimus starting dose based on a dosing algorithm instead of a standard, bodyweight-based dose. The algorithm included cytochrome P450 (*CYP*) *3A4* and *3A5* genotype, body surface area and age as covariates. The target tacrolimus C_0, measured for the first time at day 3, was 7.5-12.5 ng/mL.
Results: Between 23 February 2019 and 07 July 2020, 60 patients were included. One patient was excluded because of a protocol violation. On day three post-transplantation, 34 out of 59 patients (58%; 90%-CI 47% to 68%) had a tacrolimus C_0 within the therapeutic range. Markedly sub-therapeutic (<5.0 ng/mL) and supra-therapeutic (>20 ng/mL) tacrolimus concentrations were observed in 7% and 3% of the patients, respectively. Biopsy-proven acute rejection occurred in three patients (5%).
Conclusions: Algorithm-based tacrolimus dosing leads to the achievement of the tacrolimus target C_0 in as many as 58% of the patients on day three after kidney transplantation.

Combination of low-dose sirolimus and extended-release tacrolimus versus standard dose extended-release tacrolimus in de novo liver transplant recipients comparing long-term renal function; 24-month results from a multi-center randomized, open label, controlled study

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Background: The impact of tacrolimus (TAC) on renal function after liver transplantation (LT) has led to a number of strategies to minimize TAC exposure. The hypothesis of this study was that a combination of low-dose sirolimus (SRL) and extended-release TAC compared to normal-dose extended-release TAC will result in superior renal function with comparable rates of rejection, graft and patient survival.
Methods: This study is an open-label, multicenter randomized, controlled trial. Patients were enrolled between 02-2011 until 03-2018 and randomized between 80-100 days after LT to 1) control group once daily normal-dose extended-release TAC with trough levels: 5–10 µg/L or 2) interventional group once daily combination therapy of SRL and low-dose extended-release TAC with trough levels: 3–5 µg/L for both SRL and TAC. The primary endpoint was chronic kidney disease (CKD) defined as eGFR ≤60 mL/min/1.73m^2 at 36 months after Tx. Secondary endpoints included: treatment of biopsy proven acute rejection (tBPAR), retransplantation, mean eGFR, incidence of de *novo* diabetes mellitus (NODAT), incidence of and time to *de novo* or recurrent malignancy, and tolerability and safety. Data in this analysis were approached in an intention-to-treat (ITT) and per protocol (PP) analysis until month 24.
Results: In total, 196 patients were included and the majority was transplanted because of HCC (34.2%), cholestatic liver disease (19.9%) or (N)ASH (15.8%). At baseline, the eGFR in the control and interventional group was 72.9 and 76.9 ml/min/1.73m$^{2.}$ At 24 months, the primary endpoint was reached in 30.3% and 31% of the patients in the control and interventional group. The ITT analysis showed no relevant difference at 24 months in the eGFR for the control and interventional group: 75.7 *versus* 79.9 ml/min/1.73m^2. The TAC and SRL mean trough levels were within the target range for both groups. These results persisted in the PP analysis. Regarding the secondary endpoints, no differences were found in the control and interventional group for tBPAR (2% *versus* 5.1%), NODAT (5.1% *versus* 5.1%), retransplantation (1% *versus* 3.1%) and malignancy (3.1% *versus* 7.1%). In total, 42.3% (83/196) of the patients developed serious adverse events (SAEs, n=178). SAEs most frequently reported were fever (22.5%), infections (18.5%) and cholangitis (14.6%).
Conclusions: Low-dose sirolimus combined with extended-release tacrolimus is a safe strategy to minimize TAC exposure in LTx recipients. However, this combination does ultimately not provide a better renal function at 24 months compared to normal-dose extended-release tacrolimus.

Intra-patient variability in tacrolimus pharmacokinetics in kidney transplant patients treated with different tacrolimus formulations

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Background: High intra-patient variability (IPV) in tacrolimus exposure is increasingly recognized as a risk factor for poor long term outcomes in kidney transplantation. Previous studies have shown a reduction in IPV following a switch from the twice-daily (immediate-release) tacrolimus formulation (Prograft) to a once-daily (modified-release) tacrolimus formulation (Advagraf). There are no data available for LCP-tacrolimus (Envarsus). Envarsus has different pharmacokinetics as compared to other tacrolimus formulations with reduced peak concentrations and peak-to-trough fluctuations and the IPV may be lower. Our main objective was to investigate if the IPV in tacrolimus pharmacokinetics is reduced by switching patients from maintenance tacrolimus treatment with Prograft to either Advagraf or Envarsus.
Methods: The 'Tacrolimus IPV study' was a randomized, open label, crossover trial. Adult kidney transplant recipients who were on a stable immunosuppressive regimen which included Prograft were randomized for conversion to either Advagraf or Envarsus, and for the order in which Prograft and the once-daily formulation were taken in the cross-over design. Duration of follow up was 12 months. Patients were followed 6 months for each tacrolimus formulation, with monthly tacrolimus trough level assessments, in order to calculate IPV in tacrolimus pharmacokinetics.
Results: 92 patients were included for analysis of the primary outcome. Median interval since kidney transplantation was 46 months (IQR: 19.4-95.3). The IPV for Prograft and the once-daily formulations were 16.6% and 18.3% respectively (ns). The IPV of Envarsus (20.1%) was higher compared to the IPV of Advagraf (16.5%), but this difference was not statistically significant (+3.6%, 95%-confidence interval (CI) -0.1% – 7.3%). In the Advagraf study arm (n=47), the IPV was 17.7% and 16.5% during treatment with Prograft and Advagraf, respectively (-1.2%, 95%-CI -5.6% - 3.1%, ns). The IPV in the Envarsus study arm (n=45) was 15.5% and 20.1% during treatment with Prograft and Envarsus, respectively (+4.6%, 95%-CI: 1.2%-8.1%, p 0.01).
Conclusions: The IPV did not decrease after switching from immediate-release tacrolimus (Prograft) to either Advagraf or Envarsus. Based on the results of this study switching kidney transplant patients from a twice-daily (immediate-release) tacrolimus formulation to a once-daily (modified-release) tacrolimus formulation with the aim to lower the IPV cannot be recommended.

The risk of post-donation kidney function impairment for prospective living kidney donors with persistent isolated microscopic hematuria

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Background: According to current guidelines, a kidney biopsy is indicated in prospective living kidney donors who present with persistent isolated microscopic hematuria (PIMH) during evaluation, while post-donation risks of PIMH are unclear. Here, we investigated the risks of pre-donation PIMH on post-donation kidney outcomes.
Methods: We included 858 living kidney donors who underwent at least two urinalyses before donation and had yearly post-donation kidney function (estimated glomerular filtration rate (eGFR), proteinuria (assessed as the protein/creatinine-ratio (PCR)) and systolic blood pressure (SBP) measurements available. The association between pre-donation persistent (at least two positive measurements) isolated microscopic hematuria (≥ 1 red blood cell (RBC) per high power field (HPF) or ≥ 5 RBC per µL) and post-donation kidney function was assessed using generalized linear mixed models.
Results: Mean age was 52 (11) and median [IQR] follow-up time was 36 [12-70] months. Pre-donation PIMH was present in 78 donors of whom 74% were female, versus 48% female in the non-PIMH group (P<0.001). There was no significant association between pre-donation PIMH and the course of PCR (1.01 mg/mmol increase/year for PIMH donors and 1.03 mg/mmol increase for non-PIMH donors (P=0.34)), SBP (0.24 mmHg increase/year for PIMH donors, 0.09 mmHg increase/year for non-PIMH donors (P=0.70), or eGFR (0.62 mL/min/1.73m^2 increase/year for PIMH donors, 0.31 mL/min/1.73m^2 increase/year for non-PIMH donors (P=0.41)) over time after donation, even after adjusting for pre-donation age, sex, BMI, pre-donation eGFR, SBP and ACEi/ARB use.
Conclusions: We found no increased risk of post-donation proteinuria, hypertension or eGFR decline in donors with pre-donation PIMH. The need of a pre-donation kidney biopsy in donors with PIMH without other risk factors for kidney disease should be carefully reconsidered.

Recurrence of IgA After Kidney Transplantation in Adults

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Background: In patients with kidney failure due to IgA nephropathy, IgA deposits can recur in a subsequent kidney transplant. The incidence, impact and predictors of IgA recurrence are unclear, as most studies have been single-center and sample sizes are relatively small.
Methods: We performed a multicenter, international, retrospective study to determine the incidence, predictors and treatment response of recurrent IgA after kidney transplantation. Data was collected from all consecutive patients with biopsy-proven IgA nephropathy transplanted between 2005-2015, across 16 TANGO study centers in Europe, United States and Brazil.
Results: Our primary analysis included 504 patients. Recurrent IgA deposits were identified by kidney biopsy in 82 patients (16%; 95%CI:13%-19%). Over a median (IQR) follow-up period of 8.7 (5.5-11.2) years, Kaplan-Meier analysis showed decreased graft survival in patients with IgA recurrence (HR 1.98, 95%CI: 1.11-3.53). Multivariable Cox-regression revealed a higher risk for recurrence of IgA deposits in patients with a pre-emptive kidney transplant (HR 2.56, 95%CI: 1.59-4.17), patients with preformed donor-specific antibodies (DSA) at time of kidney transplant (HR 2.74, 95%CI:1.22-6.14) and patients with a shorter time from diagnosis to end-stage kidney disease (HR 0.84 per month, 95%CI:0.74-0.96). A steroid free immunosuppressive regimen was not associated with recurrent IgA.
Conclusions: Recurrence of IgA was associated with a 2-fold greater risk of graft loss with a cumulative risk increasing over time after transplant. Previously reported risk factors for IgA recurrence such as a steroid free immunosuppressive regimen could not be validated in our large, international cohort.

Impact of measured versus estimated GFR on living kidney donor selection: A multicenter cohort study

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Background: Most transplant centers use estimated glomerular filtration rate (eGFR) for evaluation of potential living kidney donors. Measured GFR (mGFR) allows more precise kidney function assessment, and therefore holds potential to increase the living donor pool. We aimed to address the impact of the mGFR method on donor selection and long-term safety.
Methods: In this longitudinal cohort study, we compared eGFR (CKD-EPI) before and at five years after donation in donors from one center using mGFR-based donor screening (Groningen, n=250) with two centers using eGFR-based screening (Rotterdam, n=647 and Nijmegen, n=169). Follow-up was complete in all donors.
Results: Donor age was similar among the cohorts (Groningen 53±10 years, Rotterdam 52±13 years and Nijmegen 53±9 years) with small differences in sex distribution (Groningen 54%, Rotterdam 58%, and Nijmegen 47% female, both P<0.05 vs Groningen). Before donation, eGFR was lower in Groningen (91±13 mL/min/1.73m^2) than in Rotterdam (93±15 mL/min/1.73m^2, P<0.05 vs. Groningen) and Nijmegen (94±12 mL/min/1.73m^2, P<0.05 vs. Groningen). Pre-donation mGFR was 115±22 mL/min/1.73m^2 in Groningen. At five years post-donation, eGFR was similar among the centers (Groningen 62±12 mL/min/1.73m^2, Rotterdam 61±14 mL/min/1.73m^2, Nijmegen 62±11 mL/min/1.73m^2, P=NS). The 5-year decline in eGFR was smaller in Groningen (-29±10 mL/min/1.73 m^2), compared with Rotterdam (-32 ±10, P<0.05 mL/min/1.73 m^2 vs. Groningen, P<0.05 vs. Groningen) and Nijmegen (-33 ±8 mL/min/1.73 m^2, P<0.05 vs. Groningen).
Conclusions: mGFR-based donor screening may facilitate acceptance of more donors with marginal eGFR without adverse effects on long-term kidney function, providing potential for a safe expansion of living donor pool.

Antbody mediated rejection in kidney transplantation: What is the role of complement activation?

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Background: Antibody mediated rejection (AMR) is a major cause for graft failure in kidney transplant recipients (KTR). However, its etiology is still poorly understood. Current Banff '18 classification recognizes C4d negative AMR as a phenotypic subtype, which questions the universal role of the classical complement pathway (CP) in AMR. Disappointing long-term effectiveness of complement inhibitors suggests that CP activation is an insufficient explanatory model for all AMR patients. This study aimed to clarify the role of the complement system in AMR with regard to systemic activation in serum and local deposition in renal graft tissue.
Methods: We measured systemic complement cascade activation markers C3, C3d, soluble C5b-9 (sC5b-9) in a retrospective cohort of KTR. Local complement activation was analyzed as C3d, C4d and C5b-9 deposition in kidney biopsies. Next to in vivo complement measurements, we tested classical complement activation via HLA antibodies on conditionally immortalized endothelial cells (CiGeNCs) in vitro.
Results: We included 55 KTR, which were classified based on pathology reports as AMR patients (n=20), non-AMR patients (cellular rejection, n=18) and as normal controls (n=17). Of all 20 AMR patients, 14 showed C4d deposition in peritubular capillaries and were therefore defined as C4d positive (C4d+). In C4d+ AMR, lomerular expression of C3d was significantly higher when compared to C4d- AMR (p=0.003). This was not accompanied by increased glomerular C5b-9 expression. Peritubular capillary expression of C3d and C5b-9 was not increased in AMR compared to normal controls and non-AMR patients. Additionally, no systemic evidence of increased complement pathway activation was detected in plasma of AMR patients. In line with the histological findings, flow cytometry on CiGeNCs showed expression of C4d and C3d without concomitant C5b-9 expression.
Conclusions: Our findings question the universal role of the CP in AMR. Terminal complement activation in peritubular capillaries might not be a central pathomechanism in AMR. Possibly, complement-independent mechanisms of cellular cytotoxicity are more important in AMR mediated damage. Endothelial complement regulatory processes in peritubular and glomerular capillaries might account for the heterogeneous complement profile of AMR patients. These findings might provide an explanation why terminal complement inhibitors failed to show overarching effectiveness in AMR patients.

The assesment of pre-transplant alloreactive t cells is a valuable addition in predicting patients at risk for acute rejecion

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Background: The presence of panel-reactive antibodies (PRA) is routinely measured in the screening process of kidney transplant candidates. While this screening method has proven valuable in the transplant setting, it does not account for the presence of alloreactive memory T cells. Previous studies have shown that alloreactive memory T cells are associated with the development of acute rejection. The aim of this study, was to assess the rejection risk of kidney transplant recipients by studying both T and B lymphocyte alloreactivity prior to transplantation.
Methods: PBMC samples from 114 kidney transplant recipients (transplanted between 2010-2013) were obtained pre transplantation. The frequency of IL-21 (known to provide help to B cells) producing PBMCs was analyzed by enzyme-linked immunospot assay (Elispot). Patient PBMC were stimulated with irradiated donor or third-party cells, which were completely HLA-mismatched with donor and recipient. Historical PRA and/or the presence of serum anti-HLA antibodies were used to determine which patients were sensitized to HLA antigens pre-transplantation.
Results: A total of 30 patients developed acute rejection within 6 months after transplantation. Of these patients, 16/30 (53%) were sensitized to HLA antigens prior to transplantation. Not surprisingly, this suggests that other factors contribute to this allogeneic response. Donor age and historical PRA were significantly different between patients with and without rejection (p=0.001 and 0.03, respectively) and the number of IL-21-producing alloreactive T cells showed a trend towards significance (p=0.07). In a multiple logistic regression all the above mentioned variables were shown to be indicators of an increased risk for the development of rejection (p=0.001). A 10% increase in historical PRA and 10 count increase in alloreactive IL-21 producing cells resulted in a 15% and 12% increased risk of rejection, respectively.
Conclusions: We found that B cell immunity is only present in approximately half of the patients who developed acute rejection within 6 months after transplantation. In addition to historical PRA, the donor-age and the number of pre-transplant alloreactive T cells are significant contributors to the overall risk for development of acute rejection. We propose that monitoring pre-transplant alloreactive IL-21 cells can identify more patients at risk for developing rejection shortly after transplantation.

Characterization of the immunogenicity of iPSC-derived kidney organoids

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Background: Human kidney organoids are a promising tool for studying kidney disease and regeneration. However, for successful implementation into clinical practice, the immunological acceptance of kidney organoids is crucial.
Methods: Therefore, we studied the immunogenicity of human iPSC-derived kidney organoids in an *in vitro* and *in vivo* model. Immunostaining confirmed that kidney organoids contained all the essential renal structures. Kidney organoids were co-cultured with healthy peripheral blood mononuclear cells (PBMC) for 7 days.
Results: Infiltrating CD45+ leukocytes were observed in the organoids. Particularly, CD3+ T-cells were found predominantly clustered around glomerular structures in renal stroma, and CD68+ macrophages which were diffusely distributed throughout the organoid. A mixed pattern of both pro-inflammatory M1 and regulatory M2 macrophages was observed. Immunofluorescence showed that the infiltrating cells did not proliferate as observed by the absence of Ki-67+CD45+ cells. As *in vitro* models do not support long-term culture of kidney, we subcutaneously implanted whole organoids in immune-deficient IL2Ry$^{-/-}$RAG2$^{-/-}$ mice for 1 month. Hereafter, we injected human PBMC intraperitoneally and observed a significant human CD45+ cell engraftment in the spleens and blood after 1 month. T cell populations were present in the organoids with a CD4+/CD8+ T cell ratio of 1:2 as indicated by flow cytometry, single cell sequencing (scRNAseq) and immunohistochemistry. Heterogeneous T cell populations contained activated, cytotoxic and resting/regulatory phenotypes and interestingly, the organoids also contained a population of proliferative, tissue-resident-like CD8+ T cells. There was a significant decrease in gene expression of the kidney differentiation markers PODXL, Villin-1 and CDH-1 as well as of stromal markers such as CD90 in kidney organoids that contained infiltrated T cells, suggesting immune-mediated damage had targeted both renal and stromal cell types.
Conclusions: These preliminary findings show for the first time the interaction of kidney organoids with the immune system. Understanding this interaction will advance the use of kidney organoids for disease modeling, drug testing and regenerative medicine.

Patient reported outcomes in kidney transplantation recipients, a cross-sectional overview

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Background: Patient reported outcomes (PROs) concerning Health Related Quality of Life (HRQoL) and symptom experience, which can be obtained by patient reported outcome measures (PROMs), play an important role in personalized and value-based healthcare. Yet, there is limited knowledge of these PROs from clinical implementation in kidney transplant recipients (KTRs). This study expands the insight in these healthcare outcomes in KTRs by providing a cross-sectional overview of the results of PROMs in KTRs in our center.
Methods: All adult KTRs, transplanted before October 2020 with a functioning graft, were invited to fill out our clinically implemented PROMs including the Short form-12 for HRQoL and a symptom checklist composed of the DSI and the MTSOSD-59R for symptom occurrence and burden. Results: 633 of 1495 KTRs (42%) completed the PROMs and gave consent for scientific analysis of their results. Mean age was 61.3 years (SD 11.3), 62% was male, mean time since transplantation was 11.6 years (SD 9.1), 30% underwent pre-emptive kidney transplantation and 59% had a live donor. Mean mental and physical component scores (MCS and PCS) of HRQoL were below previously studied Dutch norms (-2.8 (6%) and -7.1 (14%), respectively). Across age-groups with an interval of 10 years, MCS slightly increased until 60-69y and PCS decreased after 30-39y (both p <0.01). Male KTRs' PCS was 3.8 (9%) higher compared to female KTRs (95% CI 2.0 to 5.6; p <0.01). Mean amount of symptom experience was 16 (SD 11) out of 61 and mean symptom burden was 43 (SD 34). The top 10 most frequently reported symptoms consists of bruises, feeling tired and lack of energy, increased urge to urinate at night, dry skin, bone or joint pain, muscle cramps and weakness, trouble staying asleep and erectile problems. Sexual problems were the most burdensome symptoms, followed by lack of energy, sleeping problems, back pain and muscle weakness. KTRs with living donor experienced 3 less symptoms (95% CI -5 to -1; p <0.01) and 8.9 less burden (95% CI -14.3 to -3.4; p <0.01). Increased symptom burden showed a negative relation with mental and physical HRQoL. Conclusions: This evaluation shows a cross-sectional overview of our clinically implemented PROMs. The actionable data-driven PROs will hopefully improve our standard of care from patient counseling on the merits and expectancies of transplantation, from the design of novel diagnostic and treatment protocols targeting symptoms, or from merely giving support through listening and understanding.

Medication adherence and fear of rejection in tacrolimus treated kidney transplant recipients with and without mycophenolate mofetil: randomized controlled trial

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Background: After kidney transplantation, a strict immunosuppressive medication regimen of is necessary for graft survival. However, non-adherence to medication has been shown to occur early after transplantation and to increase over time. Weaning the medication regimen in order to lower the immunosuppresive burden, may also be a way to promote adherence, although little is known about the impact of such a regimen on fear of rejection.
Methods: We performed a nested cohort study on medication adherence and fear of rejection in a randomized, investigator-driven, open-label, single centre pilot study. Participants were randomized at 6 months post-transplant to either continue tacrolimus and mycophenolate mofetil (TAC/MMF) or to taper MMF at 6 months and discontinue MMF at 9 months (TAC monotherapy). They completed questionnaires about medication adherence (BAASIS) and fear of rejection (Perceived Threat of the Risk for Graft Rejection (PTGR)) at 6 and 12 months post-transplant.
Results: The majority of the participants at 6 months (n=78) were male (73.1%), European (65.4%), low educated (52.6%) and had a median age of 61.5 years. More than the half of the participants had a living donor (59.0%). Medication adherence was significantly higher in TAC monotherapy compared to dual TAC/MMF therapy (χ^2 (1) = 4.582; p = .032). Despite the fact that the intervention arm discontinued MMF, we found no difference in fear of rejection between the two groups of recipients (p = .887).
Conclusions: Tacrolimus monotherapy by discontinuing MMF in immunologically low-risk kidney transplant recipients, improves medication adherence and does not have an adverse effect on fear levels. Simplification of the medication regime is a potential tool for increasing adherence in clinical practice.

Impact of COVID-19 self-quarantine measures on behaviour, stress, anxiety and glycaemic control in patients with β-cell replacement therapy

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Background: Patients with severely complicated type 1 diabetes (T1D) who receive β-cell replacement therapy have multiple risk factors for a severe course of coronavirus disease, including use of immunosuppression (IS). Quarantine strategies implemented due to the coronavirus pandemic are known to impact both mental and physical health, but this impact is expected to be even greater in patients at high risk for a severe course of COVID-19. We therefore aimed to investigate the behavioural, mental and physical implications of the nationwide quarantine in pancreas and islet transplant recipients.
Methods: In order to be able to study the effect of the quarantine on glycaemic control, all patients with T1D who had received a transplantation with islets or a non-optimally functioning pancreas (i.e. with a marginal β-cell mass) using IS were eligible. As a control group, patients with T1D without IS were included. Using questionnaires, self-quarantine behaviour and self-reported changes in anxiety, stress, physical activity, weight and glycaemic control were assessed. HbA1c during quarantine was compared to the last measurement before quarantine.
Results: Transplant recipients (n=51, age 55 (48 – 59) years, BMI 23.3 (20.9 – 27.4) kg/m^2, diabetes duration 42 (34 – 48) years) adhered more stringently to quarantine measures compared to patients with T1D (n=272, age 53 (37 – 62) years, BMI 25.2 (23.0 – 27.8) kg/m^2, diabetes duration 27 (15 – 39) years). In transplant recipients as compared to T1D, 52.1% vs 18.3% (p=0.000) reported not going out for own groceries and 45.8% vs 14.0% (p=0.000) reported not leaving the house at all. Fear of coronavirus infection was higher in transplant recipients (VAS 5.0 (3.0 – 7.0) vs 3.0 (2.0 – 5.0), p=0.004) and glycaemic control worsened during quarantine (ΔHbA1c 1.67±8.74 vs -1.72±6.15 mmol/mol (p=0.006)). Among transplant recipients, 26.8% reported increased insulin use, 40.0% less physical activity, 41.7% weight gain, 29.2% increased anxiety and 33.3% increased stress since the start of quarantine.
Conclusions: Quarantine due to the coronavirus pandemic has significant impact on behaviour, stress, anxiety and glycaemic control in patients after β-cell replacement therapy. Health care professionals should be aware of these changes to be able to provide extra support.

Impact of the COVID-19 pandemic on daily lives, emotions and behaviours of kidney transplant recipients

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Background: While the COVID-19 pandemic has a huge impact on all our lives, it is important to assess the specific impact on those belonging to vulnerable groups in society. Kidney transplant recipients (KTRs) are one such group who are at extra risk of being infected with COVID-19 due to immune suppression. We investigated to what extent COVID-19 has had an impact on the daily lives, emotions and behaviours of KTRs.
Methods: We conducted a cross-sectional observational study, whereby we interviewed 153 KTRs between the end of April and the end of May 2020. We recruited KTRs who where transplanted between February 2019 and February 2020. We developed 7 open questions relating the COVID-19 pandemic. For depression, anxiety, loneliness, social support and medication adherence we used validated questionnaires. During the second wave (November 2020) we conducted a follow up online questionnaire. Results from the follow-up will be presented.
Results: The impact of COVID-19 on the lives of KTRs varied considerably. Symptoms of depression and anxiety were 8.5% and 7.2% respectively and social support was high. In contrast, half of participants reported feeling lonely. Level of medication non-adherence was 20.3%, which did not significantly differ to the rate prior to COVID-19. Furthermore, disruption of clinical care appeared to be limited (6.4%). Due to adequate adherence to regulations, concerns about catching COVID-19 were notably low.
Conclusions: These results highlight that, at group level, there is no clinically relevant impact on emotional and social well-being or health behaviours. At the individual level there may be a need for psychological support among some patients.

First promising results of CIAT: the expected future of the National living donor kidney exchange program

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Background: Computerised Integration of Alternative Transplantation (CIAT) programs was developed to increase the chances of highly immunized (HI) and long-waiting (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) patients. sHI patients are given priority, AB0-incompatible (AB0i) and/or HLA-incompatible matching (HLAi) is allowed. Long-waiting (LW) blood type 0 candidates (> 2 years dialysis) can opt for an AB0i match. In a simulation of the years 2015-2016 in 1 center, CIAT matched 8 out of 20 participating sHI patients. Desensitisation would have been indicated for 3 patients: 1 AB0i, 1 HLAi and 1 both AB0i and HLAi. Five could have been transplanted without desensitisation.
Methods: A pilot was established in our center from 2017 onwards to gain logistic experience, to test the algorithm and to optimize the program. Protocols have been created and pathways were developed for recognition of sHI and LW candidates, for patient information, and for logistics. Participation in CIAT as LW or sHI was discussed and decided by a standing committee.
Results: From 2017-2020 56 transplantations were accomplished through CIAT: 52 compatible, and 4 AB0i transplantations. Unfortunately, 2 HLAi transplantations were cancelled during COVID. 10 sHI patients were matched, 8 were transplanted: 5 compatible and 3 AB0i matches. Their median vPRA was 95% (range 85-100), median age 54 years (range 26-76) and median waiting time 5y(range 2y - 9y). 12 LW patients were transplanted: 11 compatible and 1 AB0i, median waiting time 3y (2y- 6y). 20 unspecified donors were included: 5 donated to the waitlist, 15 initiated chains (9 with 1 incompatible pair, 6 with 2 pairs). There were 6 kidney-exchange cycles with 2 incompatible pairs, 1 kidney-exchange cycle with 3 incompatible pairs. CIAT runs were performed between national runs. In the same period 16 pairs were transplanted through the national exchange program, transplanting 1 sHI patient.
Conclusions: The pilot yields very promising results for the sHI and LW candidates. Negotiations on national implementation, replacing the current cross-over program, are ongoing. Extrapolation of our results to national size would mean between 16-20 sHI candidates transplanted per year. Apart from an enormous health-gain for sHI and LW patients this means a vast reduction of healthcare costs.

The national desensitization program for HLA-incompatible living-donor kidney transplantation: an underused option for unsuccesful HLA-incompatible couples

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Background: Kidney transplant candidates with a broad panel of HLA-antibodies accumulate on the waiting list despite the Acceptable Mismatch (AM) and the national kidney-exchange program (KEP). Desensitization to remove donor-specific antibodies (DSA) against a living kidney donor in the national HLA-incompatible (HLAi) program is an additional option to transplant these candidates. We investigated the potential of waiting list candidates that could be referred to this program, and report the actual numbers of referrals and outcomes.
Methods: Eurotransplant and NTS documents were studied to identify highly immunized candidates. Electronic patient files were studied to report clinical outcomes. Eligibility criteria for the national HLAi program are a complement-dependent cytotoxicity (CDC) positive crossmatch with a living kidney donor and either two years participation in AM or one year participation in the national KEP.
Results: In 2019, 64 positive crossmatch couples participated in the national KEP; 41 remained without a transplant. In 2019, 19/57 Dutch candidates on the AM waiting list were transplanted. The number of AM candidates with a potential living donor is unknown. Since reimbursement in 2017, 30 consultations and 22 referrals for the national HLAi program took place.
22 referrals for the national desensitization program resulted in 14 kidney transplantations. After re-evaluation of potential donors, 7 of them received an HLA-*compatible* donor kidney. In nine candidates desensitization was performed. In two candidates the CDC crossmatch remained positive due to persistently high DQ6 (MFI 11.000 respectively 19.000 after 9 plasmapheresis sessions) and they could not proceed to transplantation. The 7 succesfully desensitized recipients (of which 3 also ABOi) are all alive with functioning grafts. Median eGFR is 40 ml/min (range 16-82) with a median follow-up of 26 months. Five recipients experienced early ABMR, of which 4 progressed to caABMR within one year. The anti-IL6 receptor blocker tocilizumab stabilized further loss of kidney function (see abstract xx). DSA remained detectable in Luminex SAB testing after desensitization, rebounded during AMR and mostly diminished over time. In general, class II DSA were more persistent than class I DSA.
Conclusions: The national HLAi desensitization program is an underused program for highly immunized candidates, as the majority of potential candidates is not referred for evaluation. Evaluation for eligibility may lead to (re)discovery of a suitable HLA-compatible donor. Transplantations performed in the HLAi desensitization program have been succesful.

Discrimination between Relevant vs Irrelevant HLA antibodies in Kidney Transplantation

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Background: Kidney transplantation is the best treatment for most end-stage renal failure patients. Success is limited by rejection reactions. In transplant rejection, patient antibodies against the HLA proteins from the donor play an important role, so-called donor-specific HLA antibody (DSA). Most of these DSA can be detected with complement-dependent cytotoxicity crossmatch assay (CDC-XM). While, with the recently developed single antigen bead (SAB) assays (Luminex technology), DSAs can be detected with increased level of sensitivity and specificity. This level of detail in DSA detection leads to luminex-defined DSA that do not cause a positive CDC crossmatch test. However, not all of these DSA are clinically relevant. The aim of the study is to deliver additional analysis to clarify the clinical relevance of all these DSA.
Methods: In order to determine the clinical relevance of all these DSA, the focus is shifted from molecular level to epitope level which provides new parameters an insight on HLA antibodies. This concept is denoted as donor epitope specific HLA antibody (DESA). In simple words, DESA are antibodies that bind to specific regions on donor HLA molecules. The assignment of DESA is done using the single-antigen bead (SAB) assay and the most likely high-resolution typing for donor and recipient. The used dataset in this analysis is comprised of 441 Dutch kidney transplants from 1995 to 2006.
Results: More than 2 DESA is associated with a higher risk of transplant rejection compared to <=2 DESA. However, one or a few DESA are enough to cause a transplant rejection. This indicates that the quantity of DESA alone is not a strong risk indicator of transplant rejection. In addition, DESA distance to the cell membrane is not a risk indicator, while other parameters like epitope accessibility, position of the DESA on HLA molecule, HLA molecule class, might be a possible risk indicator and should be further investigated. To this end, a software application is developed that visualises the 3D structure of donor HLA molecule and the regions on these molecules with the potential of antibody reactivity.
Conclusions: Thanks to the adopted approach and the defined DESA, there is the opportunity to look into more details and parameters that help specifying the clinical relevance of HLA antibodies. DESA related parameters like quantity, distance to cell membrane or HLA surface, HLA class, and position on the 3D structure, to name but a few. Some of these parameters do not depict much potential, while others seem to be more promising in defining the clinical relevance of the HLA antibodies

HLA Class I and HLA-DR antibody-verified eplet mismatch load is an independent determinant for graft failure in renal transplantation

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Background: Long-term renal transplant outcomes have not improved in the last twenty years, with chronic antibody mediated damage being a major factor. Refinement in HLA matching could result in improved graft outcomes. Eplets are polymorphic amino acid residues on mismatched HLA that can induce an antibody response. Eplets are shared between HLA molecules but the combination of eplets is unique for a given HLA allele. Importantly, not all eplets are immunogenic, and true immunogenic eplets are proven to interact with antibodies by means of antibody verification, which is a yet uncompleted endeavor. Matching for HLA antibody-verified eplets would theoretically improve long-term graft survival. However, large European studies on the effect of eplet matching on graft outcome are currently lacking.
Methods: We conducted a retrospective cohort study of kidney transplant recipients transplanted through the Eurotransplant Kidney Allocation System from 1996 to 2019 to evaluate the effect of antibody-verified eplet mismatches on transplant outcome. Allele level HLA-A, -B, -C, DRB1 and DQB1 typing data were imputed from serologic HLA-A, -B and DR types using Haplostats. Antibody-verified eplet mismatches were identified by an R-based program. Uni- and multivariate Cox proportional hazard models were fitted in a cohort of 34,401 unsensitized (PRA = 0%) first kidney transplant recipients with at least 1 HLA allele mismatch to assess the risk of death-censored graft failure (DCGF) by an increasing number of antibody-verified eplet mismatches.
Results: Multivariate Cox proportional hazard models demonstrated HLA class I and HLA-DR antibody-verified eplet mismatches to be an independent risk factor for DCGF with hazard ratios of 1.021 [95% CI 1.011, 1.031] and 1.014 [1.004, 1.025] respectively. In contrast, while significant in the univariate model, HLA class I and HLA-DR allele mismatches were not significantly associated with DCGF in the multivariate model. Whereas HLA-DQ antibody-verified eplet mismatches did have a significant effect on DCGF in the univariate model, it did not have a significant effect on DCGF in the multivariate model, in contrast to HLA-DQ allele mismatch (HR: 1.167 [95% CI: 1.073, 1.269]).
Conclusions: HLA Class I and HLA-DR antibody-verified eplet loads are independent risk factors for DCGF and a stronger predictor for graft failure than allele mismatch load. No significant effect was observed for antibody-verified HLA-DQ eplets. As currently a low number of HLA-DQ eplets is antibody-verified, there may be a role for HLA-DQ that have not yet been antibody-verified. Accordingly, future studies should be directed towards antibody verification of HLA eplets, especially of HLA-DQ.

A preliminary kidney transplant cohort study to define the most immunogenic HLA-DQ amino acid mismatches using HLA-EMMA

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Background: In renal transplantation, *de novo* donor-specific antibodies (*dn*DSA) can be formed against mismatched donor HLA antigens and are associated with inferior graft survival. These *dn*DSA are induced by polymorphic amino acids (AA) on mismatched HLA antigens and are mainly directed against HLA class II, and more specifically HLA-DQ. To ultimately prevent *dn*DSA formation without unnecessarily precluding transplants it is pivotal to define which polymorphic residues often result in an antibody response, and which not. Therefore, our aim was to define the most immunogenic HLA-DQ AA mismatches in a clinical kidney transplant cohort.
Methods: To facilitate this, we developed a software program, HLA-EMMA, containing all HLA known AA sequences and polymorphic solvent accessible (SA) AA positions per HLA locus. From multiple Dutch transplant centres we selected non-immunised male recipients that received their first renal transplant with at least one HLA class II antigen mismatch who subsequently lost their graft due to immunological failure. High resolution HLA typing of donor and recipient was performed and used to determine the SA AA mismatches for each mismatched donor HLA allele. Recipients' sera after graft failure were screened by luminex single antigen bead assays to determine *dn*DSA.
Results: The study cohort consisted of 79 donor-recipient couples of which 35% developed HLA-DQ-specific *dn*DSA upon graft failure. The chance of *dn*DSA formation was lower for 2 HLA-DQB1 or HLA-DQA1 allele mismatch compared to 1 allele mismatch, OR 0.260 (0.078-0.865) and OR 0.514 (0.150-1.762) respectively, as the sum of SA AA mismatches was often lower for double allele mismatches than for several single allele mismatches. For both HLA-DQB1 and HLA-DQA1 we observed a higher frequency of *dn*DSA with increasing numbers of SA AA mismatches. The HLA-DQB1 and HLA-DQA1 AA mismatches were grouped based on tertiles and this resulted in OR 3.788 (1.912 – 7.504) and OR 3.677 (1.908-7.086), respectively. Interestingly, a single AA mismatch appeared to be sufficient for inducing an antibody response. Unfortunately, due to the relatively low number of donor-recipient pairs, no specific AA positions or type preferentially resulting in *dn*DSA formation could be identified.
Conclusions: Overall, this cohort study showed that the HLA-EMMA software can be used for AA comparison of HLA datasets and the chance of *dn*DSA specific for HLA-DQ increases with an increasing number of SA AA mismatches. Future studies in context of the International Immunogenetics and Histocompatibility Workshop of a large and diverse cohort of kidney transplant recipients will be performed to identify the most immunogenic HLA-DQ amino acid mismatches.

Topics, Delivery Modes, and Social-Epistemological Dimensions of Web-Based Information for Patients Undergoing Renal Transplant and Living Donors During the COVID-19 Pandemic: Content Analysis

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Background: The COVID-19 pandemic has markedly affected renal transplant care. During this time of social distancing, limited in-person visits, and uncertainty, patients and donors are relying more than ever on telemedicine and web-based information. Several factors can influence patients' understanding of web-based information, such as delivery modes (instruction, interaction, and assessment) and social-epistemological dimensions (choices in interactive knowledge building). The aim of this study was to systemically evaluate the content, delivery modes, and social-epistemological dimensions of web-based information on COVID-19 and renal transplantation at time of the pandemic.
Methods: Multiple keyword combinations were used to retrieve websites on COVID-19 and renal transplantation using the search engines Google.com and Google.nl. From 14 different websites, 30 webpages were examined to determine their organizational sources, topics, delivery modes, and social-epistemological dimensions.
Results: The variety of topics and delivery modes was limited. A total of 13 different delivery modes were encountered, of which 8 (62%) were instructional and 5 (38%) were interactional; no assessment delivery modes were observed. No website offered all available delivery modes. The majority of delivery modes (8/13, 62%) focused on individual and passive learning, whereas group learning and active construction of knowledge were rarely encountered.
Conclusions: By taking interactive knowledge transfer into account, the educational quality of eHealth for transplant care could increase, especially in times of crisis when rapid knowledge transfer is needed.

Digitale flowvolumemeting na longtransplantatie, toepassing van een innovatie.

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Background: Acute rejectie na longtransplantatie is een risicofactor op het ontwikkelen van orgaan falen op langere termijn. Het meten van longfunctie is essentieel als graadmeter voor het herkennen van pulmonale problemen en mogelijk acute rejectie. De huidige meetmethode van longfunctie in de thuissituatie bestaat uit controle middels een analoge peakflowmeter. De trend van de longfunctie en de blaastechniek zijn niet inzichtelijk. Gevolg is dat de patiënt met klachten laagdrempelig gezien wordt op de polikliniek. Het doel van dit project was om na te gaan of een digitale flowvolumemeter, inclusief gebruik van een digitale omgeving, helpt in een zorgvuldiger monitoren van de longfunctie en om inzicht te krijgen in de gebruiksvriendelijkheid van een digitale flowvolumemeter.
Methods: In dit project zijn verschillende meetmethodes vergeleken. Als eerste stap is bij 15 gezonde proefpersonen de overeenkomst gemeten in de longfunctie tussen de huidige peakflowmeter, een digitale flowvolumemeter en de huidige ziekenhuismeting. In stap twee zijn de digitale flowvolumemeters getest door longtransplantatiepatiënten. 20 patiënten zijn geïncludeerd om de digitale flowvolume meter te gebruiken. Alle longfunctietests zijn uitgevoerd in zittende positie en in het ziekenhuis onder begeleiding van een longfunctieassistent. De vergelijkende meetmomenten bij de patiënt zijn gekoppeld aan reguliere poliklinische controles. Naast de metingen ontving de patiënt een (niet gevalideerde) vragenlijst over gebruiksvriendelijkheid en gebruiksgemak.
Results: Stap 1: 15 personen hebben 3 longfunctietests geblazen met de peakflowmeter, een digitale flowvolumemeter en de ziekenhuismeter. De metingen laten een hoge correlatie zien (r=0.95, p<0.01) . Stap 2: De uitslagen van de longfunctie middels de digitale flowvolume meter en de meting in het ziekenhuis laten eveneens een hoge correlatie zien (r=0.93, p< 0.01) . Gebruikers zijn tevreden over het gebruiksgemak en gebruiksvriendelijkheid van de digitale flowvolumemeter. Toegang en inzage in de digitale omgeving werd door de zorgverleners als eenvoudig en overzichtelijk ervaren.
Conclusions: Meting van longfunctie middels een digitale flowvolumemeter is betrouwbaar, de trend van de longfunctie is door gebruik van de digitale omgeving inzichtelijk voor de patiënt en de zorgverlener, en de digitale flowvolumemeter wordt door patiënten als gebruiksvriendelijk ervaren. Om te onderzoeken of de inzet van de digitale flowvolumemeter een bijdrage levert in het verbeteren van de kwaliteit en efficiëntie van de huidige zorg en de overleving is het nodig om de inzet van de digitale flowvolumemeter te verbreden en vervolgonderzoek te doen.

Simultaneous LC-MS/MS quantification of creatinine, iohexol and five immunosuppressants in volumetric microsamples for remote renal transplant recipient monitoring

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Background: Renal function and immunosuppressant exposure are considered key parameters in renal transplant recipient management. Microsampling techniques have enabled remote sample collection to enhance patient comfort and monitoring flexibility, as compared to conventional venous sampling. We developed a liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay for simultaneous quantification of tacrolimus, everolimus, sirolimus, cyclosporine, mycophenolic acid, iohexol and creatinine in microsamples for remote immunosuppressant and renal function monitoring.
Methods: A full and partial analytical validation, as per European Medicine Agency (EMA) guidelines on bioanalytical method validation, was performed for dried blood spot (DBS) and volumetric absorptive microsampling (VAMS) samples, respectively. In addition, a clinical validation was conducted with 60 paired DBS, VAMS and reference venous EDTA samples from 15 renal transplant recipients who participated in the RRFD trial (NTR7256). The extent of agreement between the three bioanalytical methods was evaluated using standard Passing-Bablok and Bland-Altman statistics.
Results: The analytical validation was successful for all analytes in DBS and VAMS samples. The following lower quantification limits were established in DBS: tacrolimus 1.2 µg/L, sirolimus 2.6 µg/L, everolimus 1.6 µg/L, cyclosporine 10.6 µg/L, mycophenolic acid 0.3 mg/L, iohexol 7.5 mg/L and creatinine 0.3 mg/dL. The clinical validation indicated good agreement between DBS and EDTA for tacrolimus (mean bias -8.99%; Passing-Bablok slope 0.87) and everolimus (-7.98%; 0.95). Conversion factors to translate capillary whole blood concentrations to plasma concentrations are required for mycophenolic acid (mean bias -29.1%; Passing-Bablok slope 0.76), iohexol (-51.4%;0.58) and creatinine (+12.7%;1.13). Substantial variation was observed for creatinine, but the assay was considered adequate for creatinine trend analysis. No sirolimus or cyclosporine samples were available. The validity of the assay for VAMS samples was acceptable, albeit outperformed by DBS.
Conclusions: A multi-analyte LC-MS/MS assay for remote immunosuppressant and renal function monitoring was developed, showing promising results which support gradual implementation in routine clinical care.

The clinical validation of a dried blood spot method for simultaneous tacrolimus and creatinine measurement

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Background: Monitoring tacrolimus concentrations and kidney function after transplantation is important to avoid tacrolimus under- and overexposure and its clinical consequences, including acute nephrotoxicity. Using dried blood spot (DBS) instead of a venipuncture for blood sampling has several advantages: it allows blood sampling at home and it makes it easier to draw blood samples at a specific or at multiple time points (e.g. for an AUC measurement).
Methods: In this study, a DBS sampling method for tacrolimus and creatinine concentration measurement in blood was clinically validated, by comparing pre-dose whole-blood and serum concentrations (for tacrolimus and creatinine, respectively) obtained by a venipuncture to concentrations measured via DBS. The need for a DBS correction factor and hematocrit correction using near infrared spectroscopy was evaluated. Deming regression was used for validation and potential bias was evaluated with a Bland-Altman analysis.
Results: A total of 50 solid organ transplant recipients was included in the analysis. We calculated the following conversion formula for tacrolimus: $[\text{Tacrolimus}]_{DBS}$+1.49)/1.788, with a Deming intercept of 0.272 (95%-CI -0.53 to 1.08) and a slope of 0.960 (95%-CI 0.84 to 1.07). Using this conversion formula, 92% of the tacrolimus measurements were within the 20% limits of agreement (LOA) and 76% of the tacrolimus measurements were within the 15% LOA. We calculated the following conversion formula for creatinine: $[\text{Creatinine}]_{DBS}$+0.8069)/0.9077, with a Deming intercept of -0.5261 (95%-CI -12.73 to 11.68) and a slope of 1.004 (95% CI 0.92 to 1.08), respectively. Using this conversion formula, 94% of the creatinine measurements were within the 15% LOA. For both tacrolimus and creatinine, no additional correction for hematocrit was required.
Conclusions: DBS sampling was clinically validated and can be used in clinical practice for simultaneous measurement of tacrolimus and creatinine with the use of a conversion formula. An additional correction for hematocrit was not required.

Clamping of cerebral circulation may improve left ventricular contractility after normorthermic regional perfusion after anoxic circulatory death in a porcine model

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Background: Heart transplantation from circulatory dead donors is emerging. Due to the warm ischaemic insult, the hearts suffer from circulatory death it is paramount to reperfuse the tissue with oxygenated blood. In situ thoracoabdominal regional perfusion is a method to perfuse and evaluate the hearts after circulatory death. It is speculated that cerebral reperfusion may produce a sympathetic storm that negatively impacts ventricular contractility.
The purpose of this study was to investigate the impact of cerebral reperfusion on cardiac contractile function during and after normothermic regional perfusion (NRP) after anoxic circulatory death in a porcine model.
Methods: The animals were anaesthetized and cerebral monitoring equipment was implanted. Biventricular pressure-volume catheters and a pulmonary artery catheter were placed percutaneously. Through a midline sternotomy, the heparinised animals were cannulated for extracorporeal circulation. Baseline data were obtained before cessation of mechanical ventilation. Death was determined 5 minutes after mechanical asystole and after additional 3 minutes of warm ischemia NRP was started using a heart-lung machine. The animals were randomized before reperfusion to either clamping (CL) (n=8) or non-clamping (NCL) (n=8) of the aortic arch vessels; the infra-renal aorta was clamped in both groups. The NRP-protocol includes early volume loading of the right ventricle, infusion of dobutamine and norepinephrine and gradual wean over 30 minutes. The animals were observed for 180 minutes after weaning from NRP.
Results: All animals were successfully weaned from NRP. Both groups demonstrated an acceptable cardiac function after weaning with a mean arterial blood pressure above 75 mmHg and low filling pressures. The Non-clamp group received significantly more norepinephrine ($p=0.0484$) than the clamp group. The left ventricle End-systolic pressure volume relationship as an index of contractility showed improvement in both groups after wean from NRP compared to baseline ($p=0.0009$). In the clamp group LV contractility showed a tendency to a better improvement compared to the non-clamp group ($p=0.226$). The RV showed preserved contractility in both groups.
Conclusions: LV contractility but not RV contractility improves after circulatory death and weaning from NRP. The improvement of the left ventricular contractility tends to be better when the aortic arch vessels are clamped compared to whole-body perfusion.

Case reports of ex situ heart perfusion in hearts donated following euthanasia

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Background: Heart transplantation with a donation after circulatory death (DCD) heart is currently subject of much interest. Within the DCD classification, international experience has been gained with DCD III hearts. Outcome is favorable in these DCD III hearts when preserved with machine perfusion. Literature on heart donation following euthanasia is, however, non-existent. Organ donation following euthanasia is increasingly performed and it is assumed that these hearts could be of sufficient quality to be transplanted. We share the results of two cases of heart donation following euthanasia with ex situ subnormothermic heart preservation and normothermic evaluation.
Methods: The data of two consecutive heart donations following euthanasia was collected prospectively, as part of an ongoing study. Informed consent was obtained from the patients themselves for heart donation for research purposes. It was only performed with concomitant clinical lung donation. Both hearts were preserved using an acellular oxygenated perfusate in a subnormothermic machine perfusion strategy. Subsequently, the hearts were evaluated on a cellular normothermic perfusion machine using an intraventricular balloon. Manual changes were made to the volume in the balloon. Function was assessed as developed pressure (P_{dev}), maximal rate of pressure rise (dP/dt_{max}) and fall (dP/dt_{min}).
Results: Heart donation following euthanasia was feasible without significant changes in retrieval protocols. Duration of machine perfusion preservation was 408 and 432 minutes, for heart 1 and 2, respectively. By the end of the evaluation, P_{dev} was 119 mmHg for heart 1, with a balloon volume of 30 mL. dP/dt_{max} and dP/dt_{min} were 1524 mmHg/s and -1057 mmHg/s, respectively. For heart 2, P_{dev} was 142 mmHg with 50 mL of balloon volume. dP/dt_{max} and dP/dt_{min} were 1098 mmHg/s and -802 mmHg/s, respectively.
Conclusions: Hearts donated following euthanasia are highly valuable for research purposes and can be of sufficient quality to be transplanted. Although only a minority of the DCD hearts will be procured following a euthanasia procedure, these hearts might have a superior function, as they are only subjected to a short agonal phase and period of ischemia. The two included donor hearts were preserved for a prolonged period of time and showed adequate function. With the implementation of ex-situ heart perfusion, patients who are to donate their organs following euthanasia could also be able to donate their hearts.

Prolonged normothermic machine perfusion of discarded human donor kidneys

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Background: In order to utilize the regenerative potential of kidneys using normothermic machine perfusion (NMP), continuous perfusion beyond 1 hour may be required. The aim of this study was to develop and test the feasibility of conducting a 6h protocol for NMP using discarded human donor kidneys.
Methods: Starting point to facilitate prolonged NMP was the clinically applied 1h protocol as previously published by Hosgood et al. Discarded deceased donor kidney grafts were perfused for 6h. A pulsatile pressure of 75mmHg at 37°C using an open venous drainage system and an oxygenated red blood cell (RBC) based perfusion solution was used. To ensure stable perfusion, key adjustments such as washing the RBCs, addition of albumin and urine recirculation were made. Throughout the perfusion renal haemodynamics were registered and perfusate, urine and tissue samples were collected.
Results: Seventeen kidneys were included (9 DCD, 8 DBD), median donor age was 63.4 (range 47-75). Organs were discarded for various surgical and medical reasons. Stable renal arterial flow (t=0hr 48.7±27.7 ml/min/100gr and t=6hrs 59.7±20.7 ml/min/100gr), arterial resistance (t=0 2.4±2.2 mmHg/ml/min and t=6hrs 1.4±0.6 mmHg) and pH (t=0 7.2±0.20 and t=6hrs 7.3±0.05) were maintained throughout perfusion. The majority (n=11) of grafts produced urine during NMP. Histological assessment showed no microscopic deterioration during the course of NMP.
Conclusions: This study showed that prolonged end-ischemic NMP is feasible and maintains structural kidney integrity. It also demonstrated that for prolonged NMP an adapted perfusate is desirable. Therefore, we strongly recommend the addition of albumin, urine-recirculation and washed RBCs for longer stable perfusions.

Magnetic resonance imaging to assess renal flow distribution during ex vivo normothermic machine perfusion in porcine and discarded human kidneys

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Background: With increased use of renal grafts from suboptimal donors, the need for objective pre-transplant organ quality assessment has become more important. Novel technologies could play a pivotal role in making pre-transplant donor organ assessment more objective and reliable. Ex vivo normothermic machine perfusion (NMP) is a potentially promising method for evaluating kidney viability prior to transplantation, since it mimics a physiological environment. While a growing number of transplant centers are adopting clinical normothermic ex vivo organ perfusion technology, we urgently need a better understanding of how physiological conditions within the organ evolve over time during NMP, and how these differ from in vivo physiology. This study utilized functional magnetic resonance imaging (fMRI) to determine how regional flow distribution develops during NMP and indicates an appropriate window for on-pump viability assessment.
Methods: Nine viable porcine kidneys from a local slaughterhouse and four human discarded kidneys were subjected to our MRI compatible setup for ex vivo normothermic perfusion. Longitudinally for 3 hours, arterial spin labeling (ASL) sequences were performed. This technique is used to quantify blood perfusion without the use of an exogenous contrast agent. Through an overlay of an anatomically detailed image with the ASL perfusion map, regions of interest (ROIs) were drawn in the cortical en medullary regions. For each time point, we calculated the ratio of the average cortical and medullar signal intensity on the perfusion map (CM ratio). Absolute flow values for the whole kidney were externally measured with a flow sensor.
Results: All kidneys showed a gradual increase of CM ratio during the experiments. Porcine kidneys (n=9) showed CM ratios of 1.2 after 30 minutes, 2.7 after 1 hour, 3.6 after 2 hours and 4.4 after 3 hours. The discarded human kidneys (n=4) had CM ratios of 1.2, 3.0, 4.5 and 6.6 after 30 minutes, 1 hour, 2 hours and 3 hours respectively. During the first 30 minutes of NMP the medulla is mainly perfused, while after approximately 2 to 3 hours a more physiological state is achieved in which renal flow distribution reaches a predominant cortical perfusion. Externally measured whole-kidney flow rates stabilized much earlier after 60-90 minutes. In vivo CM ratios in healthy volunteers are approximately between 5 and 7.
Conclusions: Flow distribution gradually shifted from mainly medullar to predominantly cortical. After 2 to 3 hours, CM ratios approach human in vivo perfusion conditions.

Complement is activated during normothermic machine perfusion of porcine and discarded human kidneys

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Background: The increasing gap between demand and supply of kidneys for transplantation has led to the increasing use of marginal donor kidneys. However, transplantation of marginal donor kidneys is associated with inferior outcome. Normothermic machine perfusion (NMP) provides the opportunity to assess donor kidneys and could be used to recondition and improve the quality of marginal donor kidneys. The impact of NMP on inflammation is largely unknown. We hypothesized that NMP activates the innate immune response, represented by the complement system, which leads to a pro-inflammatory cytokine response and affects renal function.

Methods: Both porcine (n=20) and discarded human (n=10) kidneys were perfused at 37 degrees Celsius for 4-6 hours with a blood-based perfusion solution in a pulsatile flow driven machine perfusion system. Perfusate samples were taken every hour to assess complement activation, pro-inflammatory cytokines and renal function.

Results: NMP of porcine kidneys leads to significantly increased levels of complement activation products C3a and C5b-9 in perfusate and both were positively correlated with IL-6, IL-8 and TNF-alpha levels. Porcine kidneys with high C5b-9 perfusate levels had a significant lower creatinine clearance after 4 hours of NMP. High complement perfusate levels, reflected by C3d/C3 ratio, were also seen during NMP of discarded human kidneys. In addition, kidneys retrieved from brain-dead donors had significantly higher complement C3d/C3 perfusate levels during NMP than kidneys retrieved after circulatory death.

Conclusions: The complement system gets activated during NMP of porcine and discarded human kidneys. Complement activation is positively correlated with the release of cytokines, leading to reduced kidney function. Therefore, inhibition of complement during NMP should be evaluated as a strategy to improve renal graft quality prior to transplantation.

Validation of flavin mononucleotide (FMN) to monitor the quality of donor kidneys during hypothermic machine perfusion -with or without oxygen- in kidney transplantation.

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Background: Hypothermic machine perfusion (HMP) provides excellent preservation superior to cold storage. It may also allow for organ assessment prior to transplantation, helping the clinical decision whether to accept or decline an organ. Flavin MonoNucleotide (FMN) is part of the mitochondrial NADH:ubiquinone oxidoreductase enzyme (complex I) and can dissociate from this complex after ischaemia-induced mitochondrial injury. Recently, it has been reported that FMN can be used as a biomarker of organ quality during hypothermic oxygenated machine perfusion of livers and kidneys. The aim of this study was to validate the use of FMN as a biomarker for clinical outcomes in the context of HMP preserved and subsequently transplanted donor kidneys.
Methods: Multiple perfusate samples (n=367) were obtained from the COMPARE trial in kidney transplantation, a paired randomized controlled trial comparing HMP with oxygenation (HMPO2) versus standard HMP in kidneys from donation after circulatory death (DCD) donors older than 50 years of age. FMN levels in the perfusates were assessed according to previous reports (fluorescence spectroscopy, excitation 450nm; emission 500-600nm). Fluorescence intensity (FI) was correlated with short- and long-term functional outcomes. Fluorescence findings were validated by targeted liquid chromatography mass spectroscopy (LC-MS).
Results: In both $HMPO_2$ and HMP groups, FI during machine perfusion increased over time ($HMPO_2$ p=0.0001; HMP p=0.0004). The observed increase was similar for both groups (p=0.829). No correlation, however, was found between FI and post-transplant outcomes, including day 5 or day 7 serum creatinine (p=0.0756 and p=0.1359, respectively), immediate graft function (p=0.1279), creatinine clearance and biopsy proven rejection within one year (p=0.1330 and p=0.6419, respectively). In the light of these negative findings standing in contrast to those from earlier liver and other kidney reports, we decided to perform targeted LC-MS based validation experiments on <10% of the perfusate samples to (dis)prove the presence of FMN. Our validation experiments detected FMN in one perfusate sample, but the majority (n=29) of the perfusate samples were negative.
Conclusions: We conclude that the fluorescence spectrum suggested to reflect FMN does not correlate with clinical outcomes in kidney transplantation. Moreover, we did not confirm presence of FMN in the majority of the perfusate samples. These data challenge the use of direct fluorescence as an estimate of perfusate FMN levels and suggests that, in the context of hypothermic kidney perfusion before transplantation, FMN cannot be used as a biomarker to predict kidney graft function after transplantation.

Torque teno virus load kinetics as predictor for both allograft rejection, polyomavirus and cytomegalovirus infection in kidney transplantation; a cohort joint modelling study

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Background: The main challenge of Immunosuppressive therapy in solid organ transplant recipients is to navigate safely between Scylla and Charybdis, epitomized by allograft rejection and infectious complications. Torque teno virus (TTV), a ubiquitous, non-pathogenic virus controlled by the human immune system has been proposed as a useful biomarker of functional immunity in immunocompromised patients. This study investigates whether individual TTV loads can signal over- as well as under-immunosuppression by predicting the risk of both infection and rejection in kidney transplantation (KTx) recipients.

Methods: In a retrospective cohort of 389 KTx recipients, individual TTV-loads in blood plasma were measured by qPCR, once before and four times after KTx during a one-year follow-up. The endpoints were the time to the first episode of kidney rejection, and the time to the first detection of BK polyomavirus (BKPyV) and cytomegalovirus (CMV) in blood, respectively. Repeated measures and survival data were jointly modelled in a mixed effects cox regression.

Results: Within 3 months after transplantation, TTV was detected in 100% of KTx recipients with a 1000-fold increase in viral load to approximately 10^7 genome copies/ml. Kidney rejection, BKPyV viremia and CMV viremia occurred in 23%, 27% and 17% of the patients, respectively. For every 10-fold TTV load-increase, the risk of rejection significantly decreased (HR: 0.74, CI 95%: 0.71-0.76), while the risk of BKPyV and CMV viremia was not associated with TTV-load (HR: 1.03, CI 95%: 1.03-1.04 and HR: 1.01, CI 95%: 1.01-1.01).

Conclusions: TTV load kinetics predict the risk of allograft rejection in KTx recipients, but not the risk of BK and CMV infection. The potential use of TTV load levels as a guide for optimal immunosuppressive drug dosage to prevent allograft rejection deserves further validation.

Clinical and molecular profiling can help in predicting the response to alemtuzumab treatment in kidney transplant recipients with severe or glucocorticoid-resistant acute rejection

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Background: Alemtuzumab is an effective drug for the treatment of severe or glucocorticoid-resistant acute kidney allograft rejection (AR), but can also cause severe adverse events. There is a clinical need for superior treatment stratification to assess which patients will respond to alemtuzumab treatment. This study aimed to find clinical variables and gene expression profiles related to alemtuzumab treatment response in AR.
Methods: One hundred and thirteen patients from the Erasmus MC, that were treated with alemtuzumab for severe or glucocorticoid-resistant AR in January 2012 until January 2018 were included in this retrospective study. Clinical characteristics were retrieved from electronic health records. mRNA was isolated from formalin-fixed paraffin-embedded tissues of diagnostic kidney transplant biopsies and used for targeted gene expression profiling using the Banff-Human Organ Transplant panel of NanoString®. Response to alemtuzumab treatment was defined as allograft survival plus an estimated glomerular filtration rate (eGFR) above 30 mL/min/1.73 m^2 at 1 year after alemtuzumab therapy. The advanced analysis module of nSolver software and SPSS statistics were used to analyze the data.
Results: For clinical variable analysis, data of 101 patients (50 responders and 51 non-responders) was available and for gene expression analysis mRNA samples of 58 patients (29 responders and 29 non-responders) were available. Multivariate analysis identified three clinical factors that were associated with a good response to treatment: early timing of AR (<3 months after transplantation: 64% of responders and 41% of non-responders, p=0.002), a low delta eGFR between baseline eGFR and eGFR at the moment of AR (<25%/25-50%/>50%: responders:18/15/4 and non-responders: 11/11/15, p=0.01), and glucocorticoid maintenance therapy at the time of AR (90% of responders and 65% of non-responders, p=0.002). In addition, gene expression analysis revealed that genes involved in the B-cell receptor signaling pathway were related to inferior response to therapy.
Conclusions: Alemtuzumab treatment appears to be most effective in patients with severe or refractory AR in whom the diagnosis is made less than three months after transplantation, kidney function loss is limited and those who are on glucocorticoid maintenance therapy. Moreover, patients with high expression of B-cell receptor signaling genes are less likely to respond to alemtuzumab therapy. These findings can add to the development of superior stratification of patients who will benefit from alemtuzumab treatment.

Evaluation study of protocol kidney transplant biopsies: the presence of subclinical rejection and its relationship to graft outcome

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Background: Previous studies have proven that protocol biopsies at three months after transplantation can show early signs of rejection, not detectable by conventional tests for monitoring graft function. These signs of subclinical rejection (SCR) can be useful in predicting kidney allograft outcome. In this study we investigated whether patients with SCR in protocol biopsies had decreased graft function in the months following. Furthermore we considered the value of inflammation in scarred areas of kidney tissue or i-IFTA in protocol biopsies.
Methods: We included 103 patients who received a donor kidney and underwent a protocol biopsy three months after transplantation within the period of June 2017 to June 2020. All biopsies were scored according to Banff classification. All patients were followed up until October 2020.
Results: Signs of SCR were seen in protocol biopsies of 32 (31.0%) patients, either borderline changes (N=23) or acute T-cell mediated rejection (N=12). There was no difference in mean plasma creatinine levels within the first year after transplantation for patients with SCR (125.3 ± 33.5 µmol/L) and patients without SCR (126.7 ± 39.5 µmol/L) (p=0.862). Banff scores in i-IFTA were higher in patients with SCR (p≤0.000), in patients with a living donor and in patients with a cold ischemia time (CIT) >16h.
Conclusions: Patients with SCR in protocol biopsies show similar graft function within the first year following transplantation without receiving treatment for rejection. i-IFTA was higher in patients receiving a graft from a living donor, potentially since HLA-mismatch was significantly higher in this group.

A single nucleotide polymorphism within the FCGR3A 158 F/V gene is associated with decreased survival of renal allografts with chronic active antibody-mediated rejection

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Background: Long-term allograft survival has shown little improvement over the last decades. An important factor compromising long-term allograft survival in kidney transplantation is chronic active antibody mediated rejection (c-aABMR). Histomorphologic lesions of c-aABMR develop over time and are associated with recurrent and episodic endothelial cell activation by immunoglobulin G (IgG)-antibodies recognizing donor-specific leukocyte antigens (HLA) (DSA) or non-HLA antigens. Immune cells expressing Fc-receptors (FCGRs) interact with IgG antibodies bound to endothelial cells and genetic variation in *FCGR* genes may affect susceptibility for antibody-mediated rejection. Natural killer (NK) cells express the Fc-receptor CD16 (*FCGR3A*) and could therefore mediate renal endothelial cell damage in cases of c-aABMR. The V/V-genotype of the *FCGR3A* 158 F/V single nucleotide polymorphism is associated with increased CD16 expression and cytotoxicity by NK cells. This study evaluated whether this genotype is associated with the diagnosis of c-aABMR and renal allograft loss. Methods: Cases of c-aABMR (N=133) and control kidney transplant recipients without c-aABMR (N=116) were genotyped for *FCGR3A* 158 F/V. In addition, CD16 expression by NK cells and CD16-dependent NK-cell function were evaluated. Follow-up of cases of c-aABMR was until 1st of January 2020 and graft loss/failure was defined as the need for dialysis or a retransplantation. The date of diagnosis of c-aABMR and date of graft failure were used to calculate graft survival upon diagnosis. Results: The distribution of the *FGCR3A* 158 F/V-genotypes was not different for c-aABMR cases compared to control kidney transplant recipients (P=0.65). The V-allele was associated with increased median fluorescence intensity (MFI) of CD16 by NK cells (MFI $3.5x10^4$ versus $1.3x10^4$ for V/V and F/F-genotype, P<0.001). Increased expression of CD16 correlated with CD16-dependent degranulation of NK cells (R=0.4; P=0.02). Moreover, the V/V-genotype was significantly associated with a higher glomerulitis score and an independent risk factor (HR 1.98; P=0.04) for decreased allograft survival. Death-censored graft survival in c-aABMR cases at 3 years follow-up was 33% for the *FCGR3A* 158 V/V-genotype versus 62% for the F/F-genotype.
Conclusions: In conclusion, the *FCGR3A* V/V-genotype increases CD16-mediated NK cell cytotoxicity and is associated with a higher glomerulitis score and decreased renal allograft survival in cases with c-aABMR.

Tocilizumab for the treatment of chronic-active antibody-mediated rejection: a case series

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Background: Chronic active antibody-mediated rejection (c-aABMR) is a major cause off late graft losses. After diagnosis the prognosis is poor with no proven effective treatment although administration of high dose methylprednisolone pulse (MPS) with IVIG may mitigate progressive eGFR loss. A publication of an uncontrolled series of c-aABMR patients indicated that treatment with the IL-6 receptor blocker tocilizumab may be able to prevent graft loss (Choi, AJT 2017). We report our experience with tocilizumab as treatment for ongoing ABMR after HLA-incompatible kidney transplantion or c-aABMR cases, unresponsive to our standard treatment MPS and IVIG.
Methods: Tocilizumab was administered once every 4 weeks 8 mg/kg intravenously with a maximum dose of 800 mg. To estimate effectiveness, eGFR and proteinuria changes over time in the 6 months before and 6 months after starting tocilizumab treatment were compared.
Results: Tocilizumab has been started in 15 recipients. In 6 HLA-incompatible (HLAi) transplant recipients, median proteinuria had decreased by 42% at month 6 after tocilizumab, while proteinuria had increased by 89% in 6 months prior to tocilizumab. Median eGFR decreased by 5% at month 6, while eGFR loss was 26% in 6 months prior to tocilizumab. In all 6 patients donor-specific antibody MFI levels decreased during treatment.
In 7 recipients of an HLA-compatible transplant, 4 had at least 6 months of follow-up. In these 4, median proteinuria increased by 2% at month 6, while proteinuria had increased by 19% in 6 months prior to tocilizumab. Median eGFR decreased by 5% at month 6, while eGFR loss was 10% in 6 months prior to tocilizumab. Two of these recipients were considered non-responders and tocilizumab was discontinued.
Two pediatric recipients aged 11 were treated with tocilizumab. Treatment was discontinued after 10 sessions because of lack of therapy (rise in creatinin by 19% and no effect on proteinuria) respectively after one infusion because of pneumonia.
Four follow-up biopsies were performed, revealing ongoing c-aABMR despite clinical response to treatment in 2 c-aABMR and 2 HLAi recipients.
One recipient contracted covid infection and recovered without hospital admission. Leucopenia was frequently seen and dose reductions were required in 5 recipients (nadir leucocytes 0.6-3.0 x10e9/L). Seven recipients developed hypertriglyceridemia (3.4-17.3 mmol/).
Conclusions: Tocilizumab treatment is safe. Although microvascular inflammation may persist, tocilizumab slows down progressive loss of eGFR in c-aABMR refractory to standard treatment in 8 out 11 recipients.

Chronic allograft enteropathy treated with vedolizumab

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Background: The most common cause of late graft loss in intestinal transplantation is chronic allograft enteropathy (CAE). The diagnosis is often delayed because of late symptoms and signs, and the only available treatment is graft enterectomy. We present a patient who developed CAE 15 years post-transplantation and was treated with vedolizumab, a gut-specific α4β7 integrin blocker that is used for inflammatory bowel disease.
Methods: We show the clinical, endoscopic, radiological (PET-CT), serological and histopathological course of CAE beginning with discovery of the first signs of disease until 15 months after the start of vedolizumab treatment.
Results: Inflammatory signs seen in endoscopies and PET-CT minimised since beginning treatment with vedolizumab. The patient underwent partial resection of the fibrotic distal end of the ileum and remains in good condition ever since. We have discovered signs of expression of the α4β7 receptor, MAdCAM-1, in the stenotic vessels of the resected ileum.
Conclusions: To our knowledge, this is the first use of vedolizumab in chronic allograft enteropathy, providing evidence of its utility as a rescue therapy to extend graft survival and maybe avoid resection altogether.

The non-muscle splitting mini-open donor nephrectomy is a safe alternative in the laparoscopic era of live kidney donation

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Background: Live donor kidney transplantation is very successful and associated with limited donor morbidity. Still, efforts to minimize the risk for otherwise healthy donors remain essential. At our center, a mini-incision open donor nephrectomy (MINI) technique has been used since the 1990s. The MINI technique is unique in its non-muscle splitting, extraperitoneal approach through the anterior abdominal wall. For more than a decade, this technique has been used parallel to full laparoscopic live donor nephrectomy (LDN). The aim of this study was to assess the results and safety of the MINI technique for donors when compared to the current gold standard of LDN.
Methods: All live kidney donors at the Leiden University Medical Center between 2011 and 2019 were analyzed (642 donors: 287 MINI and 355 LDN). Earlier nephrectomy procedures were excluded to minimize time-related effects. The primary outcome of this study was short-term (<30 days) complications, as graded by the Clavien-Dindo system. Secondary outcomes included long-term complications, operating time, first warm ischemia time and blood loss. Multivariable regression analysis was conducted including multiple perioperative factors and surgical technique to identify possible associations with outcome.
Results: No donor mortality was observed. 11.1% of all donors experienced complications, while 0.7% experienced multiple complications. 88.7% of all complications were considered minor. Seven donors (1.1%) experienced a major complication that required surgical reintervention. Six LDN procedures were converted to hand assisted procedures and three to open procedures. MINI donors were significantly older (55 ±11 yr vs LDN 52 ±12 yr, p≤0.002) compared to LDN donors. In a multiple regression analysis, MINI was not associated with higher Clavien-Dindo graded complications or prolonged hospital stay. MINI technique was associated with more blood loss (275 ±382 ml vs LDN 136 ±201 ml, p≤0.001) but also with shorter operating time (175 ±40 min vs LDN 187 ±41 min, p≤0.001) and shorter warm ischemic time (100 ±56 sec vs LDN 296 ±117 sec, p≤0.001). One-year post-operative kidney function (eGFR) was not significantly different between MINI and LDN donors (57.1 vs. 56.6 ml/min/1.73m^2, p=0.648).
Conclusions: In general, this study confirms the perioperative safety of live donor kidney donation in modern practice. Complication rates of both MINI and LDN procedures are limited. Depending on availability, experience and preference, non-muscle splitting MINI remains a safe and feasible alternative option for live kidney donation in the present laparoscopic era.

External ureteric stent or internal double J stent placement in renal transplantation: effect on the occurrence of urinary tract infections and urologic complications?

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Background: Urinary tract infections (UTIs) and urologic complications are common after renal transplantation. Next to urinary tract surgery, catheter and stent placement are important risk factors for developing UTIs. Intraoperative stent placement could reduce, however, the risk of urologic complications. In September 2014 our protocol changed from external ureteric stent (ES) to internal double J stent (DJ). We analysed the incidence of UTIs and urologic complications in renal transplant patients between ES and DJ.
Methods: We performed a retrospective study of 711 kidney recipients, transplanted between September 2012 and December 2016 (2 years before and after protocol change, 6 months protocol transition). Ureteral reimplantation was done following the Lich-Gregoir technique and ES were removed after 7-12 days and DJ 3-4 weeks after transplantation. Initial immunosuppression regimen consisted of basiliximab induction, tacrolimus or ciclosporin, mycophenolate mofetil, and steroids. Follow-up period for this study was 6 months. A UTI was defined as clinical suspicion/leukocyturia and/or positive urine culture ($\geq 10^5$ CFU/ml) and the need for antibiotic treatment. Urologic complications were defined as urinary leakage, ureter stenosis or urinary retention requiring an intervention (surgery or catheter placement).
Results: In 412 (57.9%) patients an ES was used and in 299 (41.2%) a DJ; median age was 55 years for both groups and ±40% were women. Pre-emptive transplantation was performed more frequently in the ES group compared to the DJ group (33.3% vs. 22.4%; p=0.002). There was an equal distribution in both groups regarding living and deceased donor kidneys. In the ES group, 114 (28.6%) patients experienced ≥1 UTI within the first 6 months compared to 62 (21.3%) in the DJ group (p=0.029). Also, the cumulative incidence over time of a first UTI was higher in the ES vs. DJ group (28.2% vs. 21.1%, HR 1.40 (95% CI 1.04–1.89; p=0.031). The frequency of urological complications was comparable (12.5% ES, 10.0% DJ p=0.296): urinary leakage 3.0% and 1.0%; ureter stenosis 7.0% and 5.8%; urinary retention 3.8% and 3.4% for ES and DJ respectively.
Conclusions: Intraoperative use of an external stent compared to an internal double-J stent is associated with a higher incidence of UTIs within 6 months following renal transplantation. There is no difference in urological complications between ES and DJ. The change in protocol is therefore justified.

Magnetic ureteral JJ stents in cadaveric kidney transplantation: initial results

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Background: Placement of a double-J-stent (JJ) in kidney transplantation is broadly implemented to reduce transplant ureter strictures after transplantation. However, cystoscopic removal is required. The use of magnetic ureteral stents and removal with a magnetic transurethral retrieval device offers an alternative and prevents the need for cystoscopic equipment. In this study we evaluate our first results of using the magnetic ureteral JJ stent in cadaveric kidney transplantation.
Methods: Retrospective analysis of prospectively collected data of our first 74 cadaveric kidney transplant patients with magnetic stent insertion during the operation. The 6F, 15cm long magnetic ureteral JJ stent was used in all cases and removed after approximately 3 weeks. Medical records were reviewed to obtain data on demographics, successful retrieval rate and complications.
Results: Data of 74 patients were reviewed. 38 (51.4%) males and 36 (48.6%) females received a magnetic stent with a mean age of 55.3 years. The median duration of JJ stent indwelling was 23 (+/- 7.3) days. Overall, 60 (81.1%) magnetic stents were successfully retrieved, 11 (14.9%) needed cystoscopy, in 2 (2.7%) females the stent was spontaneously dislocated. There was no significant difference in retrieval based on gender (p= .288) or pre-transplantation urine production (p=.401). No learning curve in retrieval was observed when comparing the first 37 patients to the last 37 patients (p=.597). There were 2 (2.7%) complications after removal of the stent. Both of them needed a nephrostomy catheter due to post-renal obstruction. 1 patient eventually required surgery. No patients developed an urinary tract infection.
Conclusions: In an initial series of 74 patients, removal of a magnetic JJ without cystoscopic equipment in cadaveric kidney transplant patients appeared to be safe considering the high successful retrieval and low complication rate.

Antithrombotic Management by European Kidney Transplant Professionals – A survey study

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Background: In kidney transplant recipients, renal graft thrombosis (RGT) is a rare, but feared complication due to its relentless consequences, limited treatment possibilities and the high incidence of early graft loss. Currently, there is no clear evidence-based international antithrombotic protocol for kidney transplantation, but antithrombotic prophylaxis is often used in order to prevent RGT. The aim of this survey was to obtain a pan-European view of the different antithrombotic management strategies applied in kidney transplantation.
Methods: An online 22-question survey on the use of antithrombotic agents was distributed through e-mail and through various platforms of the European Society for Organ Transplantation. Participants were medical specialists working in the field of kidney transplantation. Questions covered demographic information, whether one would start, continue, or stop specific antithrombotic agents, and which donor and recipient factors influenced their decision.
Results: In total, there were 75 responses from 21 countries and 51 transplant centers: 56 (75%) respondents had more than 10 years' experience, 48 (64%) were surgeons and 23 (31%) nephrologists. Fifty-six (75%) respondents reported the availability of a written protocol on antithrombotic management. In 8 (16%) centers, there was a disagreement between respondents from the same center. Forty-seven (78%) respondents would prefer using antithrombotic prophylaxis independent of the available protocol. Vitamin K antagonists (69%), Direct Oral Anticoagulants (79%) and at least 1 agent of Dual Antiplatelet Therapy (85%) were most likely to be discontinued prior to transplantation, because of an estimated increased risk for bleeding (92%). Intraoperatively, 32% of respondents administer intravenous unfractionated heparin in selected cases and 18% in all cases, with doses varying between 400 and 10.000 international units. Postoperatively, 50% prescribes subcutaneous LMWH and 19% intravenous unfractionated heparin. Vascular reconstruction (64%), atherosclerosis of the recipient (60%) or history of deep venous thrombosis/ pulmonary embolism (73%) were the most common reasons to optimize antithrombotic prophylaxis.
Conclusions: Despite the overall preference for antithrombotic prophylaxis in kidney transplantation, there is a high variation within Europe regarding type and dosis, most likely due to a paucity of high quality studies. This warrants further research in order to develop better guidelines.

Donor lung clots and emboli: frequency, composition and estimated age.

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Background: Apart from gas exchange, the lungs form a filter to blood-borne particles such as emboli and have great thrombolytic capacity. In lung donation, the presence of clots is linked to a lesser quality of the graft. Therefor clots are removed during lung procurement by means of a ex vivo Retrograde flush However, it is likely that retrograde flush does not remove all clots. To further improve lung graft quality, a treatment to targeting donor lung clots could be beneficial. Therefor we studied the histology of these clots.
Methods: Since January 2019, retrograde flush fluid was collected and immediately filtered. Additionally fluid obtained by a second retrograde flush fluid from lungs that went on EVLP was treated similarly. The material left in the filters was fixed on formalin, processed into two slides and stained with haematotoxylin-eosin (HE) or Martius Scarlet blue (MSB).
Age determination in this research was based on the histological aspect of fibrin and presence of red blood cells. Red blood cells are highly present in fresh clots but older clots are completely free of them. Clots were categorized in the following groups, from young to old:
Type A made up of mostly red blood cells and little fibrin. Type A is very fresh coagulation were fibrin has not yet formed fibers.
Type B Long Fibrin Fibers usually through the entire length of the clot. Further a high percentage of non-lytic red blood cells is found.
Type C The presence of Red blood cells becomes less dominant. The long fibrin fibers become dense and are connected to each other forming an mesh.
Type D Densely packed mature fibrin that lost its fiber mesh structure. Red blood cells are hardly seen.
Type E Non thrombi material/fat/bone marrow/ Bone fragment occasional findings of tissues unrelated to coagulation.
Results: 129 clots were found ranging from 0,4mm to 70mm. No lung was totally free of clots. 40 % of the lungs released additional clots at the second retrograde flush at EVLP. Most clots (90/129) were relatively fresh (Type A,B or C). Older clots, 39/129 were placed in category D, they are at least days old, and formed before donation procedure. Fat and bone marrow emboli are common, as literature has suggested. In the context of a trauma donor pieces (2mm) of Avital bone were found.
Conclusions: All donor lungs contain clots. Clots can be fresh but some are days old, making them less susceptible to thrombolysis. Current preservation procedures such as the retrograde flush remove a portion of the clots, however in 40% of the cases clots additional clots were found at a second retrograde flush at EVLP. Therefor thrombolytic treatment could be beneficial to donor lung quality.

Clinical experience with bariatric surgery prior to liver transplantation

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Background: As a result of the obesity epidemic there has been an increase in the combination of bariatric surgery (BS) with simultaneous or subsequent liver transplantation (LT). However, clinical experience with combined BS and LT is limited. This study aimed to analyze this experience in the north of the Netherlands.
Methods: A single-center retrospective observational cohort study was performed, including all patients that had both BS and LT. Patients' characteristics, weight, LT procedures, and complications were analyzed.
Results: Seven patients that had BS prior to full-size LT were identified. LT (all donation after circulatory death) was performed in 4 women (57%) between 2014 and 2020, median age 56.5 (IQR 48.6-57.0) years, LT follow-up 2.7 (IQR 1.2-3.2) years. Bariatric procedures included laparoscopic roux-en-y gastric bypass (3), omega loop gastric bypass (2), sleeve gastrectomy (1), and open biliopancreatic diversion (1). Indications for LT were non-alcoholic steatohepatitis (NASH) cirrhosis (5), hepatocellular carcinoma and NASH (1), subacute liver failure (1). Median body mass index (BMI) decrease between BS and LT was 14.5 kg/m^2 (IQR 12.2-16.2), BS-LT interval 2.2 years (IQR 1.4-5.0)). Diabetes resolved in 4 patients.
Degree of intra-abdominal adhesions during LT procedure was described as minimal (1), mild (4), and severe (2). Hepatectomy was classified as difficult in 5 cases (4 due to portal hypertension (PH)). Median surgery time, warm ischemia times and cold ischemia times were 583 (n=6) (IQR 556-657), 46 (IQR 39-49) and 444 (IQR 399-723) minutes. Median estimated blood loss was 4.5 L (IQR 3.0-5.9). Relaparotomy was required in 3 patients due to bile leakage and/or hepatic artery thrombosis, 1 requiring re-LT. This patient died 3 months later due to infections and severe critical illness polyneuropathy. Initial LT was complicated by severe adhesions (after open BS and other surgery) and PH, leading to massive blood loss. Biliary stricture developed in 4 cases, all requiring percutaneous transhepatic cholangial drainage. During follow-up 6 patients had a well-functioning graft.
Conclusions: These data show that LT after BS is challenging but feasible, in line with data from other countries. BS prior to LT may lead to difficult hepatectomy through presence of adhesions, increasing with multiple prior surgeries. Our results imply that previous BS should not be a contraindication for LT and could be of benefit for certain patients to reduce BMI and resolve diabetes prior to LT.

Modifying the RETREAT score to predict recurrence of hepatocellular carcinoma after liver transplantation: a focus on PIVKA-II, tumor differentiation grade and tacrolimus trough levels

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Background: A reliable prediction model for hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) could help in developing a surveillance strategy and early detection and treatment of HCC recurrence prolonging the survival after recurrence. Recently, the RETREAT score, based on tumor parameters, microvascular invasion and alpha-fetoprotein (AFP) at time of LT, was created and externally validated. We aimed to investigate whether the addition of new biomarkers or tumor differentiation grade improves the predictive value of the RETREAT score and studied the relationship between standard immunosuppression and its impact on HCC recurrence.
Methods: Retrospective single center cohort study including all consecutive patients transplanted for HCC between 1989 and 2020. Biomarkers such as AFP and protein induced by vitamin K deficiency or antagonist-II (PIVKA-II) were determined. Data on tumor differentiation grade and immunosuppressive regimen were retrieved from patients records.
Results: The study cohort consisted of 206 patients, 129 patients were included in the biomarker analyses, 157 in the tumor differentiation grade analyses and 174 in the analyses of tacrolimus trough levels. 165 patients (80,1%) were male and 36% had viral hepatitis as underlying liver disease. 42 patients (20,4%) exceeded Milan Criteria (MC) based on explant pathology reports. HCC recurrence occurred in 27 patients (13,1%). Median AFP was 7,0 ng/mL (4,6-20,2) and PIVKA-II 72,5 mAU/mL (41,0-211,8). In patients with a lower recurrence risk, i.e. AFP < 8 ng/mL, or within MC, a low PIVKA-II (<90 mAU/mL) was associated with a better recurrence free survival (RFS) (p=0,008 and p=0,035). A poorly differentiated tumor was associated with a worse RFS (p=0,002) compared to well or moderately differentiated tumors. Patients with HCC recurrence tended to have a higher tacrolimus trough level. A higher mean tacrolimus trough level showed a trend towards a worse RFS.
Conclusions: Addition of PIVKA-II can further optimize the predictive value of the RETREAT score and tumor differentiation grade might be useful to further stratify patients with a high RETREAT score. Finally, this study implies that the level of tacrolimus might influence HCC recurrence and therefore we should aim for the lowest tacrolimus level possible.