Discarded kidneys from deceased donors: how far can we push the boundaries?

Maria Darema

Nephrologist

Department of Nephrology and Renal Transplantation, National and Kapodistrian University of Athens Medical School,
Laiko General Hospital, Athens, Greece

Disclosures

- I have no financial relationships to disclose relevant to my presentation
- My presentation does not include a discussion of off-label or investigational drugs

Kidney transplantation vs. Long-term Dialysis

- Improved patient survival
- Better quality of life
- Reduced costs to the health service

Kidney transplantation is confronted with an organ shortage

A large proportion of deceased donor kidneys are discarded

Organ “discard” definition

“**An organ recovered for the purpose of transplantation but not transplanted**”

AST | AMERICAN SOCIETY OF TRANSPLANTATION

Discard rates

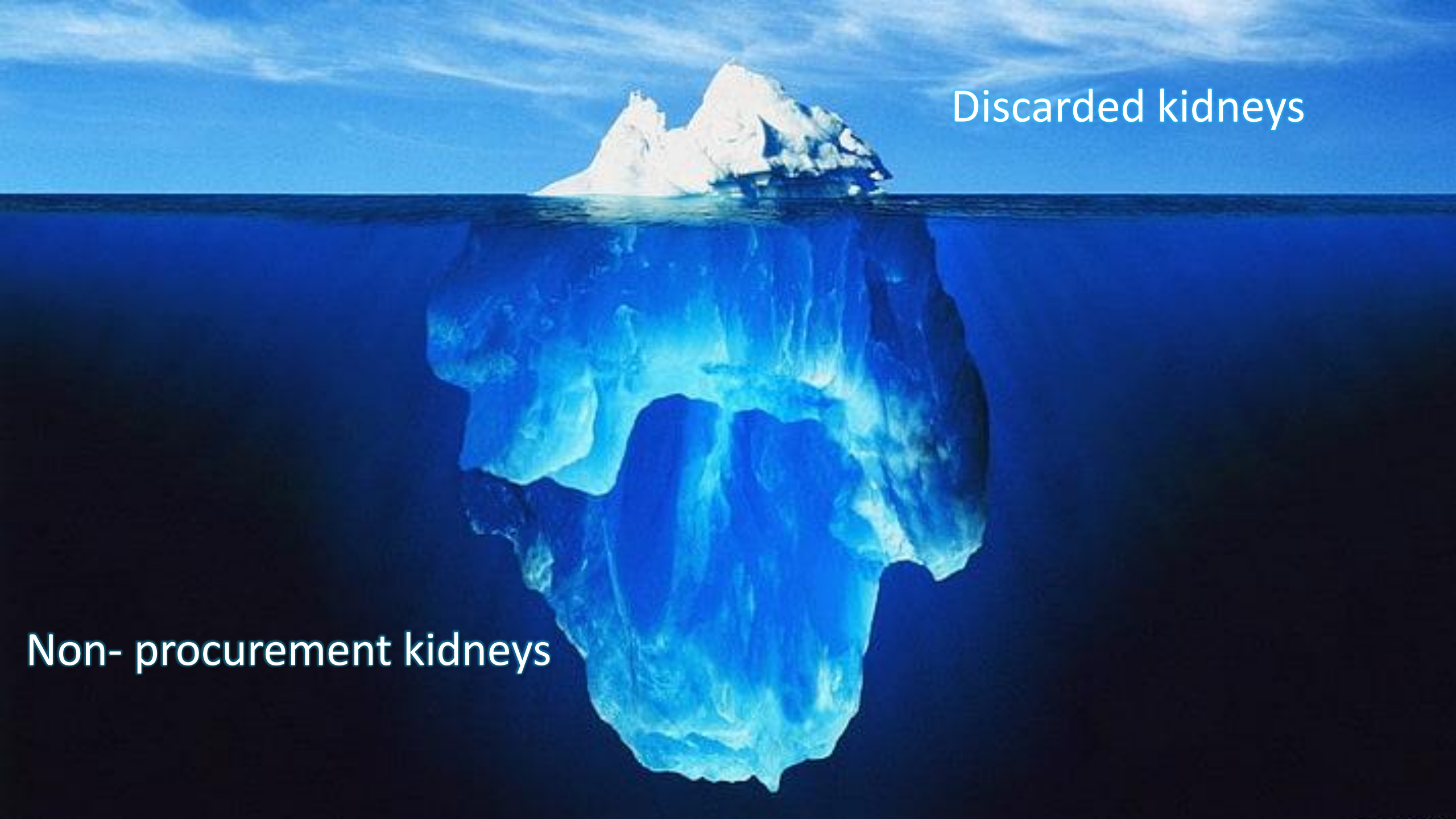
- **In the US**: 2022: **25%** (with KAS250)
  2021: 21%
  2018: 20%
  2010-2015: 18-19%
  1988: 5.1%

- **In the UK**: 10%-12%

- **In France**: 9%

- **Eurotransplant**: 8%

Curr Opin Organ Transplant 2023, 28:145–148
Am J Transplant. 2020;20:1309–1322
Curr Opin Organ Transplant 2019;24:92-96


Discarded kidneys
Non- procurement kidneys

Kidney utilization in the Netherlands – do we optimally use our donor organs?

Background

To ensure optimal utilization of deceased donor kidneys, it is important to understand the precise reason why kidneys are discarded. This study aimed to obtain a comprehensive overview of kidney utilization and discard during the entire donation process in the Netherlands.

Methods

Retrospective cohort study
The Netherlands

Kidney utilization study
3856 kidneys
2015 – 2020

Case-by-case assessment
To determine the moment of and reason for discard

Results

34.2% ...discarded for subjective presumption of impaired organ quality

66.0% ...discarded for acute kidney injury had AKI stage 1 or 2

Conclusion

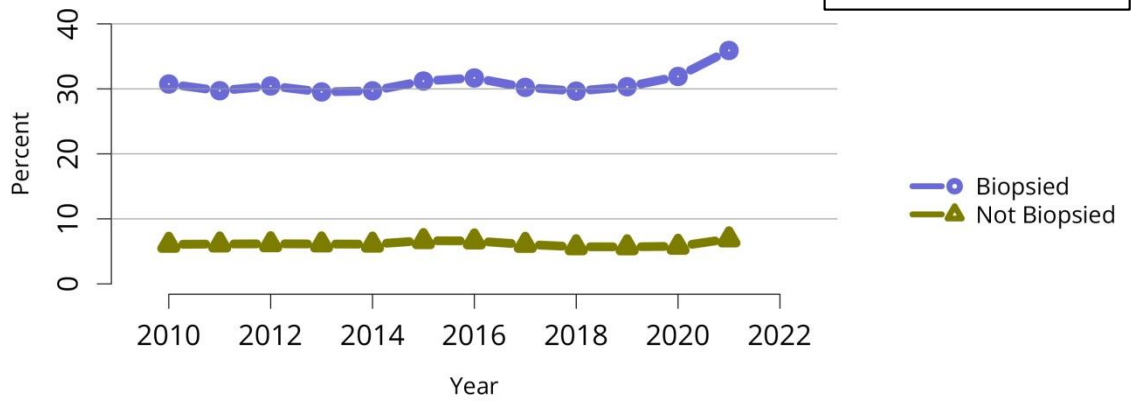
The classical definition of organ discard underestimates the non-utilization of deceased donor kidneys. Several strategies in the entire donation process could have a positive impact on kidney utilization.

NEPHROLOGY DIALYSIS TRANSPLANTATION

Schutter, R., et al. NDT (2022)
@NDTSocial

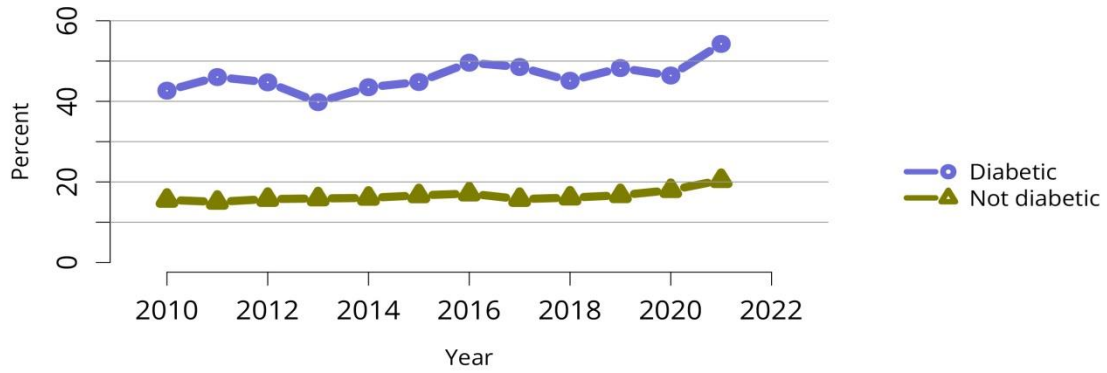
Percent of kidneys recovered for transplant and not transplanted by donor biopsy status

up to 35.9% in 2021



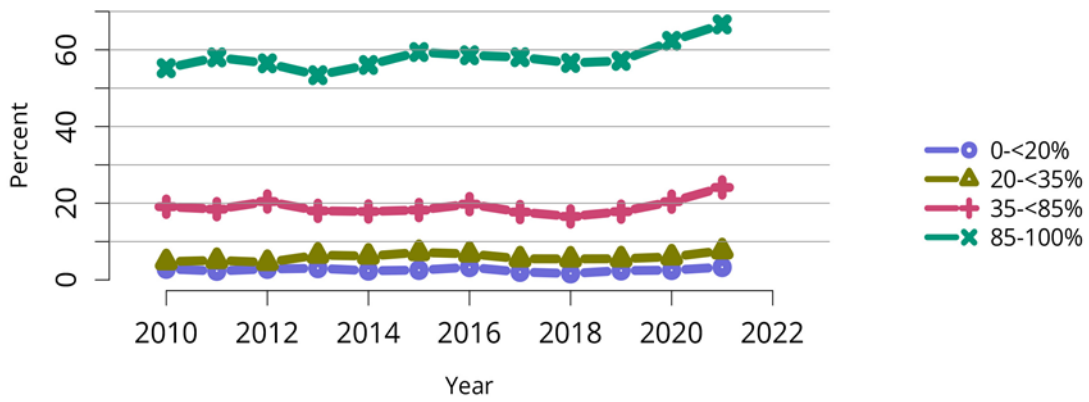
OPTN/SRTR 2021 Annual Data Report

Percent of kidneys recovered for transplant and not transplanted by donor diabetes status



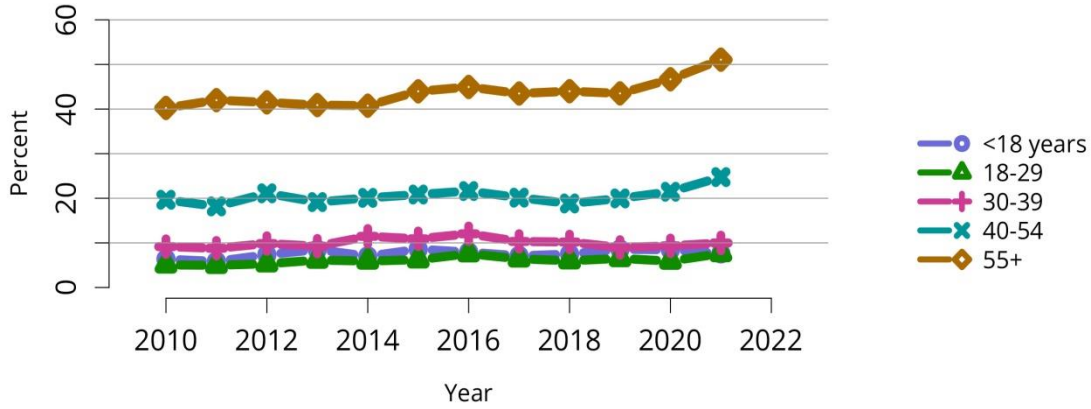
OPTN/SRTR 2021 Annual Data Report

Percent of kidneys recovered for transplant and not transplanted by KDPI



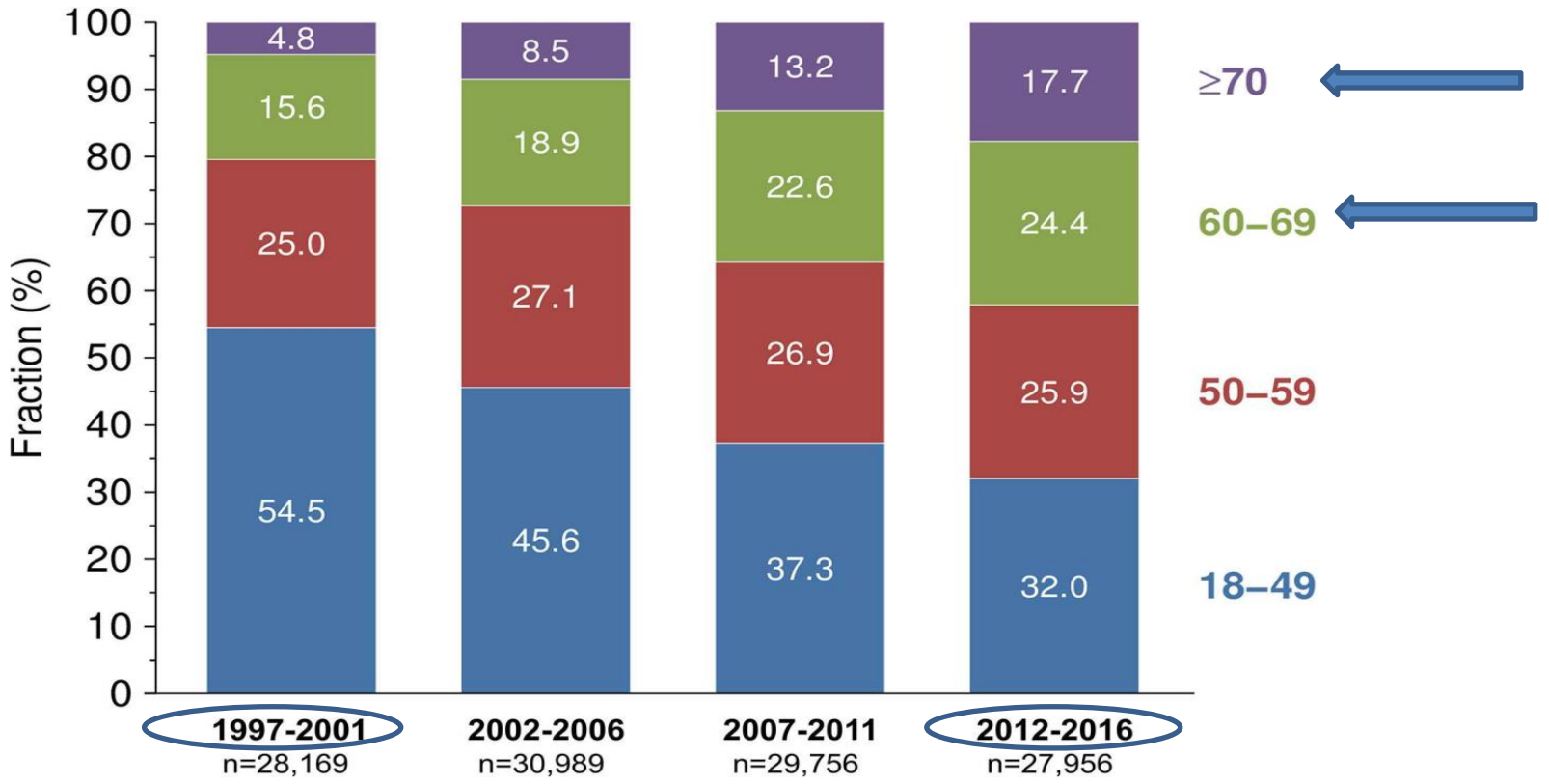
OPTN/SRTR 2021 Annual Data Report

Percent of kidneys recovered for transplant and not transplanted by donor age



OPTN/SRTR 2021 Annual Data Report

Kidneys From Elderly Deceased Donors—Is 70 the New 60?



Data: 23 European countries
116,870 patients

Development of donor age in European adult recipients of first DD kidney transplants across different time periods

Front Immunol 2019;10:2701

Kidneys From Elderly Deceased Donors—Is 70 the New 60?

- Within only one further decade (1997–2006 vs. 2007–2016) the **5-year death censored graft survival** of kidneys from **≥ 70-year-old donors** improved to the level of kidneys from 60 to 69-year-old donors in the previous decade

Data: 23 European countries
116,870 patients

Front Immunol 2019;10:2701

Factors leading to the discard of deceased donor kidneys in the United States

Sumit Mohan[1,2,3], Mariana C. Chiles[1,3], Rachel E. Patzer[4,5], Stephen O. Pastan[6], S. Ali Husain[1,3], Dustin J. Carpenter[7], Geoffrey K. Dube[1], R. John Crew[1], Lloyd E. Ratner[7] and David J. Cohen[1]

Kidney International (2018) 94, 187–198

SRTR registry

212,305 deceased donor kidneys - from 2000-2015

36,700 kidneys were discarded (17.3%)

- **bilateral discards**: both kidneys from a donor were recovered and discarded
- **single discards**: one kidney was recovered and discarded
- **unilateral discards**: one kidney was discarded while the partner kidney was transplanted

Factors leading to the discard of deceased donor kidneys in the United States

Sumit Mohan[1,2,3], Mariana C. Chiles[1,3], Rachel E. Patzer[4,5], Stephen O. Pastan[6], S. Ali Husain[1,3], Dustin J. Carpenter[7], Geoffrey K. Dube[1], R. John Crew[1], Lloyd E. Ratner[7] and David J. Cohen[1]

Kidney International (2018) 94, 187–198

SRTR registry

212,305 deceased donor kidneys - from 2000-2015

36,700 kidneys were discarded (17.3%)

'Biopsy Findings' (38.2%): the most commonly reported reason for discard

Factors leading to the discard of deceased donor kidneys in the United States

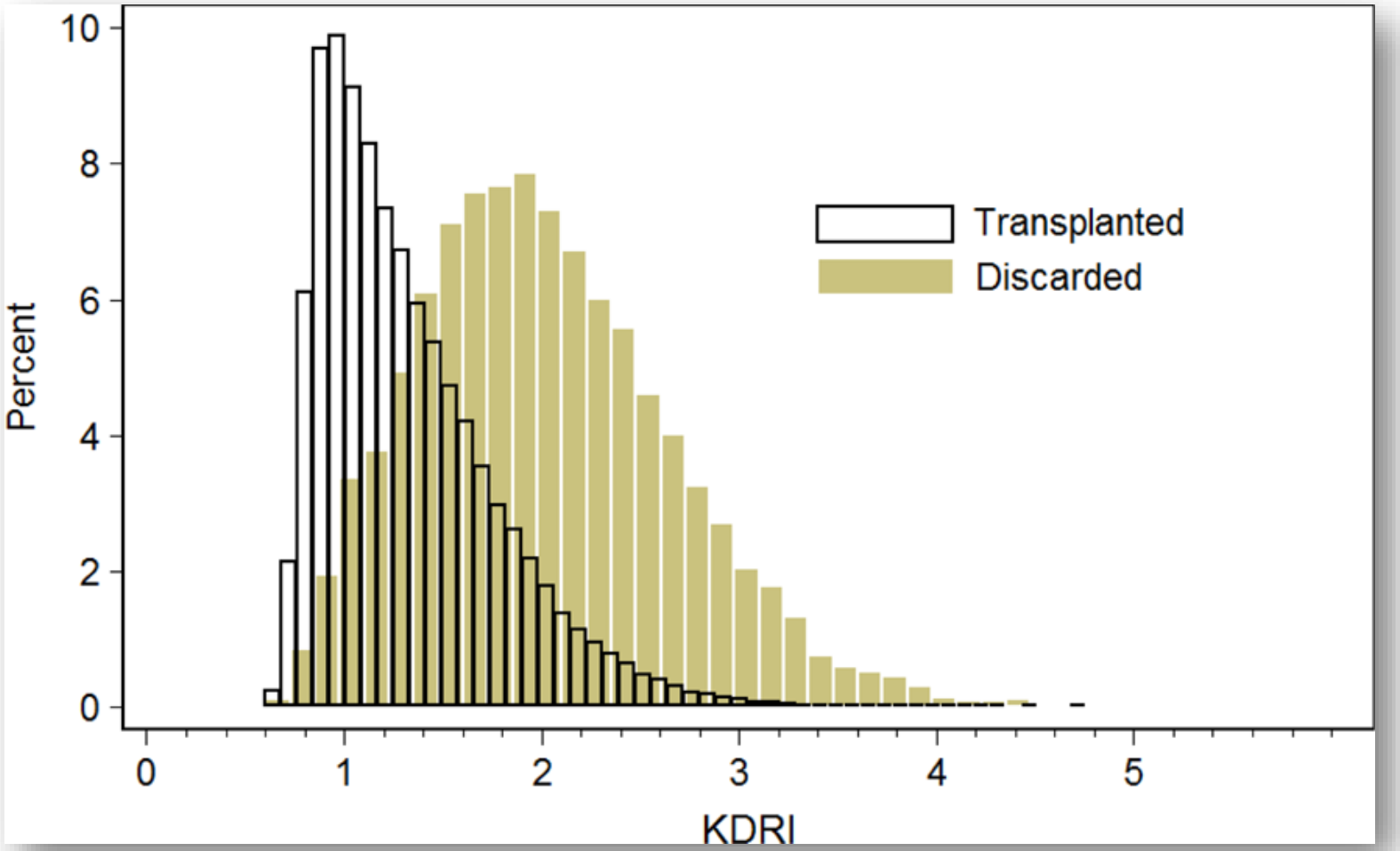
Sumit Mohan[1,2,3], Mariana C. Chiles[1,3], Rachel E. Patzer[4,5], Stephen O. Pastan[6], S. Ali Husain[1,3], Dustin J. Carpenter[7], Geoffrey K. Dube[1], R. John Crew[1], Lloyd E. Ratner[7] and David J. Cohen[1]

Kidney International (2018) 94, 187–198

Unilateral discards

- The reasons for discard: allocation system-related reasons, donor history, organ damage/anatomical abnormality, poor organ function, biopsy findings, but **the highest proportion was attributed to 'Other' (23.8%) – for reasons unrelated to graft quality**
- Recipients of unilateral transplants, irrespective of the cause of the unilaterally discarded partner kidneys, experienced a **1-year death-censored graft survival rate of > 90%**
- Recipients of the kidney whose partner kidneys were discarded due to allocation system-related reasons experienced a **1- year graft survival rate of 96.5%**

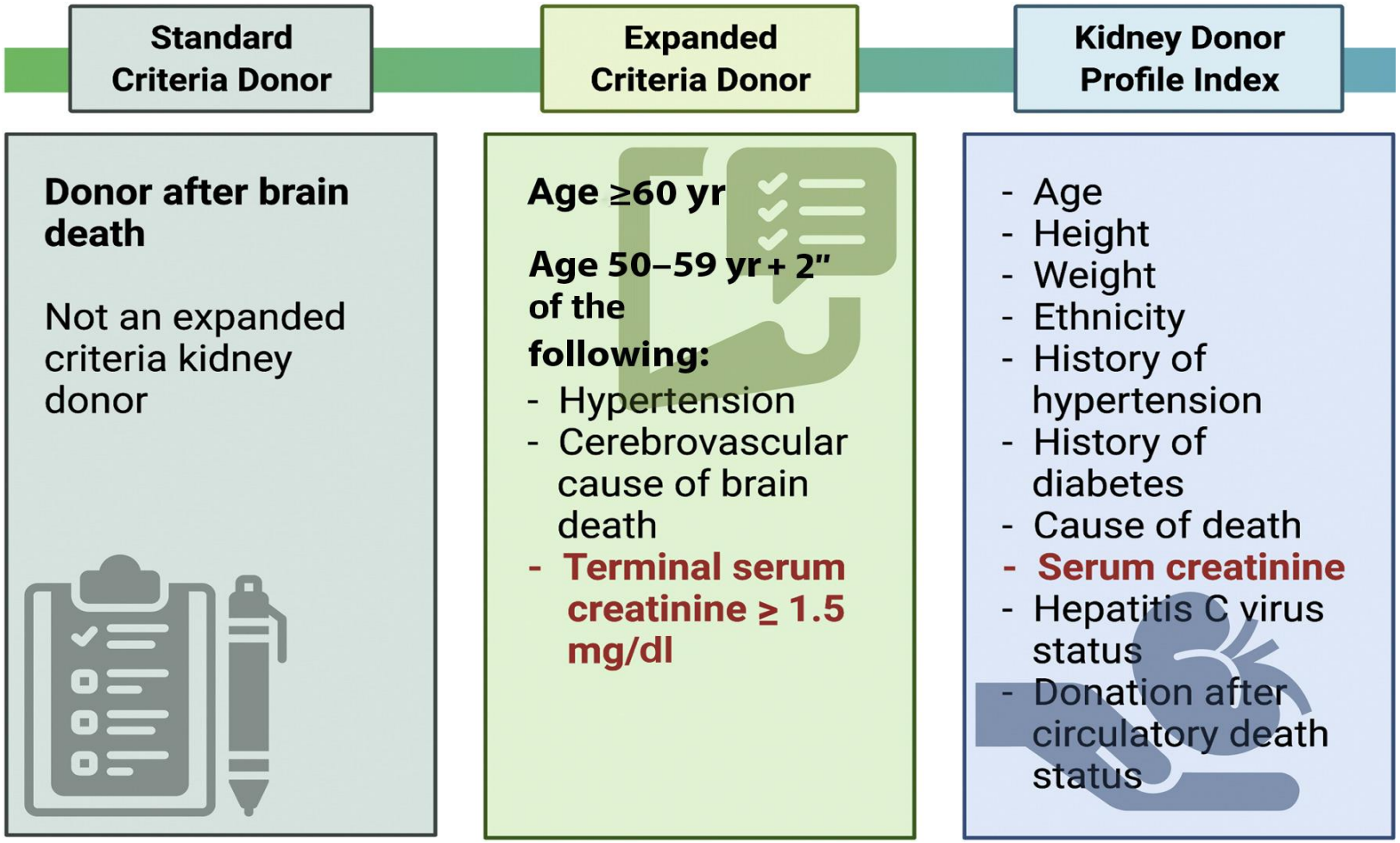
Kidney Donor Risk Index (KDRI) overlap of transplanted and discarded kidneys



Kidney Int. 2018;94:187–198

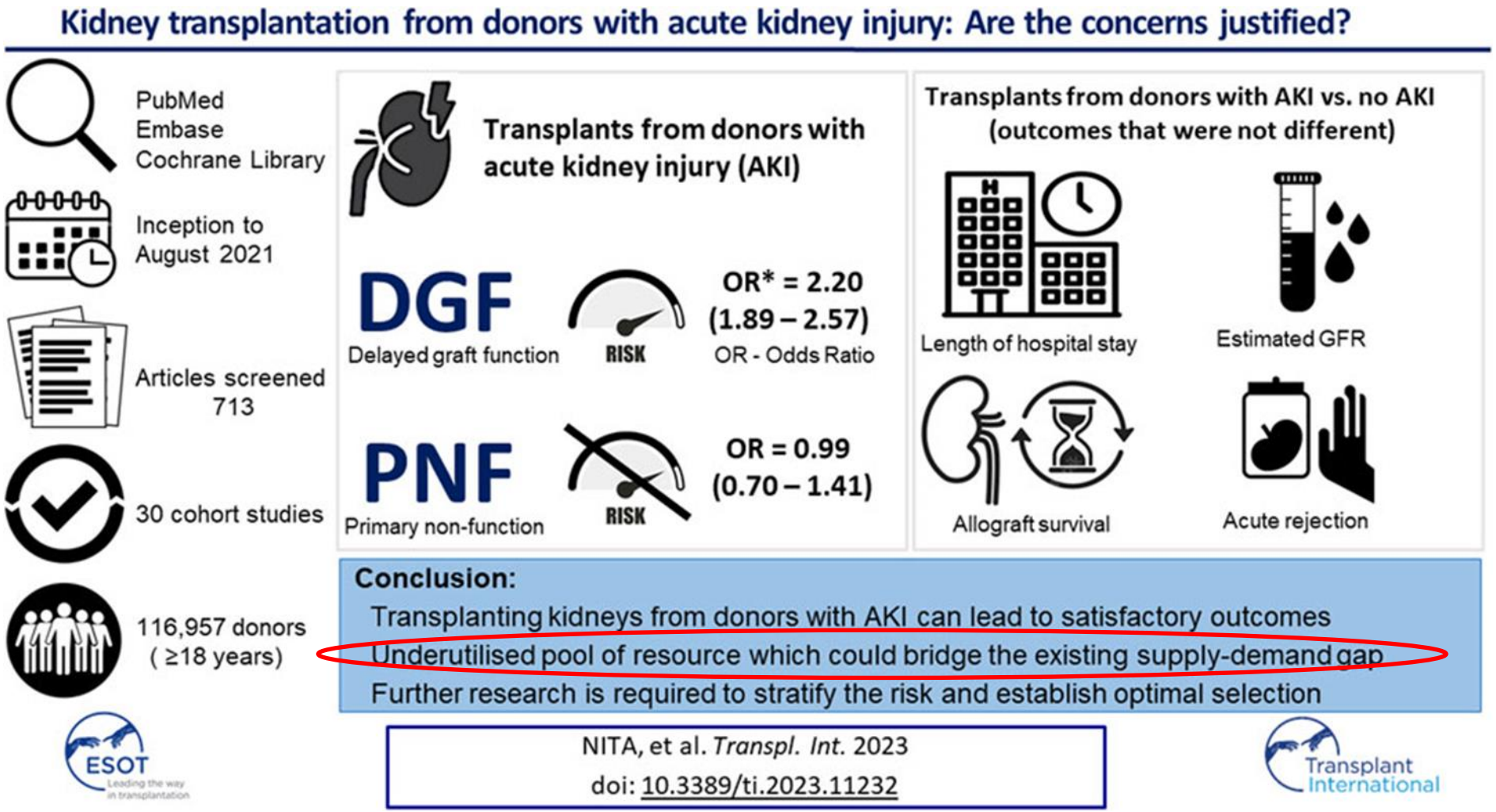
Graft quality assessment

Evolution of kidney donor risk scoring



Kidney Int Rep (2021) 6, 2025–2027

Kidney Transplantation From Donors With Acute Kidney Injury: Are the Concerns Justified? A Systematic Review and Meta-Analysis



AKI criteria
RIFLE, AKIN, KDIGO

Graft quality assessment

Visual assessment

Original Clinical Science—General

OPEN

The Association Between Macroscopic Arteriosclerosis of the Renal Artery, Microscopic Arteriosclerosis, Organ Discard, and Kidney Transplant Outcome

Anke Keijbeck, MD,[1] Rob Veenstra,[2] Robert A. Pol, MD, PhD,[2] Cynthia Konijn,[3] Nichon Jansen, PhD,[3] Harry van Goor, PhD,[4] Andries J. Hoitsma, MD, PhD,[3] Carine J. Peutz-Kootstra, MD, PhD,[1] and Cyril Moers, MD, PhD[2]

Background. During organ retrieval, surgeons estimate the degree of arteriosclerosis and this plays an important role in decisions on organ acceptance. Our study aimed to elucidate the association between macroscopic renal artery arteriosclerosis, donor kidney discard, and transplant outcome. **Methods.** We selected all transplanted and discarded kidneys in the Netherlands between January 1, 2000, and December 31, 2015, from deceased donors aged 50 y and older, for which data on renal artery arteriosclerosis were available (n=2610). The association between arteriosclerosis and kidney discard, the relation between arteriosclerosis and outcome, and the correlation between macroscopic and microscopic arteriosclerosis were explored. **Results.** Macroscopic arteriosclerosis was independently associated with kidney discard (odds ratio [OR], 1.36; 95% confidence interval [CI], 1.02-1.80; $P=0.03$). Arteriosclerosis (any degree) was not significantly associated with delayed graft function (OR, 1.16; 95% CI, 0.94-1.43; $P=0.16$), estimated glomerular filtration rate 1-y posttransplant (B, 0.58; 95% CI, −2.07 to 3.22; $P=0.67$), and long-term graft survival (hazard ratio, 1.07; 95% CI, 0.86-1.33; $P=0.55$). There was a significant association between mild arteriosclerosis and primary nonfunction (OR, 2.14; 95% CI, 1.19-3.84; $P=0.01$). We found no correlation between macroscopic and histological arteriosclerosis, nor between histological arteriosclerosis and transplant outcome. **Conclusions.** Macroscopic arteriosclerosis of the renal artery was independently associated with kidney discard and somewhat associated with primary nonfunction posttransplant. However, there was no effect of arteriosclerosis on delayed graft function, estimated glomerular filtration rate at 1 y, or long-term graft survival. Our results are valid only after inevitable exclusion of discarded kidneys that had on average more arteriosclerosis. Hence, conclusions should be interpreted in the light of this potential bias.

(*Transplantation* 2020;104: 2567–2574).

INTRODUCTION

The past few decades have seen a steady increase in the average deceased donor age.[1] A typical donor today is over 50 years old and is likely to have several relevant comorbidities.[2] Indeed, the once called "expanded criteria" donor has gradually become our standard donor. With rising donor age and associated medical conditions, it will be more likely that a substantial amount of arteriosclerosis is

Received 30 September 2019. Revision received 6 February 2020.
Accepted 9 February 2020.

[1] Department of Pathology, Maastricht University Medical Center, University of Maastricht, Maastricht, The Netherlands.
[2] Department of Surgery-Organ Donation and Transplantation, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
[3] Dutch Transplantation Foundation, Leiden, The Netherlands.
[4] Department of Pathology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

A.K. participated in the writing of the article, research design, and the performance of the research. R.V. participated in the performance of the research and data analysis. R.P. participated in data collection and proofreading of the article. C.K. participated in research design and proofreading of the article. N.J. participated in research design and proofreading of the article. H.v.G. participated in research design and proofreading of the article. A.J.H. participated in research design and proofreading of the article. C.J.P.-K. participated in data analysis, research design and performance of the research, and proofreading of the article. C.M. participated in the writing of the article, research design, the performance of the research and data analysis, and supervised conduct of the research.
The authors declare no conflicts of interest.
The authors declare no conflicts of interest.
This research was partially funded by the Dutch Transplantation Foundation.
Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com).

Correspondence: Cyril Moers, MD, PhD, Department of Surgery-Organ Donation and Transplantation-BA11, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands. (c.moers@umcg.nl).

ISSN: 0041-1337/20/10412-2567
DOI: 10.1097/TP.0000000000003189

<doi:10.1097/TP.0000000000003189>

All transplanted and discarded kidneys in the Netherlands between 1/2000, and 12/2015, from DD aged 50 y, for which data on renal artery arteriosclerosis were available (n=2610)

Macroscopic arteriosclerosis was independently associated with kidney discard and somewhat associated with PNF post-Tx , but there was no effect on DGF, eGFR at 1y, long-term graft survival

More severe degrees of renal artery arteriosclerosis were not associated with an elevated risk of PNF

There was no sign of any relation between macroscopically observed renal artery arteriosclerosis and histological indicators of intragraft arteriosclerosis

… Kidney discard based on a very subjective macroscopic assessment of renal artery arteriosclerosis should be discouraged…

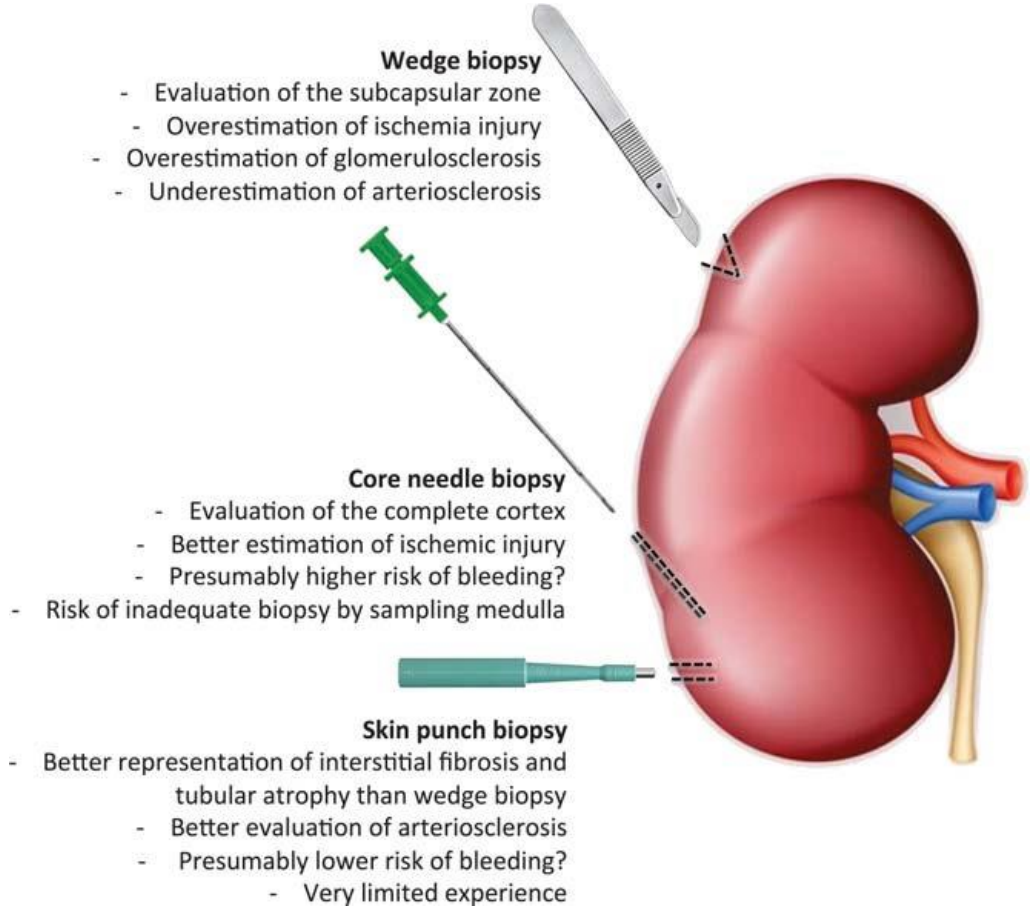
Data: from the Dutch Organ Transplantation Registry, Eurotransplant

Graft quality assessment

The role of renal transplant biopsy

Zero-Time Renal Transplant Biopsies: A Comprehensive Review

Maarten Naesens, MD, PhD[1,2]



Pathologist's Experience

Interobserver variability may affect the interpretation of the histological lesions

Techniques for obtaining zero-time biopsies vary importantly
The choice of technique impacts the diagnostic value of different histological lesions

Transplantation 2016;100: 1425–1439

Journal of Clinical Medicine

MDPI

Article

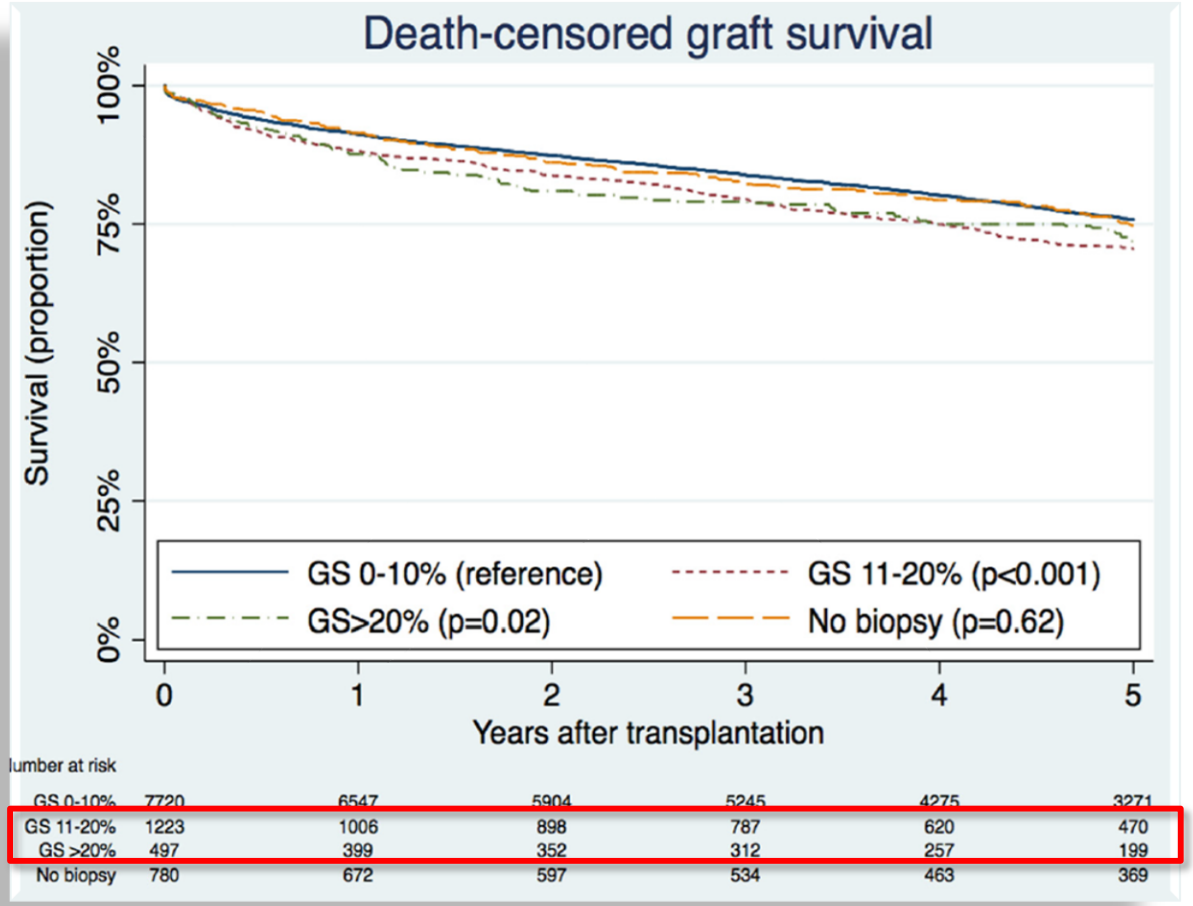
Degree of Glomerulosclerosis in Procurement Kidney Biopsies from Marginal Donor Kidneys and Their Implications in Predicting Graft Outcomes

UNOS database, 22.006 deceased-donor kidneys with a KDPI score > 85% from 2005 to 2014

Glomerulosclerosis → Rate of kidney discard

- 0–10% (58.0%) → **33.6%**
- 11–20% (13.5%) → **68.9%**
- > **20%** (19.7%) → **77.4%**

Among kidneys with >10% GS, there was no significant difference in death-censored graft survival between 11–20% GS and >20% GS.



J.Clin.Med. 2020,9,1469;doi:10.3390/jcm9051469

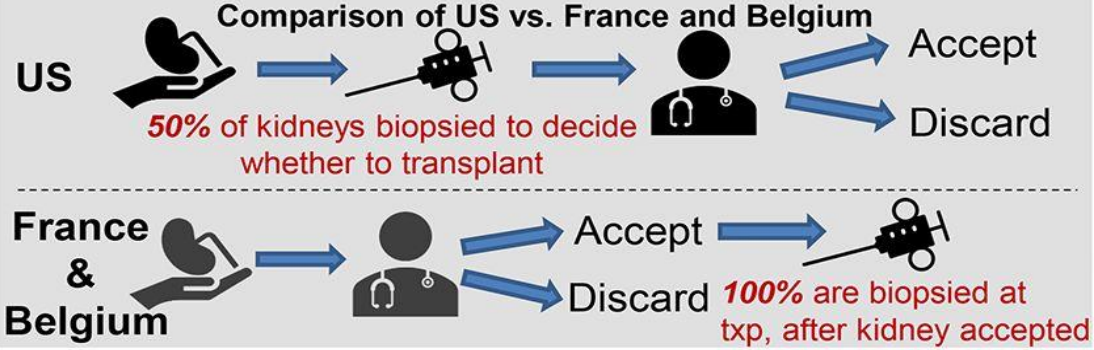
Assessment of the Utility of Kidney Histology as a Basis for Discarding Organs in the United States: A Comparison of International Transplant Practices and Outcomes

Do Allocation Kidney Biopsies Add Incremental Value in Predicting How Long A Kidney Will Survive After Transplantation?

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

BACKGROUND

Comparison of US vs. France and Belgium



METHODS

*Multivariable Cox regression model of death-censored allograft failure in development set (2 French centers) and validation set (2 Belgian centers)

**Compared predictive accuracy between baseline model and then model with addition of biopsy data

*Matched kidneys discarded in US due to histology to nearly identical kidneys transplanted in France

RESULTS

*1,629 kidney recipients at 2 French centers:
- C-stat without histology: 0.635
- C-stat with histology added: 0.646

*Similar results at Belgian centers

*493 kidneys (45%) discarded in 2015 – 2016 in the US matched to 493 transplanted French kidneys

*Those matched and transplanted kidneys had acceptable allograft survival: 93.1%, 80.7%, and 68.9% at 1, 5, and 10 years, respectively

CONCLUSION

Kidney histology did not provide additional value in determining organ quality. Many kidneys discarded due to biopsy findings would have benefitted US wait-listed patients.

doi: 10.1681/ASN.2020040464

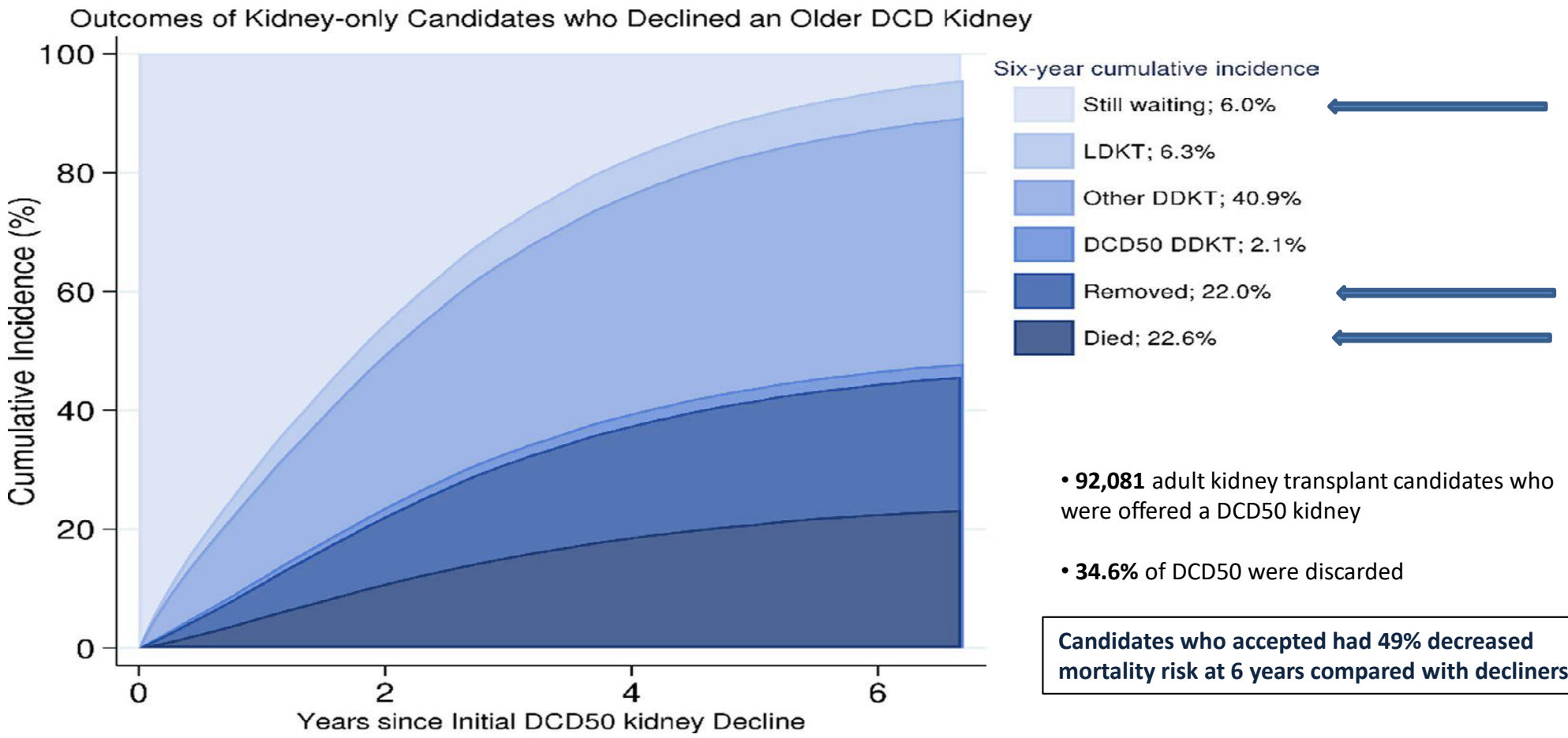
JASN February 2021;32(2):397-409

How far can we push the boundaries?

To 'push the boundaries' is to **act in a way that goes beyond what's established or expected…**

… expected for whom? For patients or for transplants?

Survival benefit of accepting kidneys from older donation after cardiac death donors



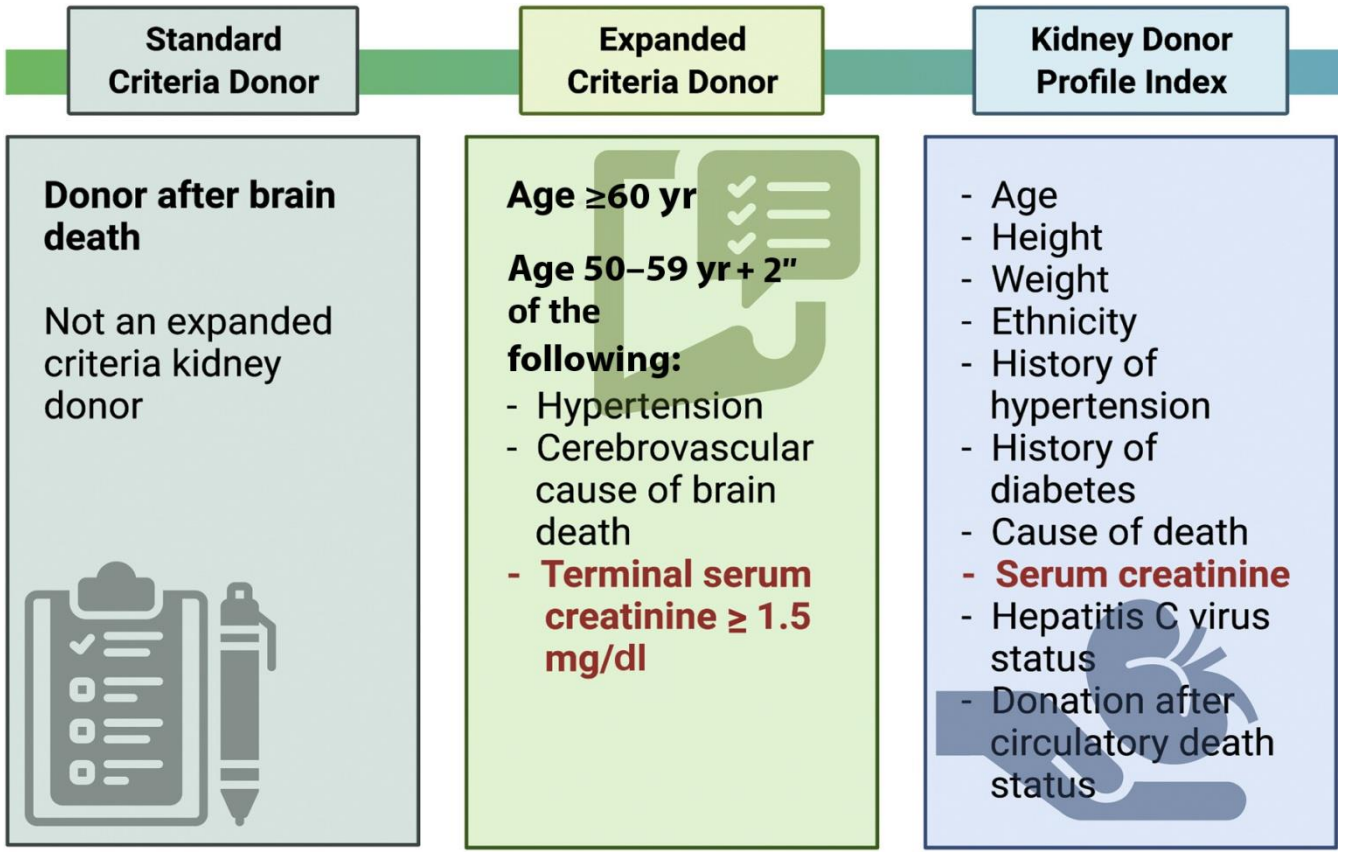
- **92,081** adult kidney transplant candidates who were offered a DCD50 kidney
- **34.6%** of DCD50 were discarded

Candidates who accepted had 49% decreased mortality risk at 6 years compared with decliners

Outcomes following the initial decline of a DCD50 kidney among candidates who declined a DCD50 kidney between 1/1/2010 and 12/31/2018 – **SRTR data**

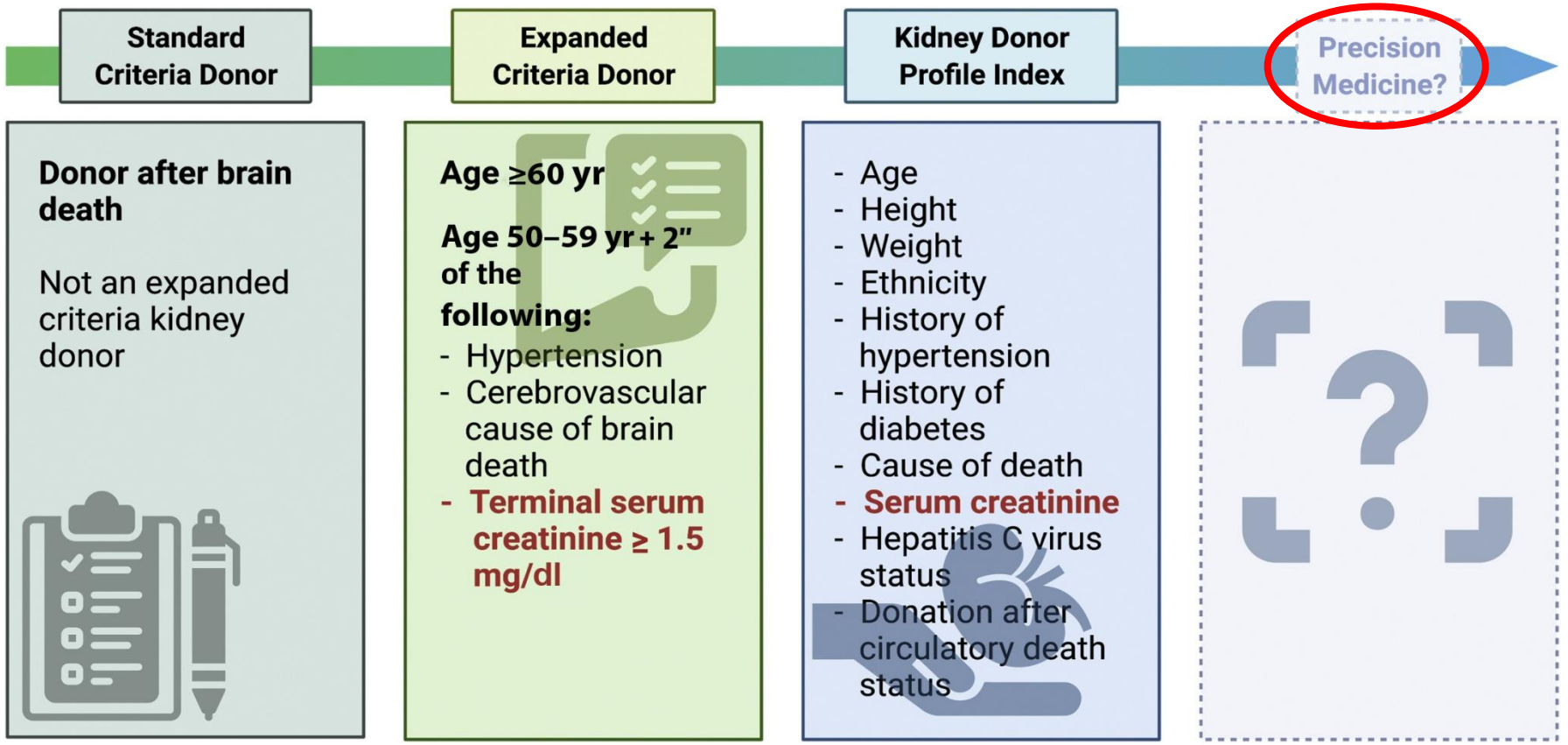
Am J Transplant. 2021;21:1138–1146

Evolution of kidney donor risk scoring



Kidney Int Rep 2021; 6: 2025–2027

Evolution of kidney donor risk scoring



Kidney Int Rep 2021; 6: 2025–2027

Rapid and accurate assessment of organ quality

Prognostic tools - Non-invasive biomarkers:

- change the landscape of allocation
- reduce the number of discarded deceased donor kidneys
- improve organ availability to countless patients on the waiting list

➢ ***Deceased donor biomarkers and genetic variations - under investigation***

- Uromodulin (UMOD) /Osteopontin (OPN) ratio
- Urinary chitinase 3-like protein 1 (YKL-40)
- Apolipoprotein L1 genotypes
- 'Omics' technologies

➢ ***Advanced magnetic resonance imaging (MRI) techniques***

J Clin Med 2022;11:487
ASN Kidney News, August 2022;14(8):19
J Clin Invest. 2021;131(22)
Transplantation 2021; 105:876–885

Optimum utilization of renal allografts

- Reduced cold ischemia time
- Dual transplantation (both kidneys from one donor into the same recipient)
- Recondition marginal organs

- Preservation techniques: promising results, need further results from the clinical setting

  - *Oxygenated hypothermic machine perfusion*

  - *Normothermic machine perfusion (NMP): pre-transplant organ assessment tool*
    active organ reconditioning

J Clin Med 2023;12:3871
J Clin Med 2022;11:487
ASN Kidney News, August 2022;14(8):19
J Clin Invest. 2021;131(22)
Transplantation 2021; 105:876–885

Received: 26 March 2020 | Revised: 15 May 2020 | Accepted: 21 May 2020
DOI: 10.1111/ajt.16100

ORIGINAL ARTICLE

AJT

Novel delivery of cellular therapy to reduce ischemia reperfusion injury in kidney transplantation

Emily R. Thompson[1,2] | Lucy Bates[1,2] | Ibrahim K. Ibrahim[1] | Avinash Sewpaul[1] | Ben Stenberg[3] | Andrew McNeill[3] | Rodrigo Figueiredo[1] | Tom Girdlestone[1,2] | Georgina C. Wilkins[1,2] | Lu Wang[1,2] | Samuel J. Tingle[1] | William E. Scott III[1,2] | Henrique de Paula Lemos[2] | Andrew L. Mellor[2] | Valerie D. Roobrouck[4] | Anthony E. Ting[5] | Sarah A. Hosgood[6] | Michael L. Nicholson[6] | Andrew J. Fisher[1,2] | Simi Ali[1,2] | Neil S. Sheerin[1,2] | Colin H. Wilson[1,2]

[1]NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation, Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne, UK
[2]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK
[3]Department of Radiology, Freeman Hospital, Newcastle upon Tyne, UK
[4]ReGenesys, Leuven, Belgium
[5]Athersys Inc., Cleveland, OH, USA
[6]NIHR Blood and Transplant Research Unit, Department of Surgery, Addenbrooke's Hospital, University of Cambridge, Cambridge, UK

Correspondence
Emily Thompson
Email: Emily.Thompson3@ncl.ac.uk

Funding information
This study was supported by Kidney Research UK, the National Institute for Health Research (NIHR) Newcastle Biomedical Research Centre and the NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation at the University of Cambridge, in collaboration with Newcastle University and in partnership with National Health Service

Ex vivo normothermic machine perfusion (NMP) of donor kidneys prior to transplantation provides a platform for direct delivery of cellular therapeutics to optimize organ quality prior to transplantation. Multipotent Adult Progenitor Cells (MAPC®) possess potent immunomodulatory properties that could minimize ischemia reperfusion injury. We investigated the potential capability of MAPC cells in kidney NMP. Pairs (5) of human kidneys, from the same donor, were simultaneously perfused for 7 hours. Kidneys were randomly allocated to receive MAPC treatment or control. Serial samples of perfusate, urine, and tissue biopsies were taken for comparison. MAPC-treated kidneys demonstrated improved urine output ($P = .009$), decreased expression of injury biomarker NGAL ($P = .012$), improved microvascular perfusion on contrast-enhanced ultrasound (cortex $P = .019$, medulla $P = .001$), downregulation of interleukin (IL)-1β ($P = .050$), and upregulation of IL-10 ($P < .047$) and Indolamine-2, 3-dioxygenase ($P = .050$). A chemotaxis model demonstrated decreased neutrophil recruitment when stimulated with perfusate from MAPC-treated kidneys ($P < .001$). Immunofluorescence revealed prelabeled MAPC cells in the perivascular space of kidneys during NMP. We report the first successful delivery of cellular therapy to a human kidney during NMP. Kidneys treated with MAPC cells demonstrate improvement in clinically relevant parameters and injury biomarkers. This novel method of cell therapy delivery provides an exciting opportunity to recondition organs prior to transplantation.

Abbreviations: ANOVA, analysis of variance; CEUS, contrast-enhanced ultrasound; DBD, donation after brainstem death; DCD, donation after circulatory death; DGF, delayed graft function; ECD, extended criteria donors; ELISA, enzyme linked immunosorbent assay; FMN, flavin mononucleotide; HMEC-1, human microvascular endothelial cell line 1; HPLC, high performance liquid chromatography; ICAM-1, intracellular adhesion molecule 1; IDO, indolamine 2, 3 dioxygenase; IRI, ischemia reperfusion injury; KIM-1, Kidney injury marker -1; MAPC, multipotent adult progenitor cells; MFI, microflow imaging ultrasound; MHC, major histocompatibility complex; MSD, MesoScale Discovery; NGAL, neutrophil gelatinase-associated lipocalin; NHSBT, National Health Service Blood and Transplant; NMP, normothermic machine perfusion; RCT, randomized controlled trial; S1PR1, shingosine-1-phosphate receptor 1.

- Ex vivo normothermic machine perfusion (NMP) of donor kidneys prior to transplantation

- Multipotent Adult Progenitor Cells (MAPC®) possess potent immunomodulatory properties that could minimize IRI

Received: 26 March 2020 | Revised: 15 May 2020 | Accepted: 21 May 2020
DOI: 10.1111/ajt.16100

ORIGINAL ARTICLE

AJT

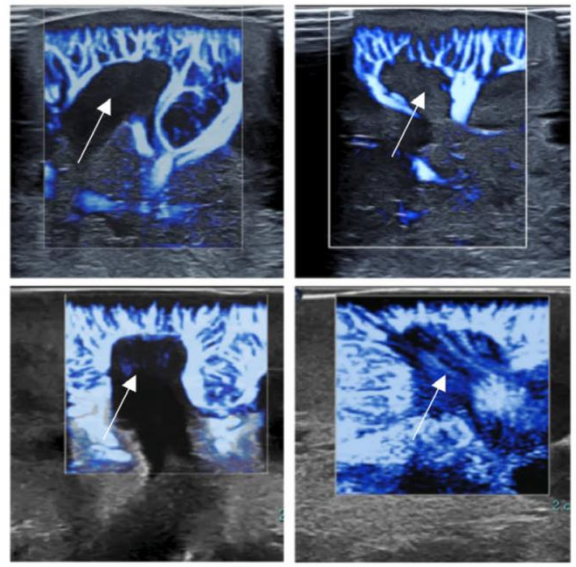
Novel delivery of cellular therapy to reduce ischemia reperfusion injury in kidney transplantation

Emily R. Thompson[1,2] | Luc
Ben Stenberg[3] | Andrew McN
Georgina C. Wilkins[1,2] | Lu W
Henrique de Paula Lemos[2] | A
Anthony E. Ting[5] | Sarah A. H
Simi Ali[1,2] | Neil S. Sheerin[1,2]

[1]NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation, Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne, UK
[2]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK
[3]Department of Radiology, Freeman Hospital, Newcastle upon Tyne, UK
[4]ReGenesys, Leuven, Belgium
[5]Athersys Inc., Cleveland, OH, USA
[6]NIHR Blood and Transplant Research Unit, Department of Surgery, Addenbrooke's Hospital, University of Cambridge, Cambridge, UK

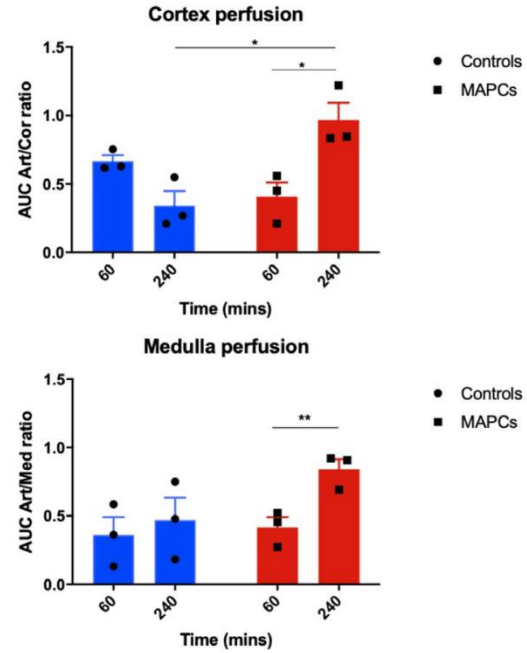
Correspondence
Emily Thompson
Email: Emily.Thompson3@ncl.ac.uk

Funding information
This study was supported by Kidney Research UK, the National Institute for Health Research (NIHR) Newcastle Biomedical Research Centre and the NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation at the University of Cambridge, in collaboration with Newcastle University and in partnership with National Health Service



ment in clinically relevant parameters and injury biomarkers. This novel method of cell therapy delivery provides an exciting opportunity to recondition organs prior to transplantation.

Abbreviations: ANOVA, analysis of variance; CEUS, contrast-enhanced ultrasound; DBD, donation after brainstem death; DCD, donation after circulatory death; DGF, delayed graft function; ECD, extended criteria donors; ELISA, enzyme linked immunosorbent assay; FMN, flavin mononucleotide; HMEC-1, human microvascular endothelial cell line 1; HPLC, high performance liquid chromatography; ICAM-1, intracellular adhesion molecule 1; IDO, indolamine 2, 3 dioxygenase; IRI, ischemia reperfusion injury; KIM-1, Kidney injury marker -1; MAPC, multipotent adult progenitor cells; MFI, microflow imaging ultrasound; MHC, major histocompatibility complex; MSD, MesoScale Discovery; NGAL, neutrophil gelatinase-associated lipocalin; NHSBT, National Health Service Blood and Transplant; NMP, normothermic machine perfusion; RCT, randomized controlled trial; S1PR1, shingosine-1-phosphate receptor 1.



Who can tolerate a marginal kidney? Predicting survival after deceased donor kidney transplant by donor–recipient combination

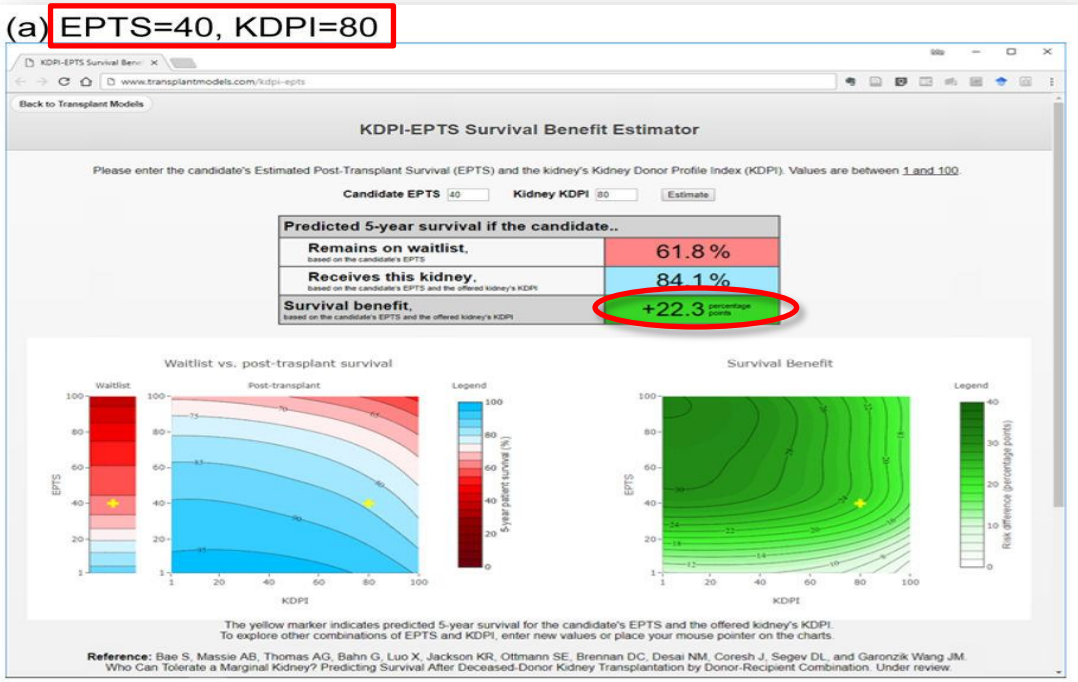
- Estimation of 5-year post-KT survival and wait-list survival
  - **Combinations of KDPI and EPTS score**

Survival benefit was defined as ''absolute reduction in mortality risk with KT''

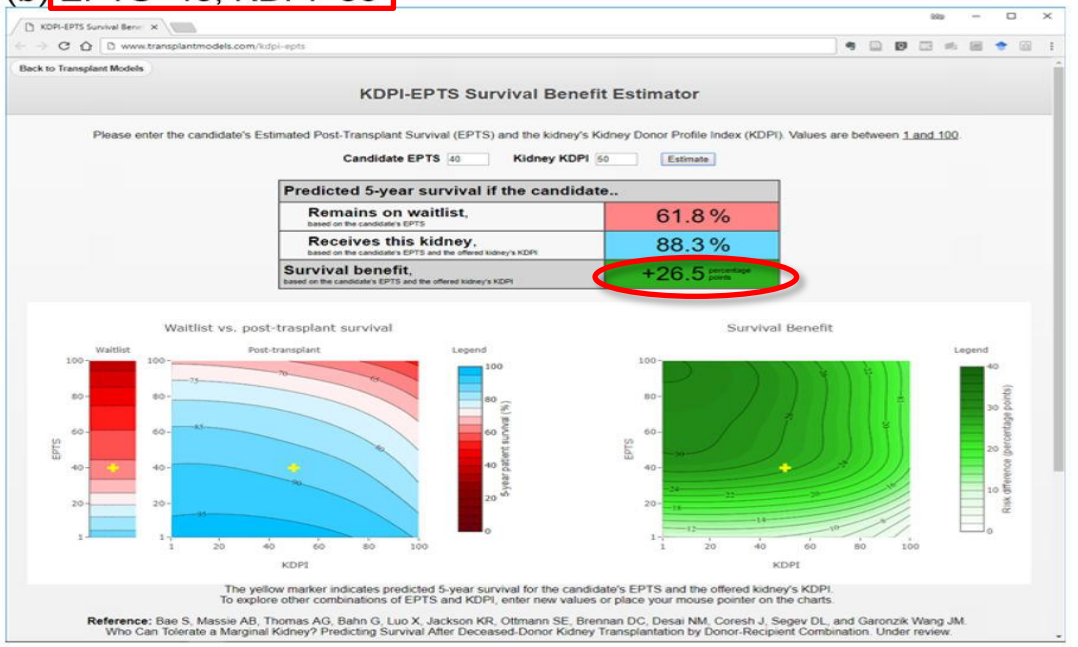
Estimated Post Transplant Survival (EPTS) score
Candidate time on dialysis
Current diagnosis of diabetes
Prior solid organ transplants
Candidate age

- ***DD KT recipients*** *(n=120.818)*
- ***Waitlisted candidates*** *(n=376.272)*
- *SRTR data*

(a) EPTS=40, KDPI=80



(b) EPTS=40, KDPI=50



Am J Transplant. 2019;19:425–433

Commentary

Trash or Treasure: Rescuing Discard Kidneys

Yunwei Zhang, MS,[1] Germaine Wong, PhD,[2] and Jean Yee Hwa Yang, PhD[1,3]

THANK YOU!

Yunwei Zhang et al, Transplantation 2021;9:105