





# **Donor Quality Assessment**

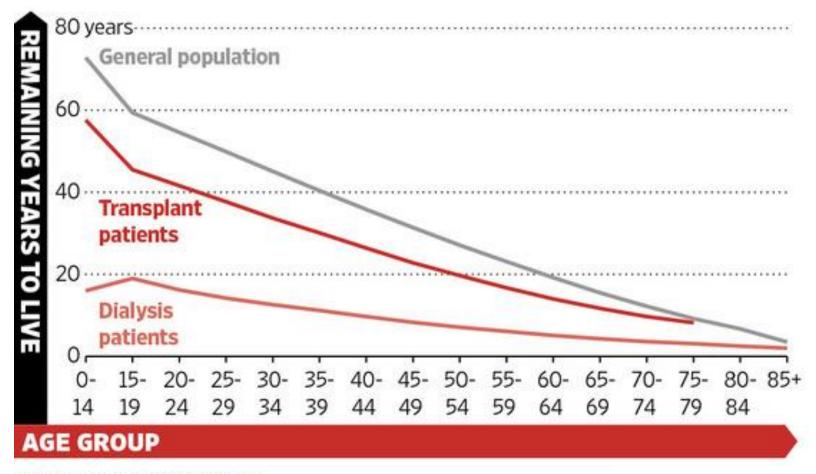
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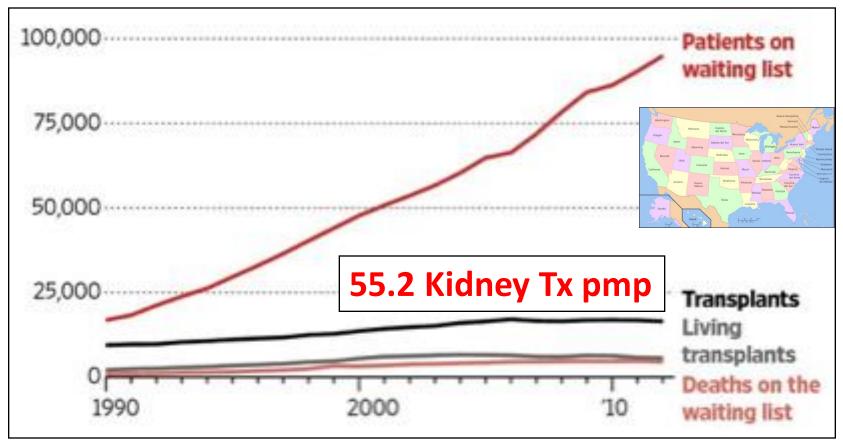




Across all age ranges, but especially for the young, kidney patients on dialysis tend to have fewer remaining years to live than those who recevied a kidney transplant.

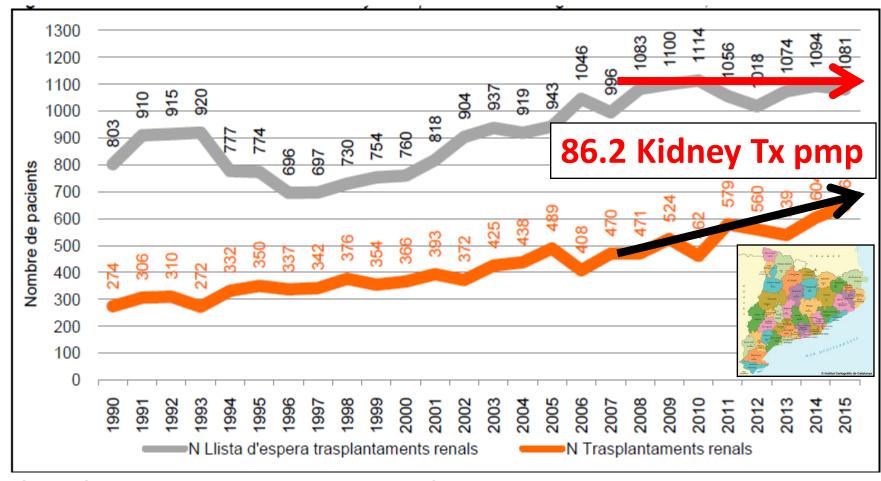


The number of patients in the waiting list increases exponentially while the number of transplanted patients increases slightly.



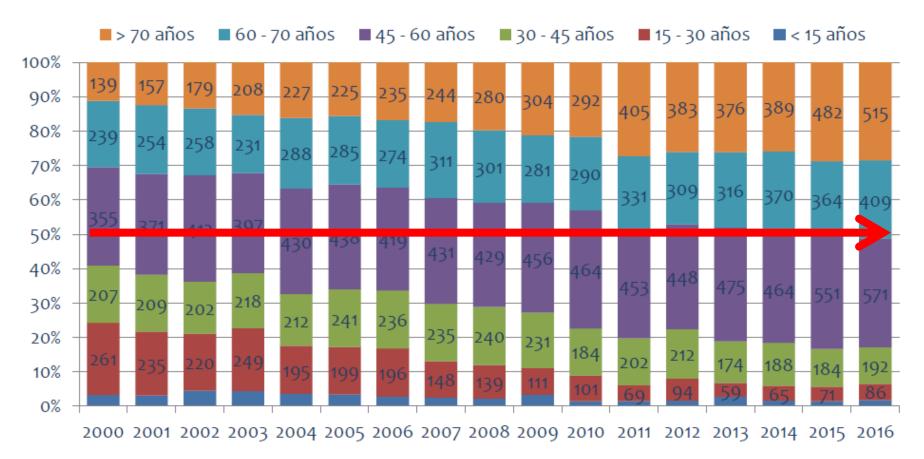
Source: US Renal Data System

The number of patients in the waiting list stabilizes despite the number of transplanted patients increases linearly.



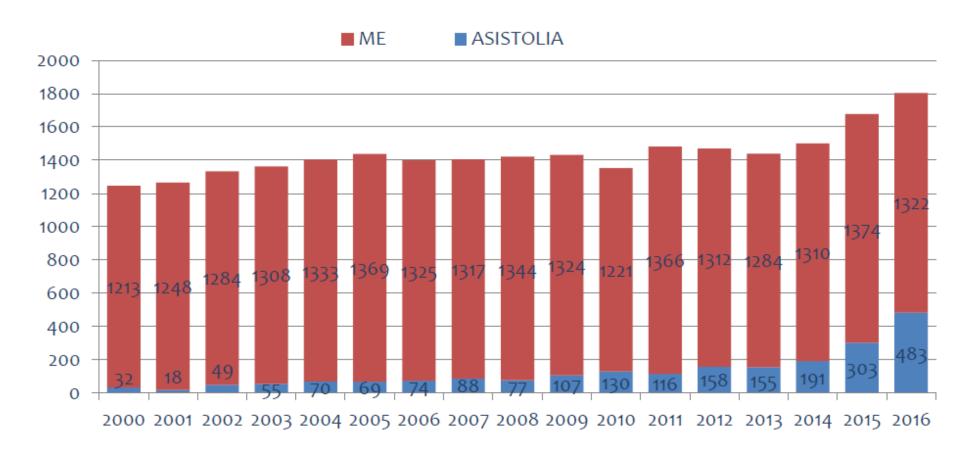
Source: Organ Donation and Transplantation Activity in Catalonia. 2015 Report

#### Age of deceased kidney donors in Spain



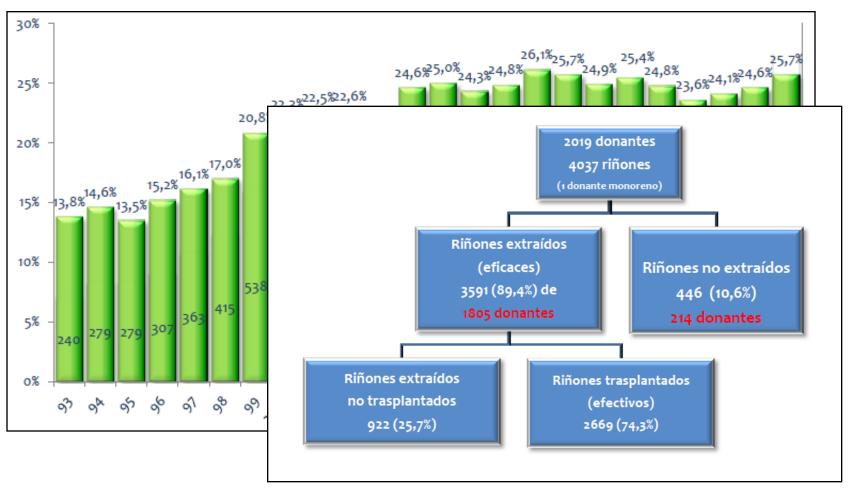
Source: Organización Nacional de Trasplantes 2016

#### Donors after cardiac death in Spain



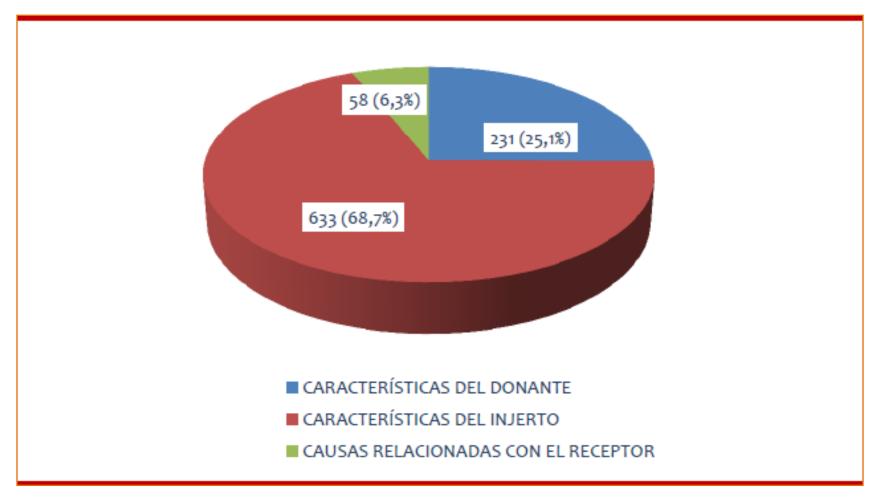
Source: Organización Nacional de Trasplantes 2016

# Kidney discard rate in Spain



Source: Organización Nacional de Trasplantes 2016

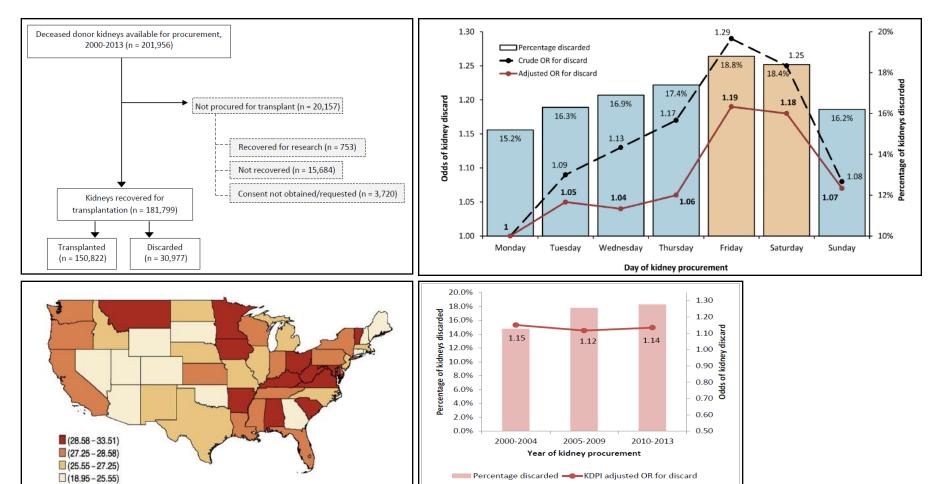
## Reasons for kidney discard in Spain



Source: Organización Nacional de Trasplantes 2016

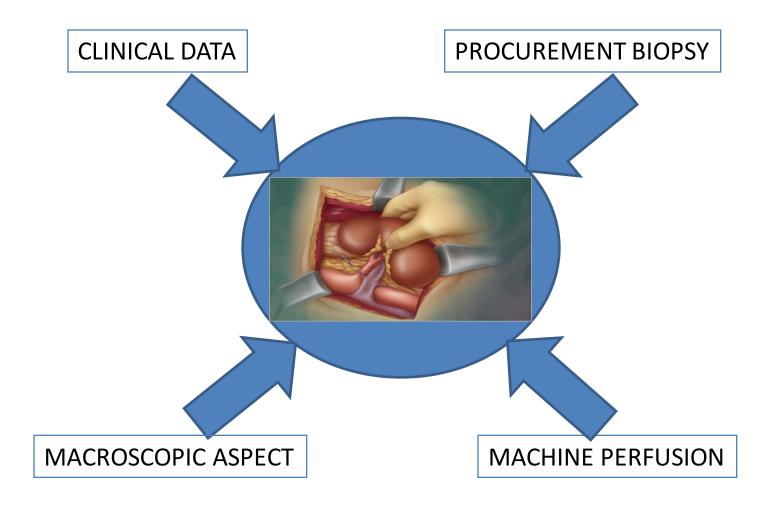
Biopsy: 234 (25.4% of discarded) (6.8% of retrived)

Discard rate varies across different areas and there exists a "week-end effect".



Mohan S et al. Kidney Int 2016. USRDS 2000-2013

## How to Assess Donor Quality

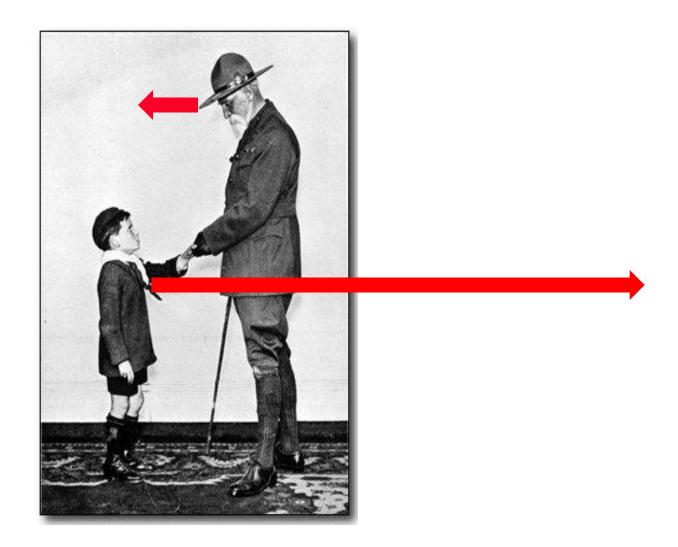


# EXPANDED CRITERIA DONORS (2002)

- 1. Donors older than 60 years
- 2. Donors older than 50 years who have at least 2 criteria: History of arterial Hypertension Cerebrovascular accident as the cause of death Terrminal serum creatinine > 1.5 mg/dL

RR of graft failure >1.7 compared with a reference group of "ideal donors" (aged 10 to 39 years, without AHT, did not die of CVA, and predonation SCr < 1.5 mg/dL)

# Lifespan and kidney transplantation



## KDPI instead of ECD (2014)

- •KDPI incorporates 10 donor factors (instead of 4 in the ECD definition) and is a more predictive measure of donor quality.
- •KDPI is a continuous "score" instead of a binary (yes/no) indicator.
- KDPI illuminates the fact that not all ECDs are alike
  - -Some ECD kidneys have good estimated quality
  - -Some SCD kidneys have lower estimated quality than some ECDs

#### **KDRI-KDPI** calculation

The association between these donor factors and graft survival was determined by estimating a multivariable Cox proportional hazards regression model using graft outcomes from nearly 70,000 adult, solitary, first-time deceased donor kidney recipients in the U.S. from 1995-2005

Table 1: KDRI Donor Factors and Model Coefficients

Donor Characteristic	Applies to:	KDRI Coefficient ("Beta")	KDRI "XBeta" Component
	All donors	0.0128	0.0128*(age-40)
Age (integer years)	Donors with age < 18	-0.0194	-0.0194*(age-18)
	Donors with age > 50	0.0107	0.0107*(age-50)
Height (cm)	All donors	-0.0464	-0.0464*(hgt-170)/10
Weight (kg)	All donors w/ weight < 80kg	-0.0199	-0.0199*(wgt-80)/5
Ethnicity	African American donors	0.1790	0.1790
History of Hypertension	Hypertensive donors	0.1260	0.1260
History of Diabetes	Diabetic donors	0.1300	0.1300
Cause of Death	Donors w/ COD=CVA	0.0881	0.0881
Serum Creatinine	All donors	0.2200	0.2200*(creat-1)
Serum Creatinine	Donors with creat > 1.5 mg/dL	-0.2090	-0.2090*(creat-1.5)
HCV status	HCV positive* donors	0.2400	0.2400
DCD Status	DCD donors	0.1330	0.1330

#### **KDRI-KDPI** calculation

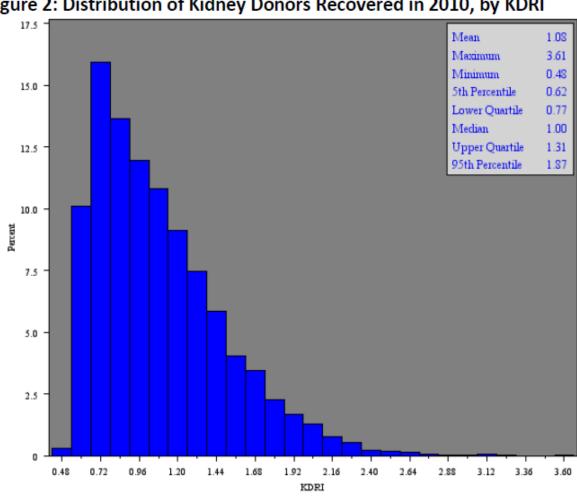


Figure 2: Distribution of Kidney Donors Recovered in 2010, by KDRI

#### **KDRI to KDPI Mapping Table**

Reference population: All Deceased Kidney Donors Recovered for the Purpose of Transplantation in 2015 in the U.S.

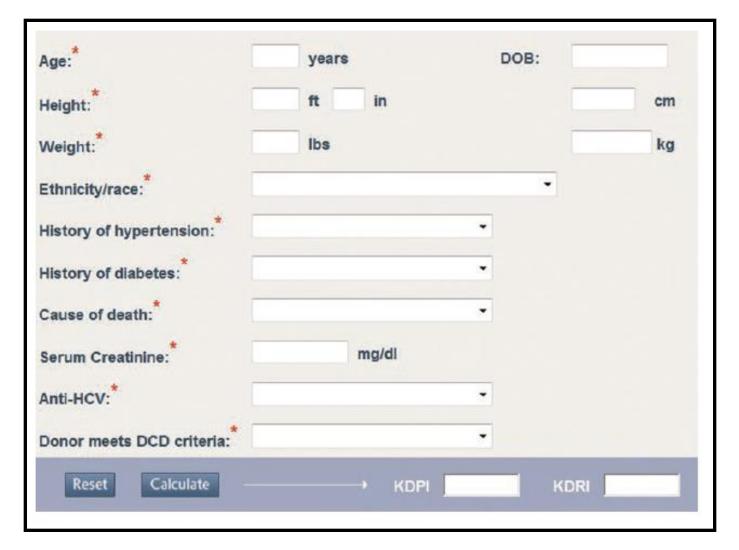
KDRI Scaled (Normalized) such that Median Donor has KDRI=1.0

Based on the OPTN database as of March 4, 2016

If KDRI is		TI IZDDI !-	
>	≤		Then KDPI is
0.0000000000000000	0.492707296641464	>	0%
0.492707296641464	0.578999305993018	^	1%
0.578999305993018	0.593519815451300	^	2%
0.593519815451300	0.608227919270311	^	3%
0.608227919270311	0.620169035598301	^	4%
0.620169035598301	0.629417808691665	^	5%

\_\_\_\_\_\_

1.734501409337510	1.790043640923710	>	95%
1.790043640923710	1.856784076117470	>	96%
1.856784076117470	1.931675961552560	>	97%
1.931675961552560	2.043369171016590	>	98%
2.043369171016590	2.217757166762110	>	99%
2.217757166762110	3.428992204105320	>	100%
3.428992204105320	99999999	>	100%



http://optn.transplant.hrsa.gov/resources/allocationcalculators.asp?index=81.

Donor age: 40 years

Height: 160 cm

Weight: 60 kg

White

No History of AHT

Non DM

Death: Trauma

SCr 0.6 mg/dL

**HCV** negative

Non DCD

KDRI: 0.85

**KDPI: 34%** 

Donor age: 65 years

Height: 170 cm

Weight: 80 kg

White

History of AHT 6-10 y

Non DM

Death: CVA

SCr 0.9 mg/dL

**HCV** negative

Non DCD

KDRI: 1.61

**KDPI: 91%** 

Donor age: 72 years

Height: 160 cm

Weight: 80 kg

White

History of AHT 6-10 y

History of DM 0-5 y

Death: CVA

SCr 0.9 mg/dL

**HCV** negative

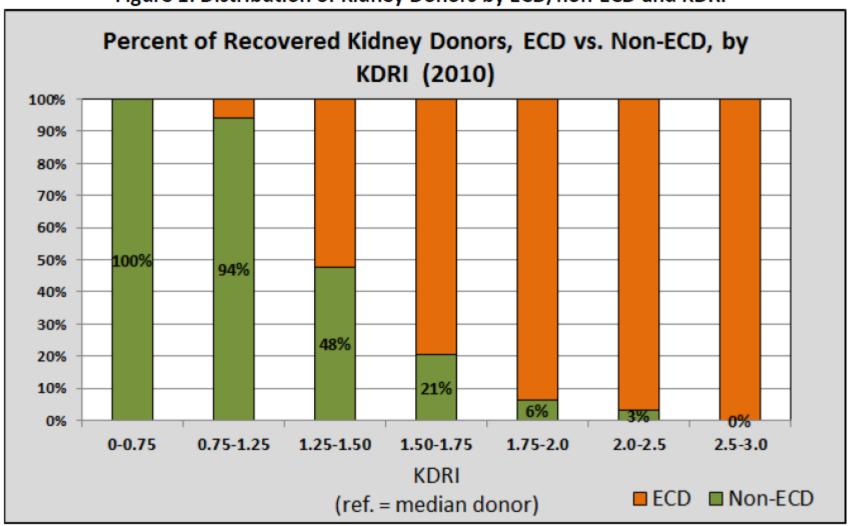
DCD

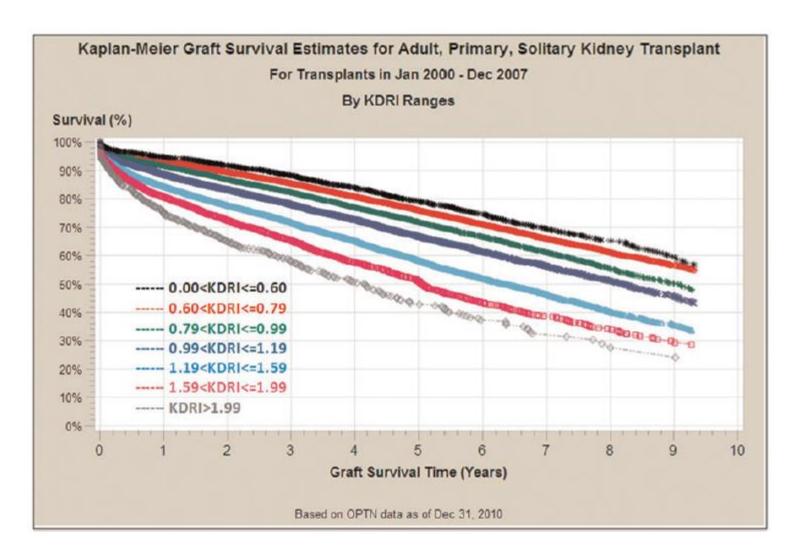
KDRI: 2.58

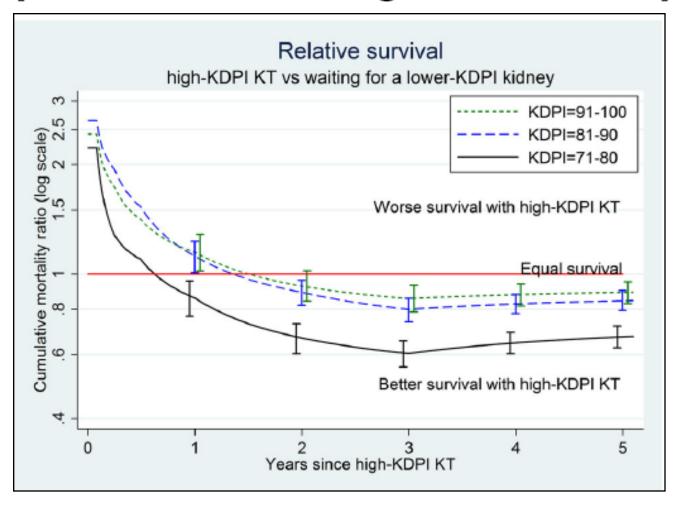
**KDPI: 100%** 

http://optn.transplant.hrsa.gov/resources/allocationcalculators.asp?index=81.

Figure 1: Distribution of Kidney Donors by ECD/non-ECD and KDRI





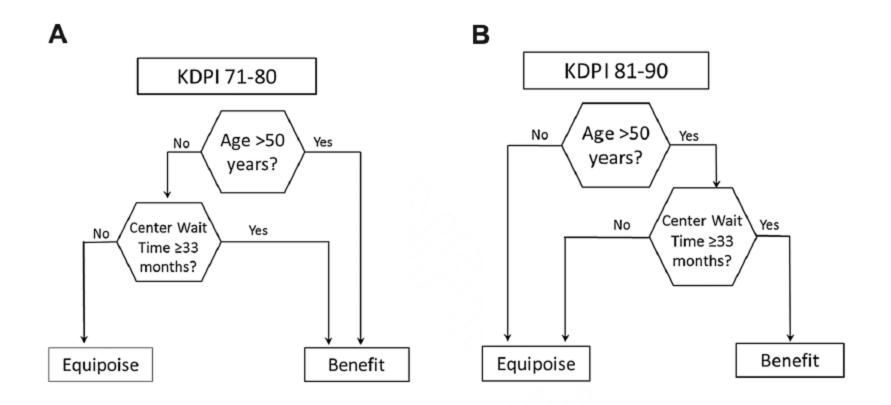


Massie AB et al. Am J Transplant 2014.. SRTR registry 2002-2011. N = 184.277

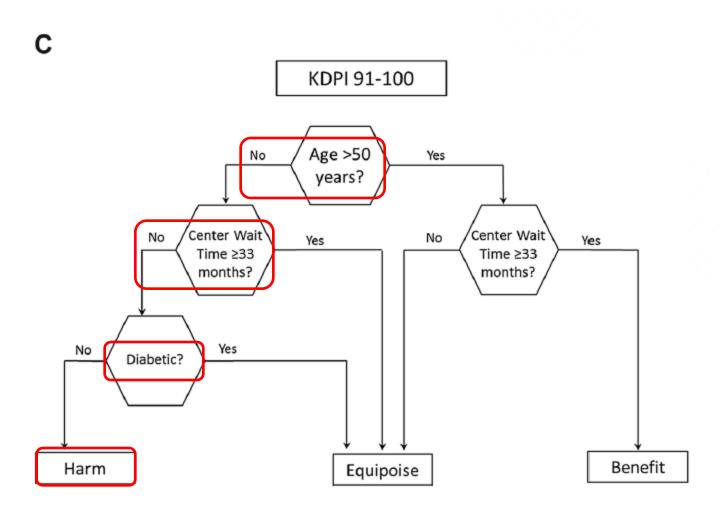
**Table 3:** Time to equal risk, and equal survival, incurred by accepting a high-KDPI kidney transplant versus the conservative approach of waiting for a lower KDPI kidney

	Time to equal risk (months)	Time to equal survival (months)
KDPI 71–80 vs. waitlist or KDPI 0–70	1.7	7.7
KDPI 81–90 vs. waitlist or KDPI 0–80	6.0	18.0
KDPI 91–100 vs. waitlist or KDPI 0–90	7.2	19.8

KDPI, Kidney Donor Profile Index.



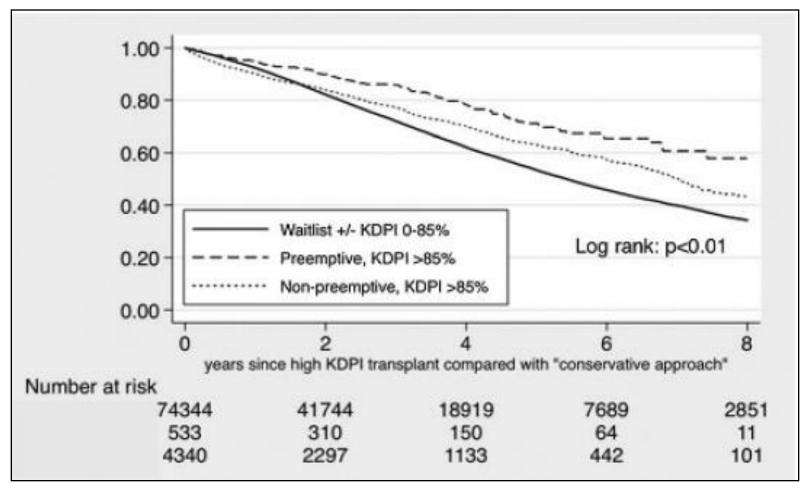
Massie AB et al. Am J Transplant 2014.. SRTR registry 2002-2011. N = 184.277



Massie AB et al. Am J Transplant 2014.. SRTR registry 2002-2011. N = 184.277

#### Survival Benefit in Older Patients Associated With Earlier Transplant With High KDPI Kidneys

Patient survival in recipients > 60 y (ITT analysis)



Jay JC et al. Transplantantation 2017

# Is the Kidney Donor Risk Index a step forward in the assessment of deceased donor kidney quality?

#### Alison P. K. Lee and Daniel Abramowicz

Department of Nephrology, University Hospital of Antwerp, Edegem, Belgium

The KDRI is an easily applicable scoring system which provides a uniform platform to initiate and to compare clinical studies. We expect more studies to be published in the near future, to further validate this scoring system in several populations.

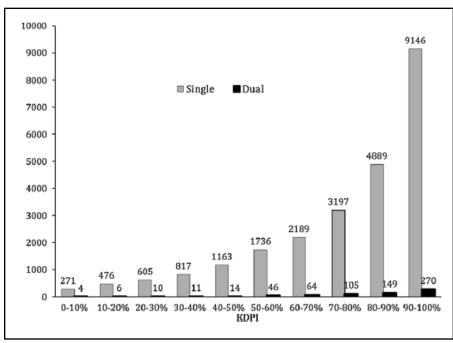
In Europe, this might be an opportunity to acquire a standardized uniform policy to meet the growing demand of donor kidneys and to maximize the use of both the best kidneys as well as those from 'marginal' donors.

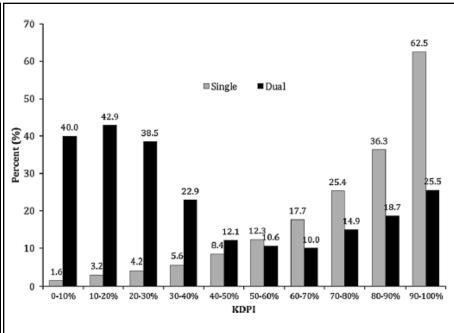
Nephrol Dial Transplant (2015) 30: 1285–1290 doi: 10.1093/ndt/gfu304

#### HIGH KDPI KIDNEYS AND RATE OF DISCARD

KDPI: 80-90% 36.3%

**KDPI: 90-100%** 62.5%





Tanriover B et al. Am J Transplant 2014.. UNOS registry 2002-2012

#### **ZERO-TIME RENAL TRANSPLANT BIOPSIES**

•When to perform the biopsy?
Procurement, preimplantation, postreperfusion

•How to perform the biopsy?
Wedge, core needle, skin punch

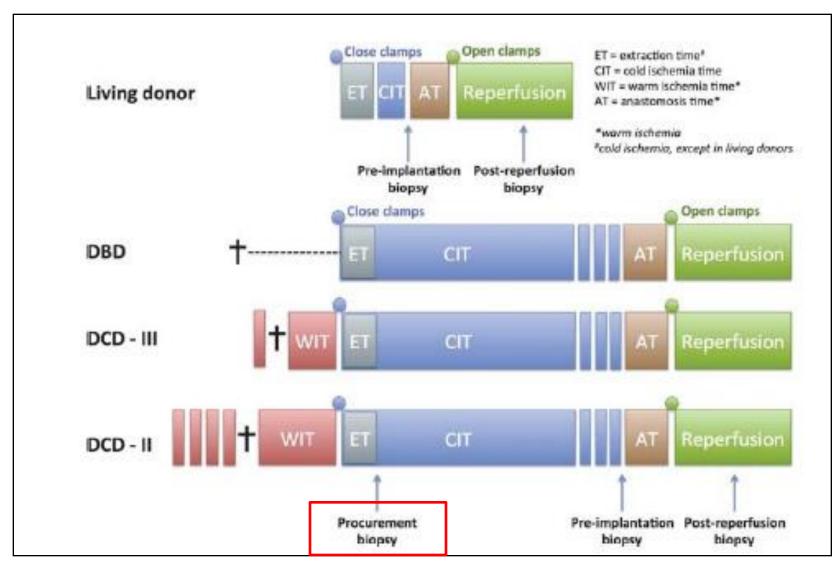
•How to process the obtained sample?
Paraffin-embedded, frozen

•How to evaluate the biopsy?
Glomerular sclerosis, Banff criteria, Remuzzi's score

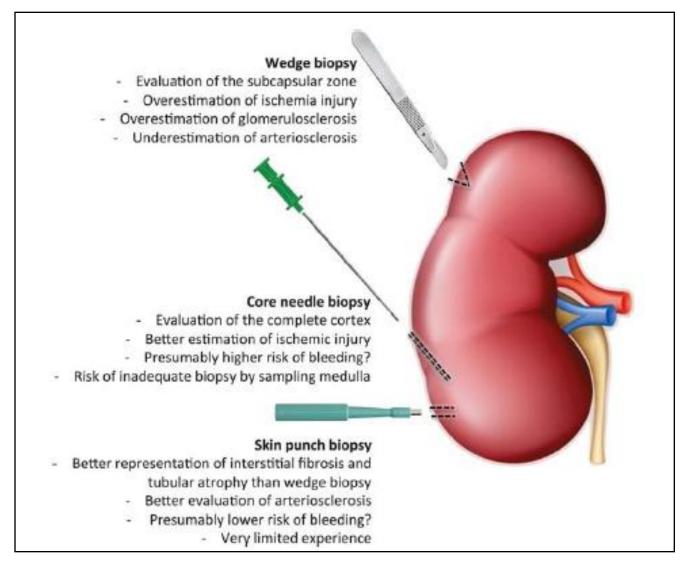
•How to interpret the results?
Sampling error, reproducibility

•When should a kidney be discarded?

#### **ZERO-TIME RENAL TRANSPLANT BIOPSIES**



#### **ZERO-TIME RENAL TRANSPLANT BIOPSIES**



#### LIMITATIONS OF ZERO-TIME RENAL TX BIOPSIES

- 1. Low predictive value on outcome
- 2. Low reproducibility between observers / samples
- 3. Thresholds to discard a kidney are define "a priori"
- 4. Donors with high KDPI (>80%) will display "frequently" advanced chronic damage

#### LOW PREDICTIVE VALUE ON OUTCOME

	Reference	Calculation	Range	Development	Clinical Application
Composite histological scores		Caroliation	Hange	Бечегорителя	оппост Аррисской
"Pirani Score"	Pirani et al; Remuzzi et al; Karpinski et al <sup>55-57</sup>	gs + ct + ci + cv ( $gs 0\% = 0$ ; $<20\% = 1$ ; 20-50% = 2; $>50% = 3$ ; ct, ci and cv scores are not in full concordance with Banff grading)	0-12	Clinical judgment	Associates with graft failure, but poor predictive performance. <sup>22,58</sup> Used in some centers for decisions on dual kidney transplantation, despite unclear waitlist effects
"Donor Score"	Azancot et al <sup>27</sup>	gs + ct + ci + cv + ah $(gs\ 0\% = 0;\ 1-10\% = 1;\ 11-20\% = 2;\ >20\% = 3)$	0-15	Clinical judgment	Associates with graft function up to 1 y posttransplantation, and with a composite of graft failure and graft functional decline. <sup>27</sup> The predictive performance is unclear.
CADI	Ortiz et al <sup>59</sup>	gs + ct + ci + cv + mm + i (gs 0% = 0; 1-15% = 1; 16-50% = 2; >50% = 3)	0-18	Clinical judgment	Associates with posttransplant CADI and could be used as baseline for posttransplant comparison as ΔCADI correlates with graft function up to 2 y after transplantation Association with graft failure was not evaluated. 59
"Chronicity Index"	Sund et al <sup>60</sup>	gs + if/ta + cv + ah + i (gs score = combination of global glomerulosclerosis and grades of sclerosis in preserved glomeruli)	0-15	Clinical judgment	Not established.
"Total Chronic Banff Score"	Snoeijs et al <sup>61</sup>	cg + mm + ct + ci + cv + ah + gsfraction x 3 (gsfraction = 0 to 1)	0-21	Clinical judgment	Associates with graft failure, but the predictive performance is poor. <sup>22,61</sup>
"CIV Score"	Balaz et al <sup>62</sup>	ci + cv	0-6	Modeling	Associates with delayed graft function, but the predictive performance is poor. 62
"Donor Chronic Damage Score"	Lopes et al <sup>49</sup>	$ci + cv + gs (gs \le 10\% = 0; > 10\% = 1)$	0-7	Modeling	Associates with graft function and graft failure, <sup>22,49</sup> but the predictive performance is poor. <sup>22</sup>
"MAPI Score"	Munivenkatappa et al <sup>24</sup>	ah (absent = 0; present = 4) + periglomerular fibrosis (absent = 0; present = 4) + arterial wall-to-lumen ratio ( $<0.5 = 0$ ; $\ge 0.5 = 2$ ) + scar (absent = 0; present = 3) + gs ( $<15\% = 0$ ; $\ge 15\% = 2$ )	0-15	Modeling + independent validation	Associates with graft failure, but the predictive performance is moderate at best. <sup>24</sup>
Clinical-histological score					
'Paris Composite Score" (for donors ≥ 50 years)	Anglicheau et al <sup>63</sup>	donor creatinine (<150 $\mu$ mol/L =0; $\geq$ 150 $\mu$ mol/L) and/or donor hypertension (absent 0; present = 1) + gs (gs <10% = 0; $\geq$ 10% = 1)	0-2	Modeling + independent validation	Associates with eGFR at 1 y after transplantation, and with graft failure. The predictive performance is good for eGFR at 1 y, but poor for graft failure. 63
"Leuven Donor Risk Score"	De Vusser et al <sup>22</sup>	donor age ( <i>years</i> ) + gs + 3 x if/ta ( $gs < 10\% = 0$ ; $\ge 10\% = 1$ )	1	Modeling + independent validation	Associates with graft failure. The predictive performance for graft failure is moderate. <sup>22</sup>

# The reproducibility and predictive value on outcome of renal biopsies from expanded criteria donors

M. Antonieta Azancot<sup>1</sup>, Francesc Moreso<sup>1</sup>, Maite Salcedo<sup>2</sup>, Carme Cantarell<sup>1</sup>, Manel Perello<sup>1</sup>, Irina Torres<sup>1</sup>, Angeles Montero<sup>2</sup>, Enric Trilla<sup>3</sup>, Joana Sellarés<sup>1</sup>, Joan Morote<sup>3</sup> and Daniel Seron<sup>1</sup>

Table 1 | Relationship between donor biopsy scores obtained by On-call pathologists and the renal pathologist (MS)

			On-call pathologist					
Renal pathologist	Total	Mild damage ≤3	Moderate damage 4–5	Advanced damage 6–7	Unacceptable ≥8			
Mild damage ≤3	36	17	15	4	0			
Moderate damage 4–5	53	3	31	19	0			
Advanced damage 6–7	25	3	4	16	2			
Unacceptable ≥8	8	0	0	0	8			
Total	122	23	50	39	10			

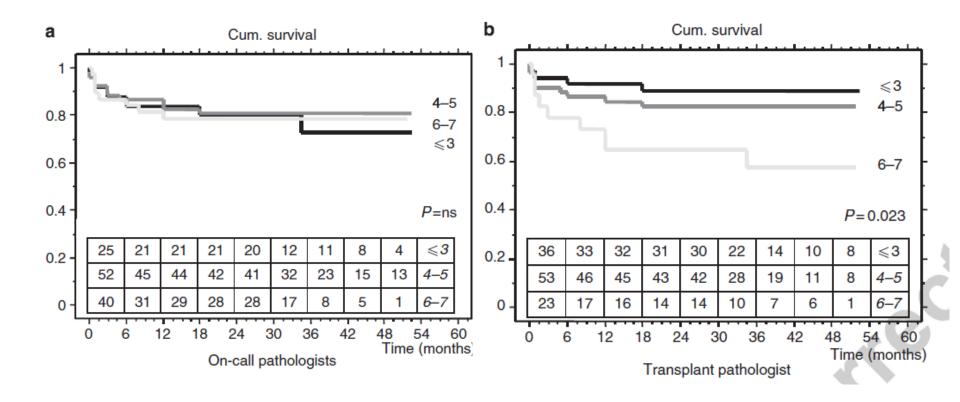
*P*-value < 0.001 ( $\chi^2$ ).

Kappa value=0.41

Azancot MA et al. Kidney Int 2014

# The reproducibility and predictive value on outcome of renal biopsies from expanded criteria donors

M. Antonieta Azancot<sup>1</sup>, Francesc Moreso<sup>1</sup>, Maite Salcedo<sup>2</sup>, Carme Cantarell<sup>1</sup>, Manel Perello<sup>1</sup>, Irina Torres<sup>1</sup>, Angeles Montero<sup>2</sup>, Enric Trilla<sup>3</sup>, Joana Sellarés<sup>1</sup>, Joan Morote<sup>3</sup> and Daniel Seron<sup>1</sup>



Azancot MA et al. Kidney Int 2014

# Pre-implantation analysis of kidney biopsies from expanded criteria donors: testing the accuracy of frozen section technique and the adequacy of their assessment by on-call pathologists

**Table 3.** Distribution of the Remuzzi score for frozen sections in the original report and frozen sections evaluated by the trained pathologist (n = 82). The results are expressed as the number of cases and percentage (N [%]).

	Remuzzi sc	Remuzzi score									
	0	1	2	3	4	5	6	7	8		
OR	3 (3.66)	20 (24.39)	15 (18.29)	21 (25.61)	17 (20.73)	3 (3.66)	2 (2.44)	0 (0)	1 (1.22)		
TP FS	0 (0)	9 (10.98)	16 (19.51)	23 (28.05)	20 (24.39)	9 (10.98)	3 (3.66)	2 (2.44)	0 (0)		

OR: original report, frozen section; TP FS: trained pathologist, frozen section.

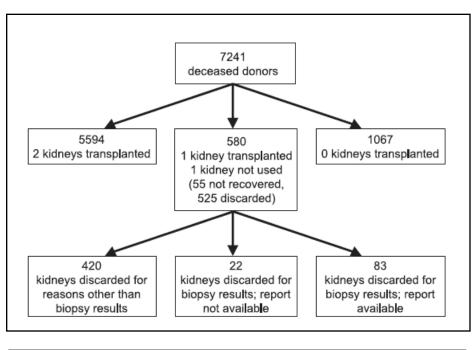
**Table 4.** Distribution of Remuzzi score for FS and PS evaluation revised by the same observer (n = 92). The results are expressed as the number of cases and percentage (N[%]).

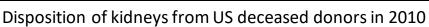
	Remuzzi score									
	0	1	2	3	4	5	6	7	8	
FS PS	0 (0) 2 (2.17)	10 (10.87) 8 (8.7)	18 (19.57) 17 (18.48)	23 (25) 27 (29.35)	22 (23.91) 26 (28.26)	12 (13.04) 8 (8.7)	4 (4.35) 3 (3.26)	2 (2.17) 1 (1.09)	1 (1.09) 0 (0)	

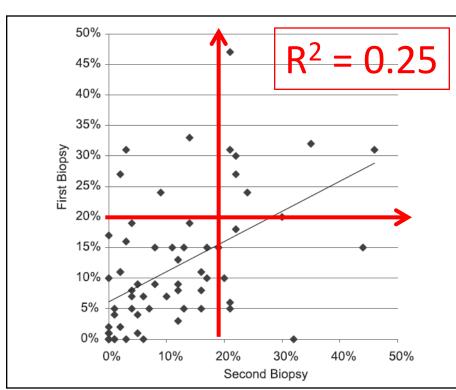
FS, frozen section; PS, paraffin section.

#### Two biopsies obtained from the same donor (N=64)

discarded, n=24 implanted with contralateral discarded, n=16 matched controls, n=24







Percentage of globally sclerotic glomeruli

Kasiske B et al. Clin J Am Soc Nephrol 2014

### Banff Histopathological Consensus Criteria for **Preimplantation Kidney Biopsies**

#### Circle appropriate findings:

Donor Biops	Interstitial fibrosis	None Mild Moderate Severe <5%; 6-25% 26-50% >50% of cortex involved							
Type of specim	Tubular atrophy	None Mild Moderate Severe 0%; <25% 26-50% >50% of cortical tubules involved							
Specimen ID: _	Interstitial inflammation	None Mild Moderate Severe <10%; 10-25% 26-50% >50% of cortex involved							
Number of glor Number of glob	Arterial intimal fibrosis	None Mild Moderate Severe 0%; <25% 26-50% >50% vascular narrowing							
Percentage of g Number of arte	Arteriolar hyalinosis hyalin restricted to subendothelial layer	None Mild * Moderate * Severe *							
*Periglomerular so **Vessel with inte	*Mild: at least one arteriole Moderate: more than one arteriole Severe: multiple arterioles affected, circumferential								
glomerulus cut in	Glomerular thrombi None Mild * Moderate* Severe*								
	*mild <10% of capillaries occluded; moderate: 10-25% occlusion; severe: >25% occlusion evaluate in the most severely affected glomerulus								
Liapis H et al.	†Mild: ATI – epithelial flattening, tubule dilation, nuclear dropout, loss of brush border; Moderate – focal COAGULATIVE TYPE necrosis; Severe – infarction.								
/9/2017	Other findings: (FSGS, nodular glomerulosclerosis, tumor, etc.)								

### Banff Histopathological Consensus Criteria for Preimplantation Kidney Biopsies

Consensus best practices and suggestions for future studies for performing and interpreting donor biopsies

- 1. Good **wedge biopsies** not restricted to the subcapsular cortex can be superior to needle biopsies.
- 2. Histopathologic parameters with **good or fair reproducibility** include number of glomeruli, **percentage of globally sclerosed glomeruli**, **interstitial fibrosis and arteriosclerosis**.
- 3. Although only percentage of glomerulosclerosis was identified as statistically significant parameter that associated with graft function, other studies noted that significant interstitial fibrosis and arteriosclerosis can also adversely affect graft function.

Liapis H et al. Am J Transplant 2017

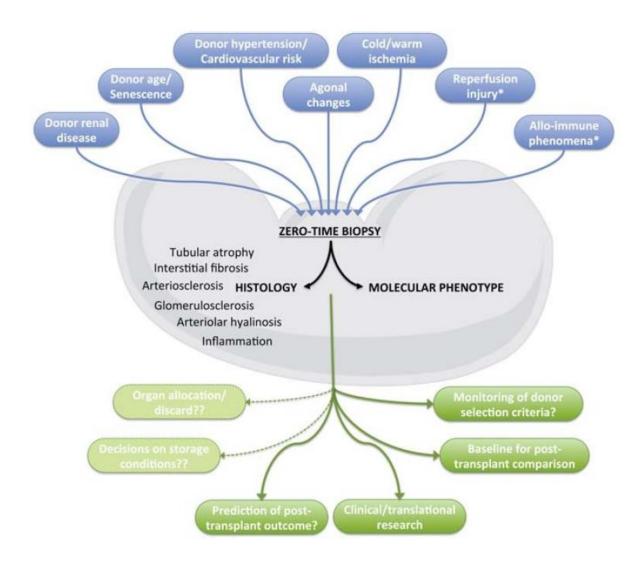
### Banff Histopathological Consensus Criteria for Preimplantation Kidney Biopsies

Consensus best practices and suggestions for future studies for performing and interpreting donor biopsies

- 4. Rigidly defined histologic <u>cutoffs such as 20% glomerulosclerosis should</u> <u>not be used in isolation to discard kidneys</u>.
- 5. Comprehensive clinical evaluation such as that required in calculation of KDPI is an important part of donor evaluation; however, the **C-statistic (ability to predict graft failure) for KDPI is only 0.6**, and further studies seeking to rigorously evaluate the incremental value of biopsy readings over clinical assessment alone need to be performed.
- 6. **Training of general pathologists** to read donor biopsies using consistent criteria **is recommended**.
- 7. Adoption of rapid formalin-fixation and paraffin-embedding protocols that have the potential to eliminate problems associated with interpreting frozen sections need to be studied further.

Liapis H et al. Am J Transplant 2017

### **ZERO-TIME RENAL TRANSPLANT BIOPSIES**



Naesens M. Transplantation 2016; 100: 1425-1439

# The Kidney Donor Profile Index (KDPI) of Marginal Donors Allocated by Standardized Pretransplant Donor Biopsy Assessment: Distribution and Association With Graft Outcomes

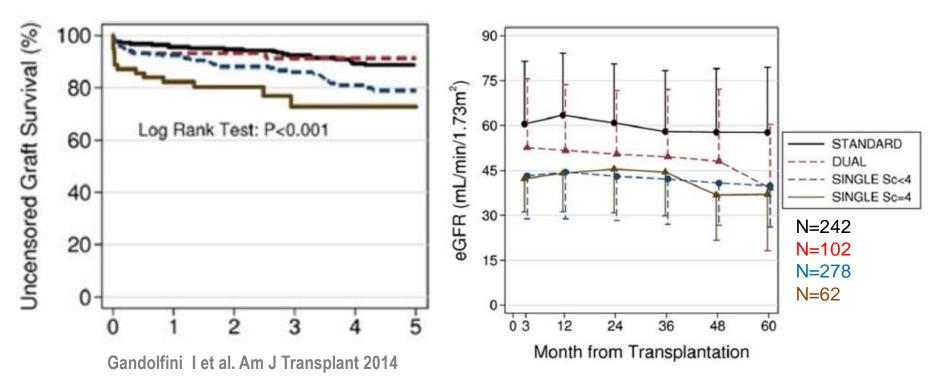
Emilia-Romagna (Italy). 2001-2012.

Marginal donors: donor age > 65 y, eCr Cl < 60 mL/min, Proteinuria > 1g/d

Remuzzi's score

1479 offered kidneys. 182 (12%) discarded. 37 due to score > 6.

**KDPI=80-90% Discard rate 15%. KDPI >90% Discard rate 37%.** 



## Long-Term Outcomes and Discard Rate of Kidneys by Decade of Extended Criteria Donor Age

Turin University Hospital (Italy). 2003-2013. 647 Tx from ECD.

Reumuzzi's score. From 2006 score 4 allocated as single transplant

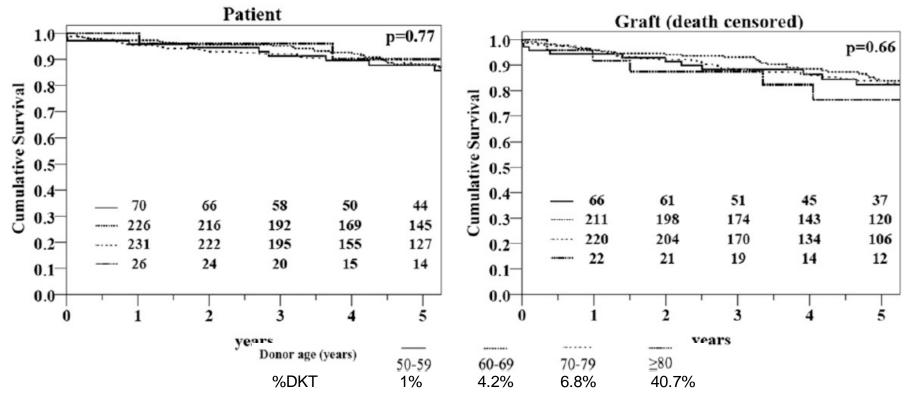
Table 3. Causes of KDR per donor age decades									
KDR and KDR causes	50–59 yr ( <i>n</i> =188), %	60–69 yr ( <i>n</i> =587), %	70–79 yr ( <i>n</i> =604), %	≥80 yr ( <i>n</i> =110), %	Total ( <i>n</i> =1489), %	P Value			
Organ recovered and transplanted Organ recovered but not transplanted (KDR)	84.6 15.4	81.8 18.2	78.1 21.9	51.8 48.2	79.4 20.6	<0.001 <0.001			
KDR causes Suspected donor neoplasia or other comorbidities	0	2.7	2.6	1.8	2.3	0.15			
Organ macroscopic appearance or anatomic anomalies	4.8	7.2	10.3	20	9.1	< 0.001			
Preimplantation kidney biopsy Technical problems	3.7 4.3	5.1 0.9	4.6 2.3	11.8 3.6	5.2 2.1	<0.001 <0.001			
No available recipients Others	2.1 0.5	1.8 0.5	2.1 0	10.9 0	2.6 0.3	< 0.001			

Messina M et al. Clin J Am Soc Nephrol 2016

## Long-Term Outcomes and Discard Rate of Kidneys by Decade of Extended Criteria Donor Age

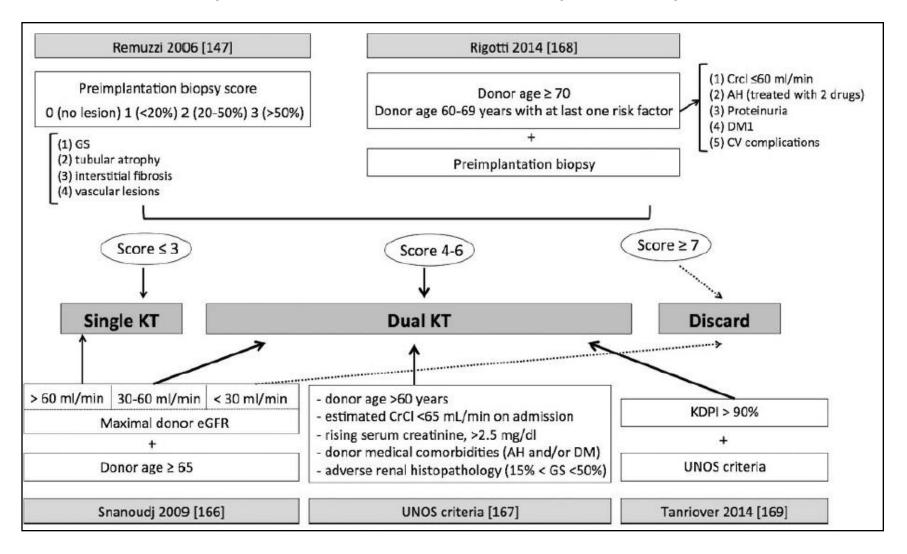
Turin University Hospital (Italy). 2003-2013. 647 Tx from ECD.

Reumuzzi's score. From 2006 score 4 allocated as single transplant



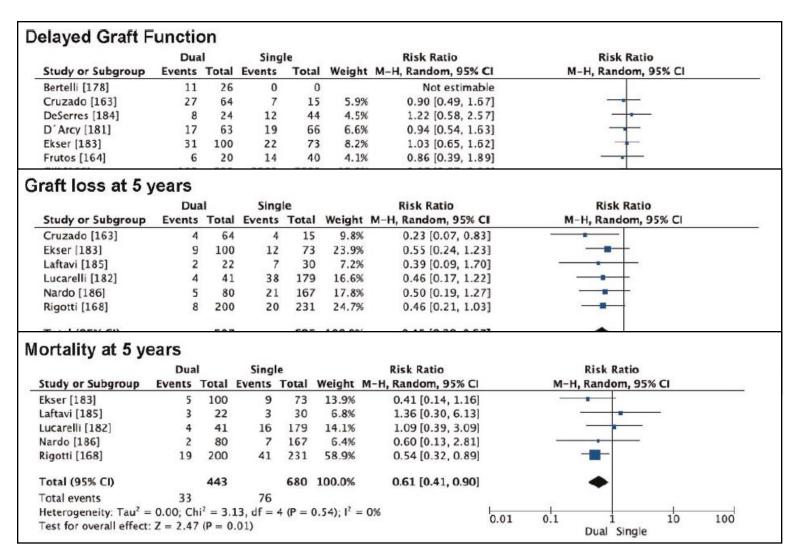
Messina M et al. Clin J Am Soc Nephrol 2016 4/9/2017

### There is a place for dual kidney transplantation?



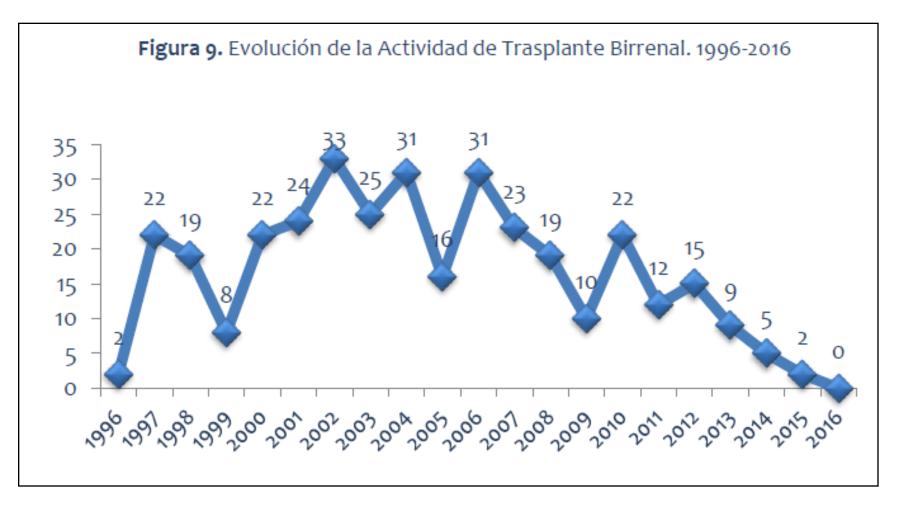
Perez-Saez MJ et al. Transplantation 2017

### There is a place for dual kidney transplantation?



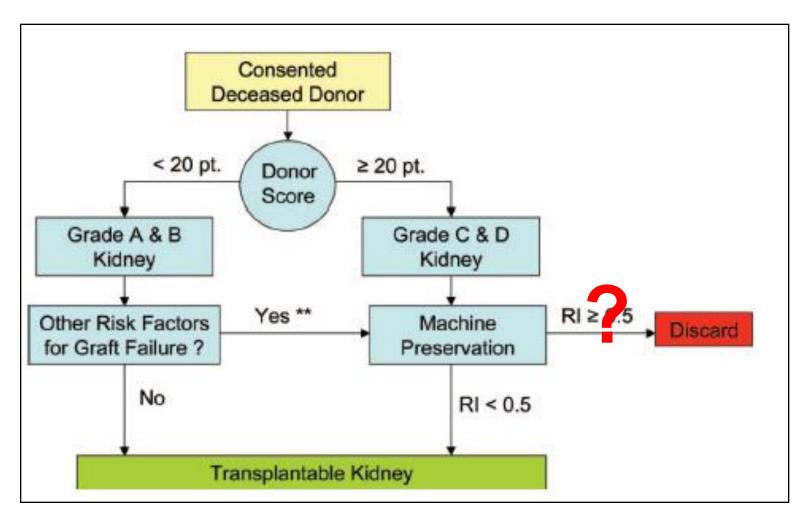
Perez-Saez MJ et al. Transplantation 2017

### There is a place for dual kidney transplantation?



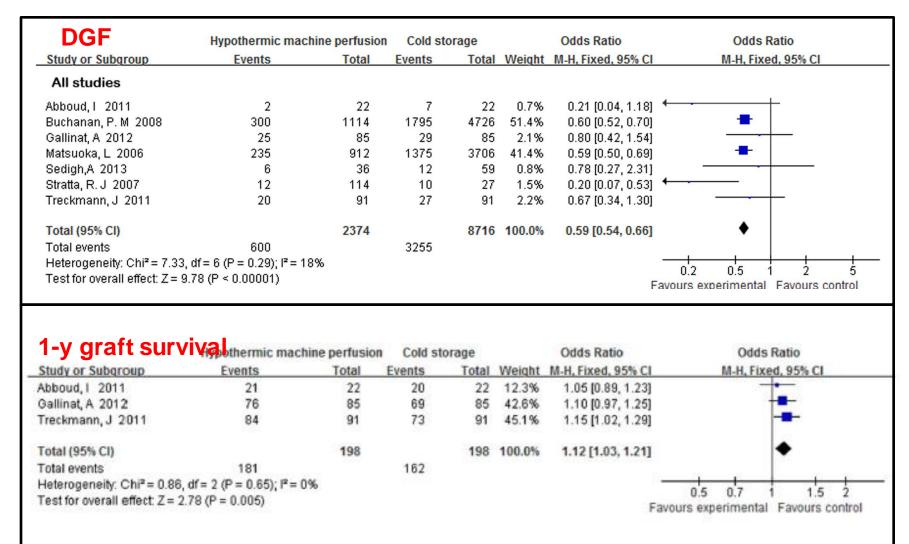
Source: ONT report 2016

#### MACHINE PERFUSION FOR OLD KIDNEYS



Nyberg SL et al. Transplantation 2005

### MACHINE PERFUSION FOR OLD KIDNEYS



Jiao B et al. Plos One 2014

### Summary

- 1. New tools such KDPI seem adequate to evaluate the kidney quality from clinical data but it is necessary to validate its performance in other populations. Additionally, we need to develope algorythms to allocate organs in order to minimize the kidney discard and assure better survival with very expanded kidneys than remaining in the kidney waiting list for a standard donor.
- 2. Procurement biopsies help to characterize pre-existing lesions but should not be used to discard kidneys due to the low predictive value on outcome, sampling error and low reproducibility of scores.
- 3. The combination of clinical data (KDPI) and procurement biopsies allow to design algorythms (including or not dual kidney transplantation) for using high risk kidneys with low discard rates and similar outcomes than low risk kidneys.