

Prélèvements hépatiques : enjeux actuels et améliorations futures

Dr Niccolo Petrucciani



ABM 2015

Tableau F1. Evolution de la liste d'attente et devenir des candidats en greffe hépatique

	2010	2011	2012	2013	2014	2015	2016
Liste d'attente							
- malades restant en attente au 1er janvier de chaque année	806	932	941	1106	1267	1296	1265
dont malades en attente au 1er janvier et en CIT	191	250	299	285	420	562	633
% des malades en CIT parmi les malades en attente au 01/01	24%	27%	32%	26%	33%	43%	50%
- nouveaux inscrits dans l'année	1580	1532	1724	1822	1787	1756	
- décédés dans l'année	170	137	183	208	216	181	
% de décès parmi les inscrits*	7,1%	5,6%	6,9%	7,1%	7,1%	5,9%	
- sortis de la liste d'attente	192	222	215	212	262	251	
dont sortis de la liste d'attente pour aggravation	112	105	110	116	138	122	
Greffes	1092	1164	1161	1241	1280	1355	
- dont greffes avec donneur vivant apparenté	17	14	9	13	12	15	
- dont greffes avec donneur vivant domino	8	19	8	7	5	9	
- dont greffes avec donneur DDAC-ACI	3	5	3	2	4	2	
- dont greffes avec donneur DDAC-LAT	0	0	0	0	0	6	
Greffes (pmh)	16,9	17,9	17,7	18,9	19,3	20,4	

* receveurs en attente au 1er janvier de l'année en cours + nouveaux inscrits

pmh : par million d'habitant

CIT : contre-indication temporaire

Données extraites de CRISTAL le 01/03/2016

DDAC_ACI = Donneur décédé après arrêt circulatoire suite à un arrêt cardiaque inopiné

DDAC_LAT=Donneur décédé après arrêt circulatoire suite à la limitation ou l'arrêt des thérapeutiques

ABM 2015

Tableau F2. Evolution des principaux indicateurs de pénurie en greffe hépatique

	2010	2011	2012	2013	2014	2015
Nouveaux inscrits pour un greffon	1,4	1,3	1,5	1,5	1,4	1,3
Receveur en attente au 1er janvier pour un greffon	0,7	0,8	0,8	0,9	1,0	1,0
Receveur en attente au 1er janvier pour un greffon hors malade en CIT	0,6	0,6	0,6	0,7	0,7	0,5
Total candidats pour un greffon	2,2	2,1	2,3	2,4	2,4	2,3

CIT : Contre-indication temporaire

Données extraites de CRISTAL le 01/03/2016

Organ shortage → extended criteria donors

Extended criteria donors

Table 1 Donor factors defining ECD	
Risk of Impaired Graft Function	Risk of Disease Transmission
Donor age (>60 years)	Positive hepatitis B and C serologies
Donor obesity	Unexplained cause of death
Steatotic livers (>40% macro)	Known donor malignancy
Donation after cardiac death	"High-risk" lifestyle
Hypernatremia (serum Na > 155 mEq/L)	Active bacterial/viral infections
Hypotension and inotropic support	Elderly donors
Prolonged intensive care stay	
Long ischemia times (CIT > 12 hours)	
Partial liver grafts (split/live donor)	

Gastroenterol Clin North Am. 2011 Sep;40(3):641-58. doi: 10.1016/j.gtc.2011.06.007.

Liver transplantation in the 21st century: expanding the donor options.

Sass DA¹, Reich DJ.

Parameters

Age:

- | | |
|-------|-----------------------|
| <40 | <input type="radio"/> |
| 40-49 | <input type="radio"/> |
| 50-59 | <input type="radio"/> |
| 60-69 | <input type="radio"/> |
| >69 | <input type="radio"/> |

DONOR RISK INDEX CALCULATOR

Cause of Death

- | | |
|--------------------------------|-----------------------|
| Trauma | <input type="radio"/> |
| Anoxia | <input type="radio"/> |
| Cerebrovascular Accident (CVA) | <input type="radio"/> |
| Other | <input type="radio"/> |

Race

- | | |
|------------------|-----------------------|
| African American | <input type="radio"/> |
| White | <input type="radio"/> |
| Other | <input type="radio"/> |

Donation after Cardiac Death (DCD)

- | | |
|-----|-----------------------|
| Yes | <input type="radio"/> |
| No | <input type="radio"/> |

Partial/Split Liver Graft

- | | |
|-----|-----------------------|
| Yes | <input type="radio"/> |
| No | <input type="radio"/> |

Height

Enter height in centimeters

Organ Location

- | | |
|----------|-----------------------|
| Local | <input type="radio"/> |
| Regional | <input type="radio"/> |
| National | <input type="radio"/> |

Cold time

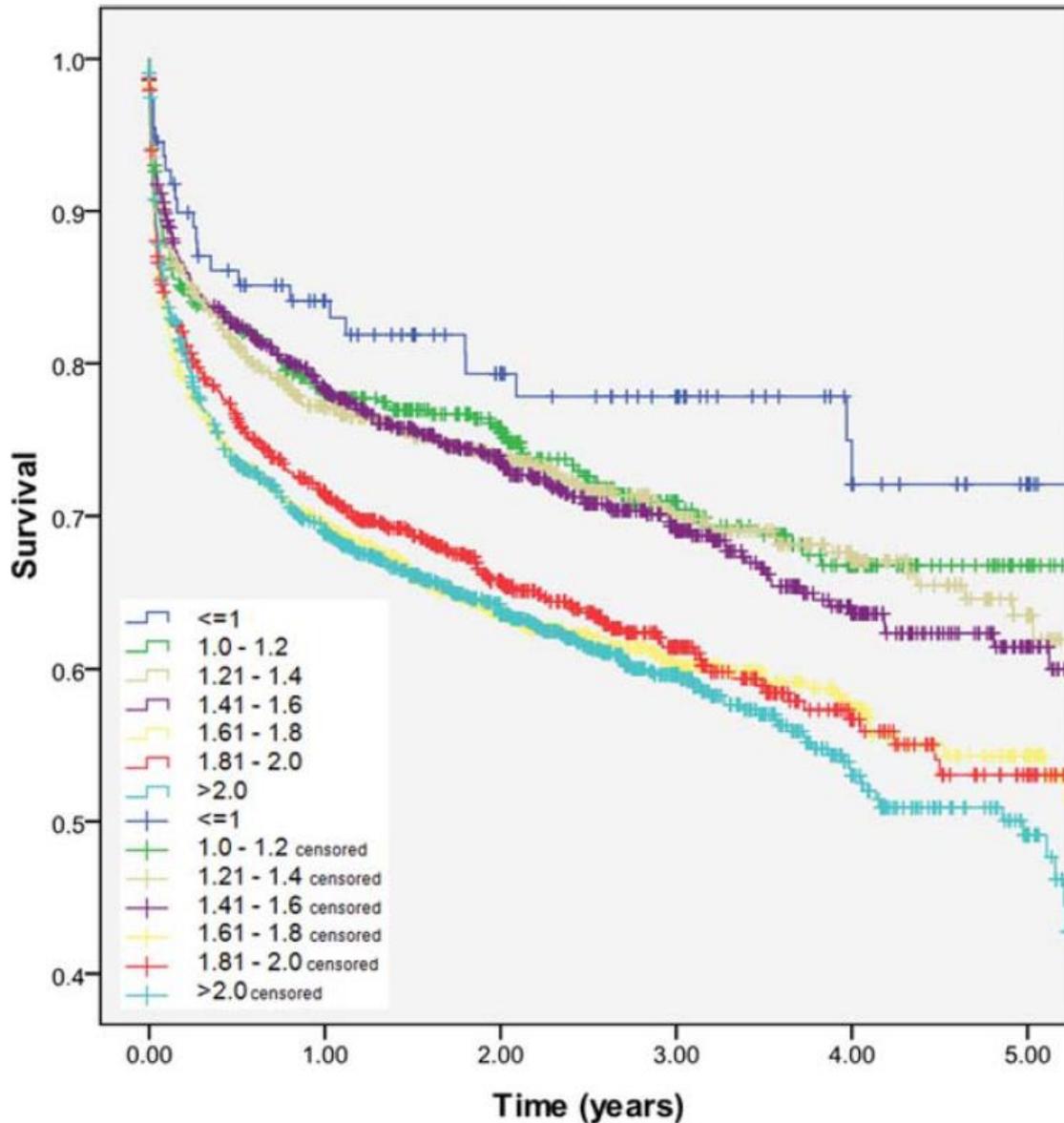
Enter cold time in hours

Validation of the Donor Risk Index in Orthotopic Liver Transplantation Within the Eurotransplant Region

LIVER TRANSPLANTATION 18:113-120, 2012

- 5939 liver transplants in Eurotransplant
- DRI was higher in Eurotransplant versus OPNT (USA)
- DRI was strongly correlated with outcomes and the most significant factors influencing outcomes

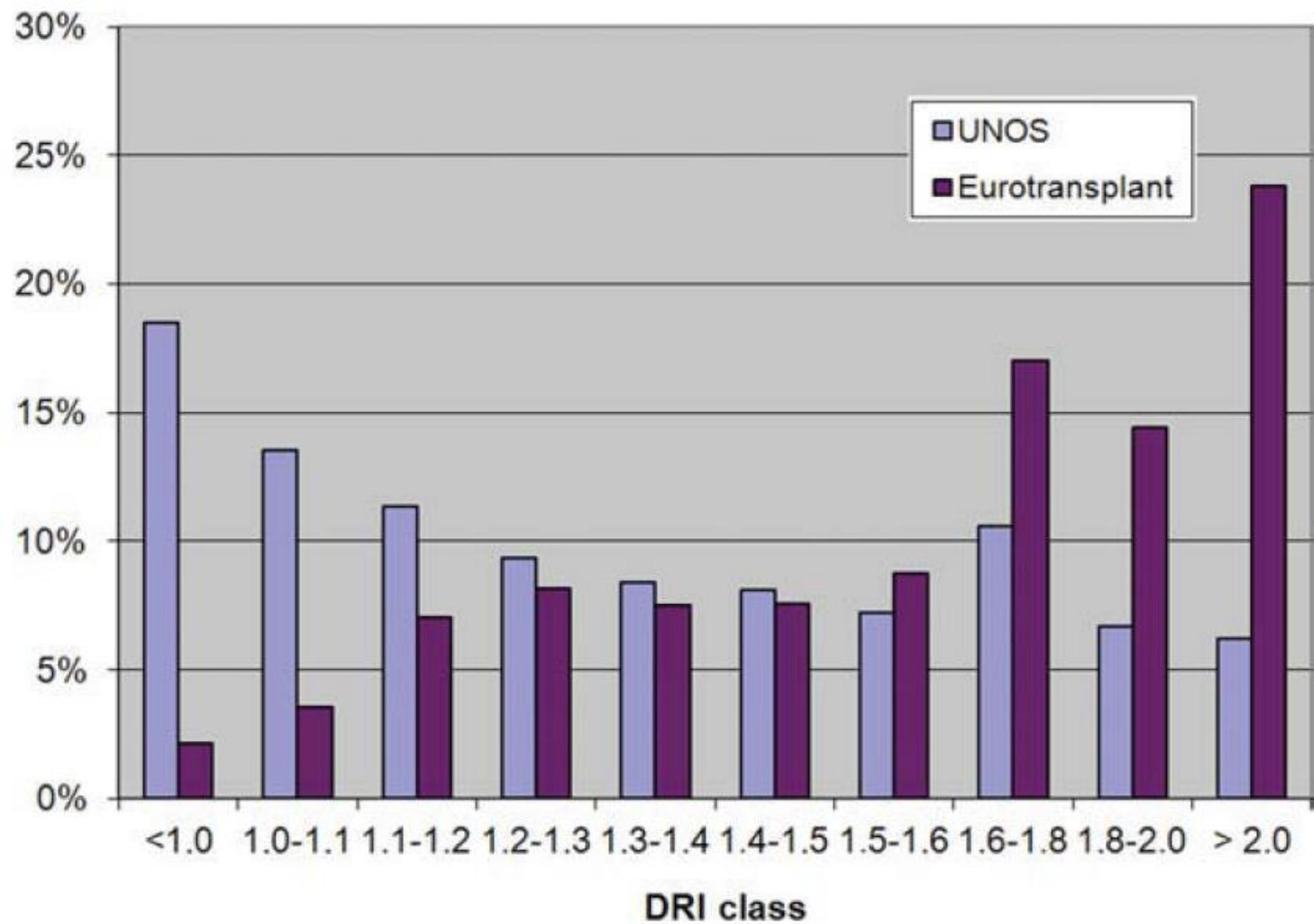
Figure 2. Failure-free survival of adult orthotopic liver transplants from deceased donors in the Eurotransplant region between January 1, 2003 and December 31, 2007 per DRI category.



Validation of the Donor Risk Index in Orthotopic Liver Transplantation Within the Eurotransplant Region

LIVER TRANSPLANTATION 18:113-120, 2012

This study confirms the idea that the results of liver transplantation should always be seen in the light of liver donor quality. When we are looking at outcome data, it is important for us to refer to this donor quality, and the DRI would be a valid tool for this. Of course, the outcome also depends on recipient factors.



The Eurotransplant Donor Risk Index in Liver Transplantation: ET-DRI

American Journal of Transplantation 2012;

- DRI was modified to ET-DRI
- ET-DRI includes all covariates of DRI except race and weight
- GGT and rescue offer were added
- Location was modified (local, regional, extra-regional)

The Eurotransplant Donor Risk Index in Liver Transplantation: ET-DRI

American Journal of Transplantation 2012;

Table 6: Three-month, 1-year and 3-year failure free survival per ET-DRI category

ET-DRI	N (%)	Graft survival (95% confidence interval)		
		3 Months	1 Year	3 Years
0.0 <ET-DRI ≤ 1.0	62(1.2)	90.3 (97.9–82.7)	83.6 (93.2–74)	81.6 (91.6–71.6)
1.0 <ET-DRI ≤ 1.2	262(5.2)	87.6 (91.8–83.4)	81.9 (86.7–77.1)	75.0 (80.8–69.2)
1.2 <ET-DRI ≤ 1.4	635(12.7)	84.0 (87.0–81.0)	76.5 (79.9–73.1)	70.1 (74.1–66.1)
1.4 <ET-DRI ≤ 1.6	786(15.7)	84.2 (86.8–81.6)	78.0 (81.0–75.0)	69.6 (73.2–66.0)
1.6 <ET-DRI ≤ 1.8	908(18.1)	81.2 (83.8–78.6)	73.6 (76.6–70.6)	65.7 (69.1–62.3)
1.8 <ET-DRI ≤ 2.0	879(17.5)	82.4 (85.0–79.8)	71.1 (76.1–70.1)	61.2 (64.8–57.6)
2.0 <ET-DRI	1481(29.5)	77.7 (79.9–75.5)	67.5 (69.9–65.1)	58.2 (61.0–55.4)

ET-DRI and FFS-data complete in 5013 cases (84.4% of total 5939).

- ET-DRI had high predictive value for outcomes after LT

External validation of the Donor Risk Index and the Eurotransplant Donor Risk Index on the French liver transplantation registry

23 January 2017

Audrey Winter^{1,2}  | Cyrille Féray³ | Etienne Audureau⁴ | René Écochard⁵
Christian Jacquelin⁶ | Françoise Roudot-Thoraval³ | Christophe Duvoux³ |
Jean-Pierre Daurès^{1,2} | Paul Landais^{1,7}

- Neither the DRI nor the ET-DRI were validated against French dataset.
- Important donor and candidates differences
- New adaptation of DRI?

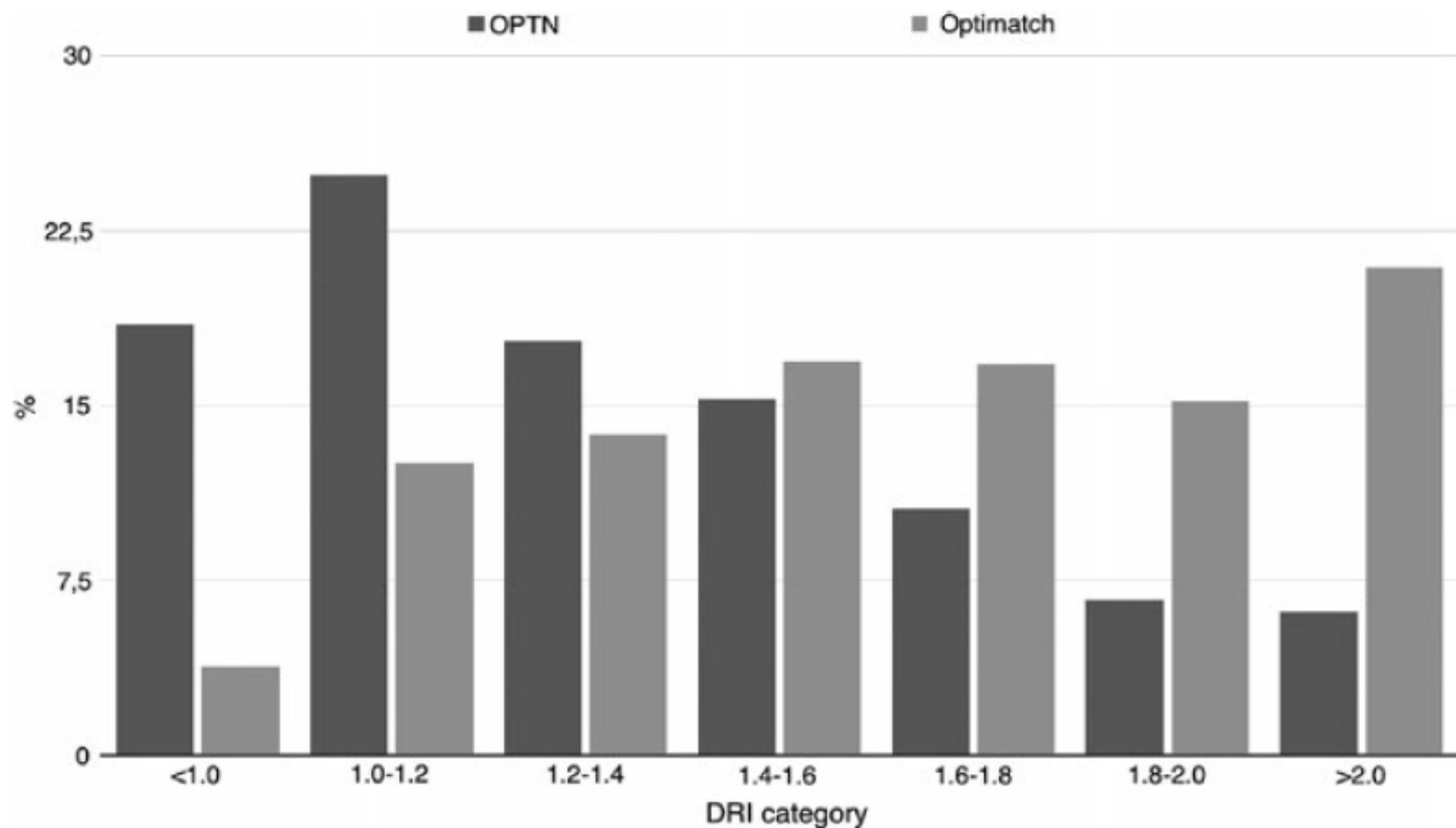


FIGURE 1 Distribution of the DRI for the OPTN and the French datasets

ABM 2015

- 1361 prélèvements hépatiques/1782 donneurs (76.4%)
- Age moyenne de donneur: 56.2 ans
- Donneurs >65 ans = 38%

Age

- The proportion of older donors has continuously increased in France
- Concerns: biliary complications, arterial thrombosis, poor initial function, overall graft survival (especially in HCV+ recipients)

Outcome of liver transplantation using donors older than 60 year of age

Serrano et al.

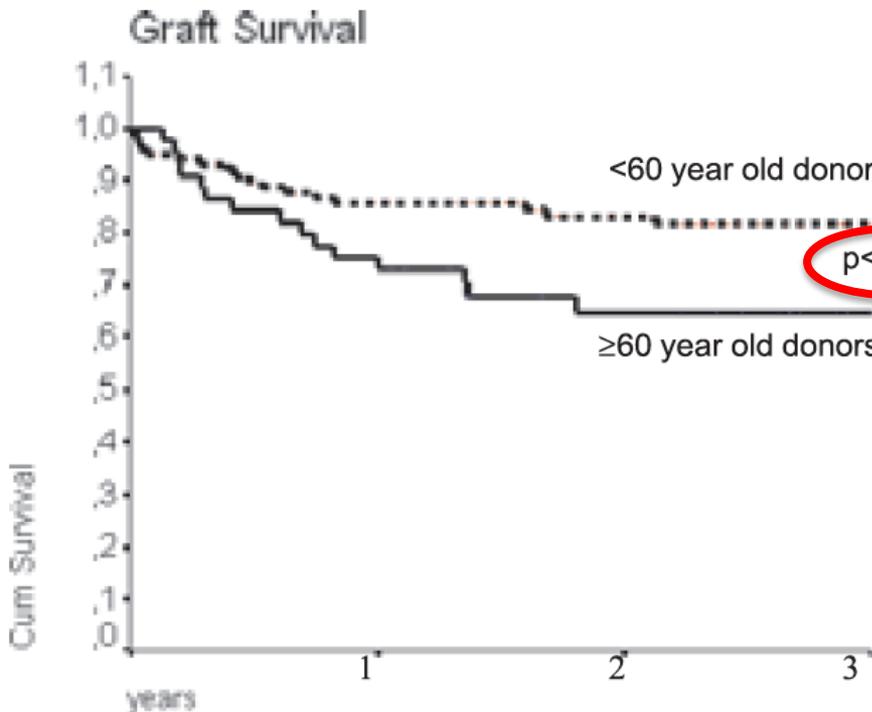
Clin Transplant 2010

- 149 LTs, donor age >60 y in 47 and <60 in 102
- In older donors group:
 - > non anastomotic biliary strictures
 - < graft survival

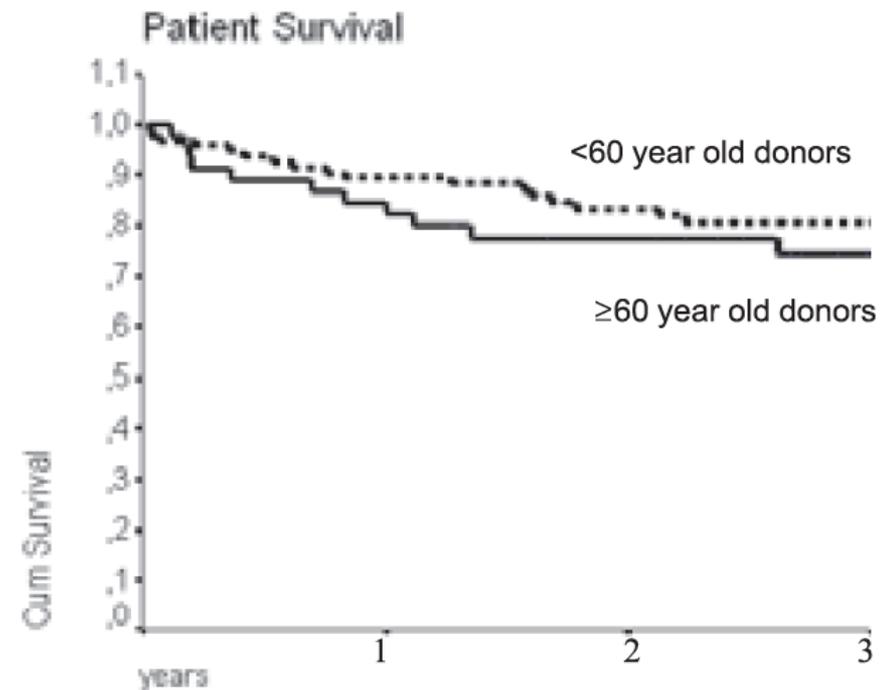
Outcome of liver transplantation using donors older than 60 year of age

Serrano et al.

Clin Transplant 2010



Graft Survival	1 y	2 y	3 y
Donor <60 years	0.85	0.81	0.79
Donor ≥ 60 years	0.74	0.65	0.65



Patient Survival	1 y	2 y	3 y
Donor <60 years	0.89	0.84	0.81
Donor ≥ 60 years	0.82	0.77	0.73

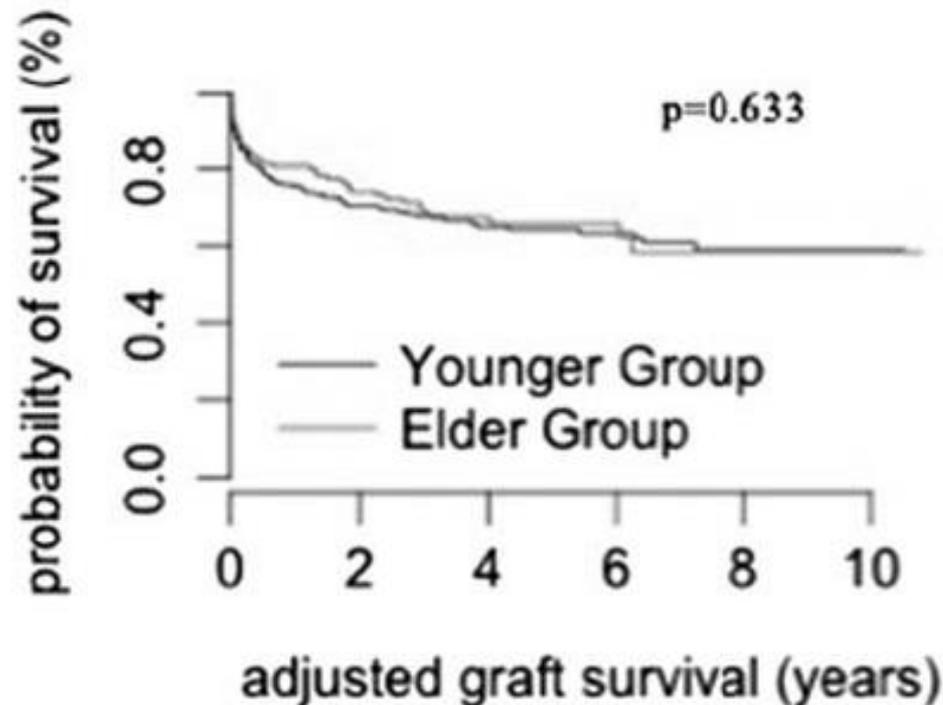
Liver Transplantation With Older Donors: A Comparison With Younger Donors in a Context of Organ Shortage

Louise Barbier, MD,¹ Manuela Cesaretti, MD,¹ Federica Dondero, MD,¹ François Cauchy, MD,¹
Linda Khoy-Ear, MD,² Takeshi Aoyagi, MD,¹ Emmanuel Weiss, MD, PhD,² Olivier Roux, MD,³ Safi Dokmak, MD,¹
Claire Francoz, MD, PhD,³ Catherine Paugam-Burtz, MD, PhD,² Ailton Sepulveda, MD,¹
Jacques Belghiti, MD, PhD,¹ François Durand, MD, PhD,³ and Olivier Soubrane, MD, PhD¹

- 157 donors >75 y compared with 253 <60y
- Older group: better liver tests, only 3 cardiac arrests
- No differences in complications (biliary, arterial, non-function) and graft survival

Liver Transplantation With Older Donors: A Comparison With Younger Donors in a Context of Organ Shortage

P



Years	0	2	4	6	8	10
Younger Group (N)	253	152	105	64	20	2
Elder Group (N)	157	80	35	17	6	4

FIGURE 1. Grafts' survival in the older group and in the younger group after adjustment on HCV infection and MELD score. The table below the survival curves displays the numbers of patients at risk.

Age

- Results highly variables in the different studies
- No cut-off

D-MELD, a Simple Predictor of Post Liver Transplant Mortality for Optimization of Donor/Recipient Matching

American Journal of Transplantation 2009;

**J. B. Halldorson*, R. Bakthavatsalam,
O. Fix, J. D. Reyes and J. D. Perkins**

- Study on UNOS database
- D-MELD (donor age x recipient MELD) accurately predicts patients and graft survival
- Useful for allocation

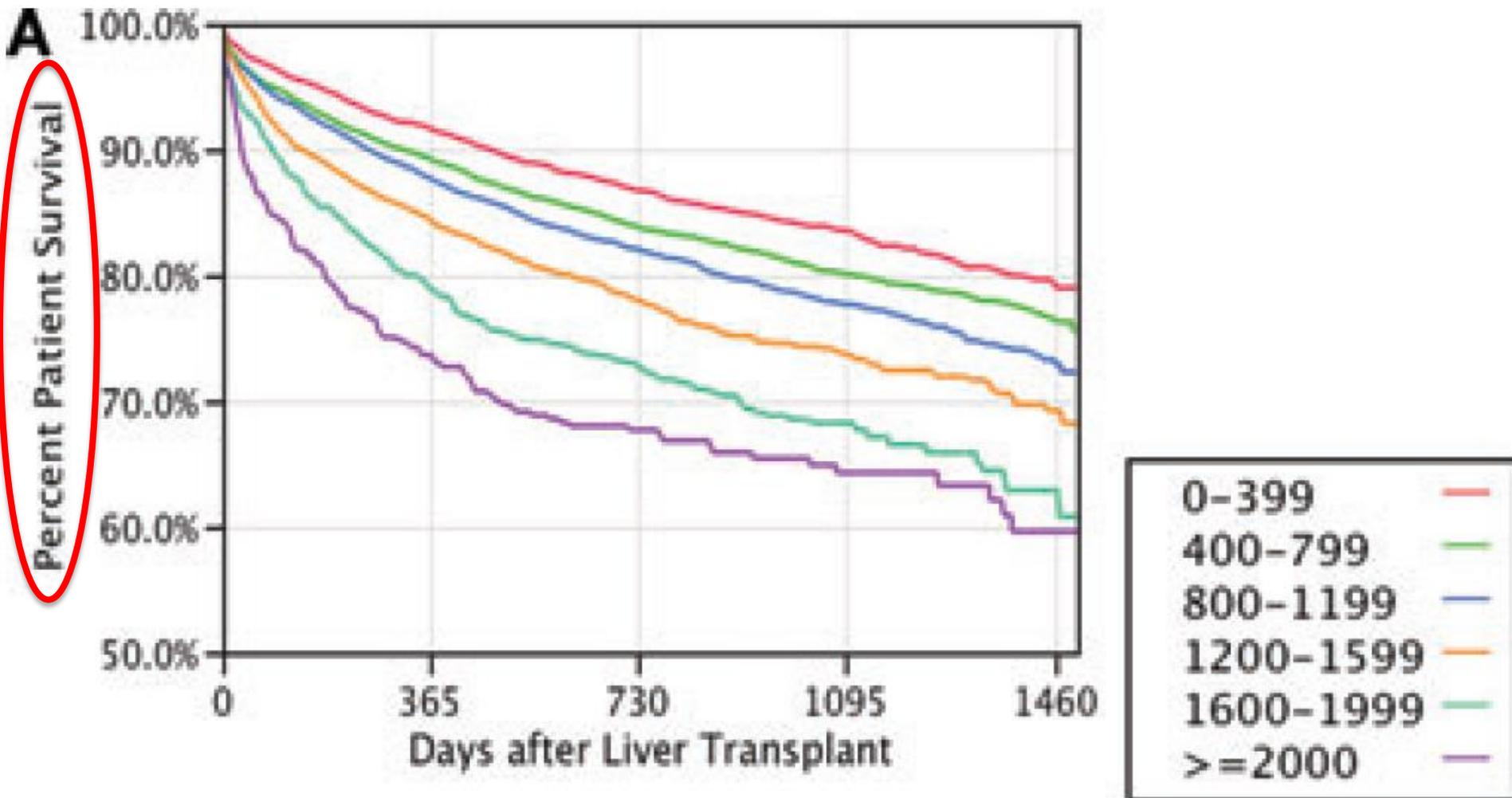
D-MELD, the Product of Donor Age and Preoperative MELD, Predicts Surgical Outcomes After Living Donor Liver Transplantation, Especially in the Recipients With HCV-positive and Smaller Grafts

A. Tanemura, S. Mizuno*, H. Kato, Y. Murata, N. Kuriyama, Y. Azumi, M. Kishiwada, M. Usui, H. Sakurai, and S. Isaji

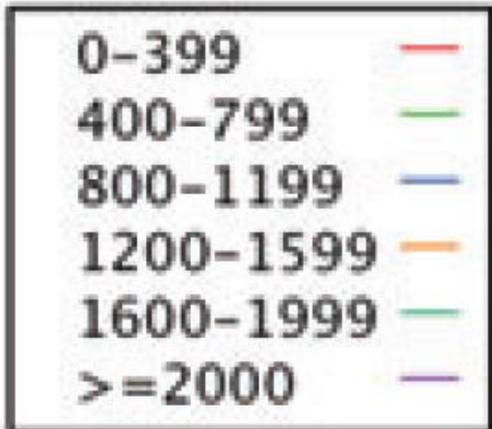
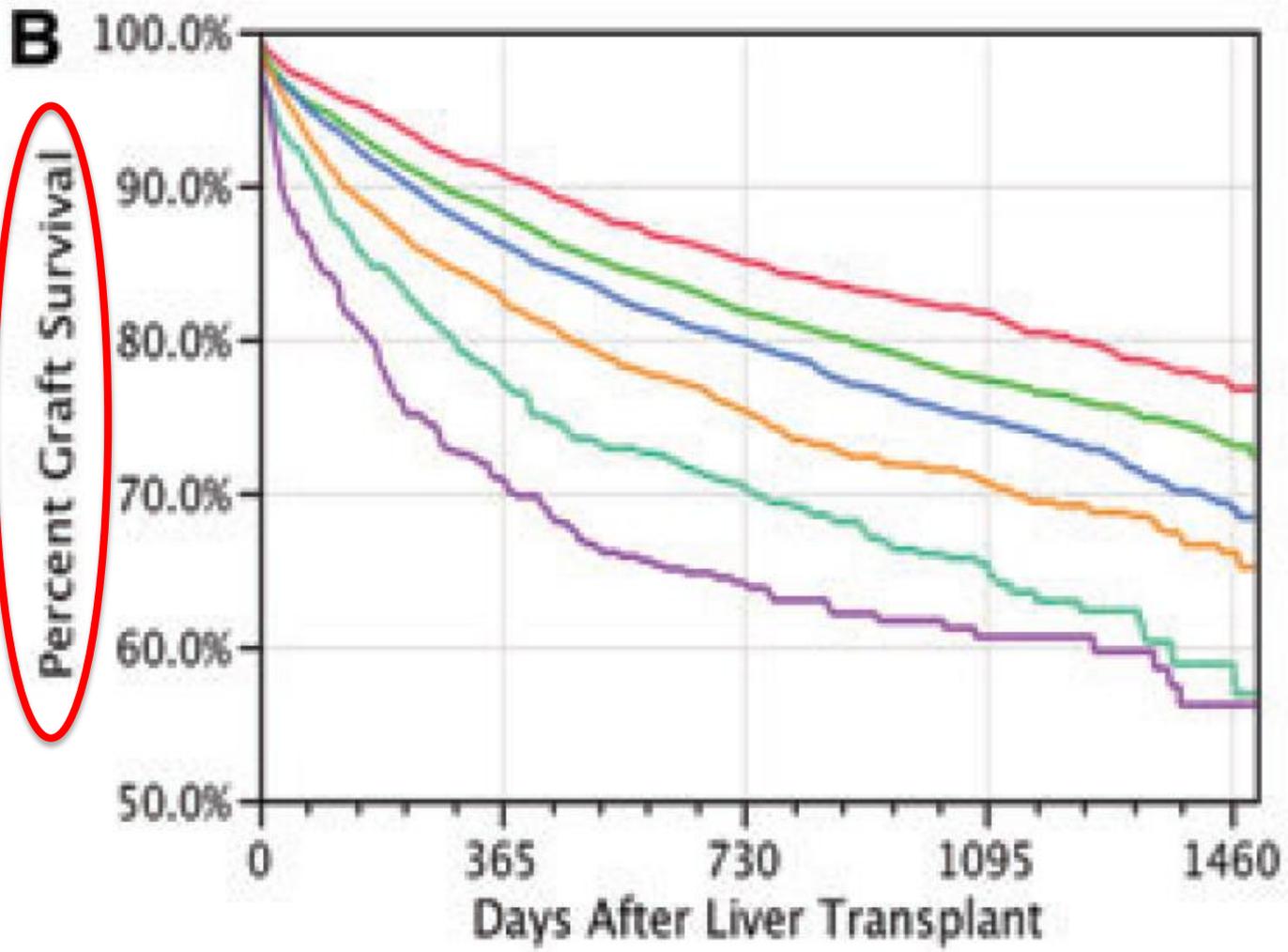
Transplantation Proceedings, 48, 1025–1031 (2016)

- 120 patients classified according to D-MELD (donor age x recipient MELD)
- D-MELD <1000 = 101
- D-MELD >1000 = 19

D-MELD, the Product of Donor Age and Preoperative MELD, Predicts Surgical Outcomes After Living Donor Liver Transplantation, Especially in the Recipients With HCV-positive and Smaller Grafts



D-MELD, the Product of Donor Age and Preoperative MELD, Predicts Surgical Outcomes After Living Donor Liver Transplantation, Especially in the Recipients With HCV-positive and Smaller Grafts



Other factors

- Liver steatosis
- Rescue liver (hors tours)
- Cold ischemia
- DCD donors

Interpretation of all donor's and recipient's factors to define the risk

Are There Better Guidelines for Allocation in Liver Transplantation?

A Novel Score Targeting Justice and Utility in the Model for End-Stage Liver Disease Era
Dutkowski et al.

- Risk analysis in 37255 patients of UNOS
- 6 predictors of survival after LT identified: recipient MELD, cold ischemia time, recipient age, donor age, previous OLT, life support dependence
- BAR (Balance of Risk) score stratified patients better than previous scores

Are There Better Guidelines for Allocation in Liver Transplantation?

A Novel Score Targeting Justice and Utility in the Model for End-Stage Liver Disease Era

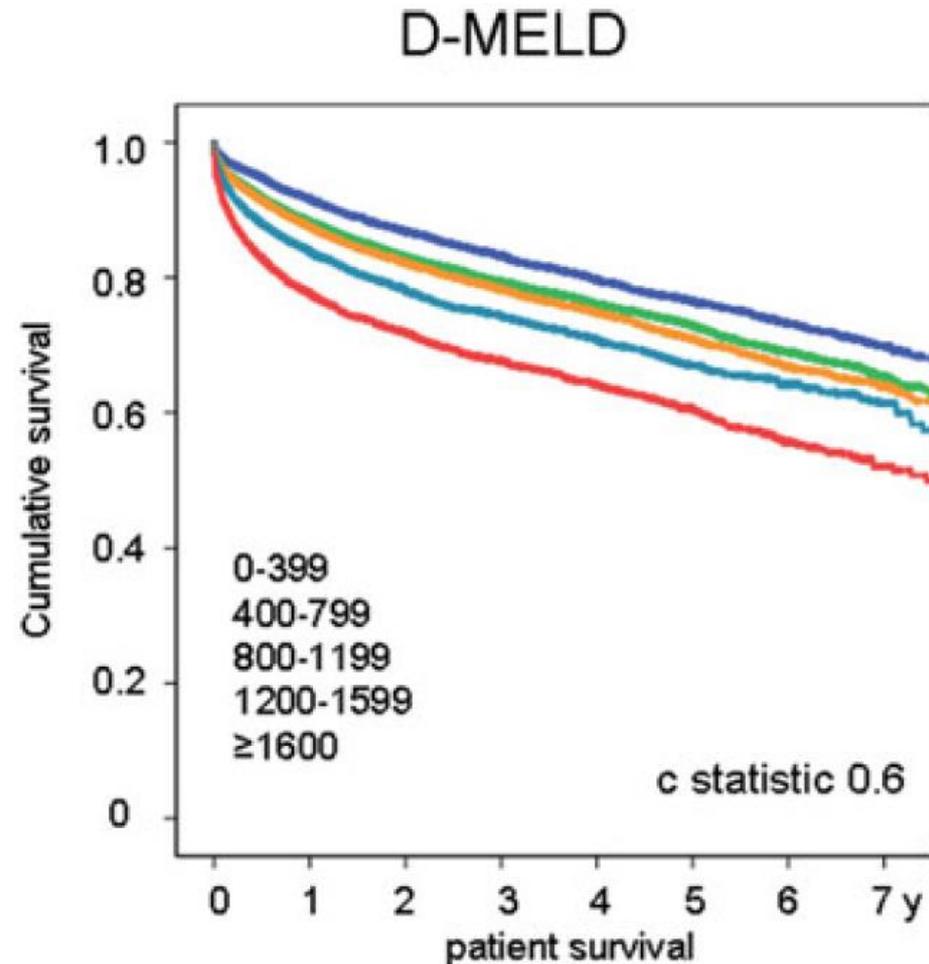
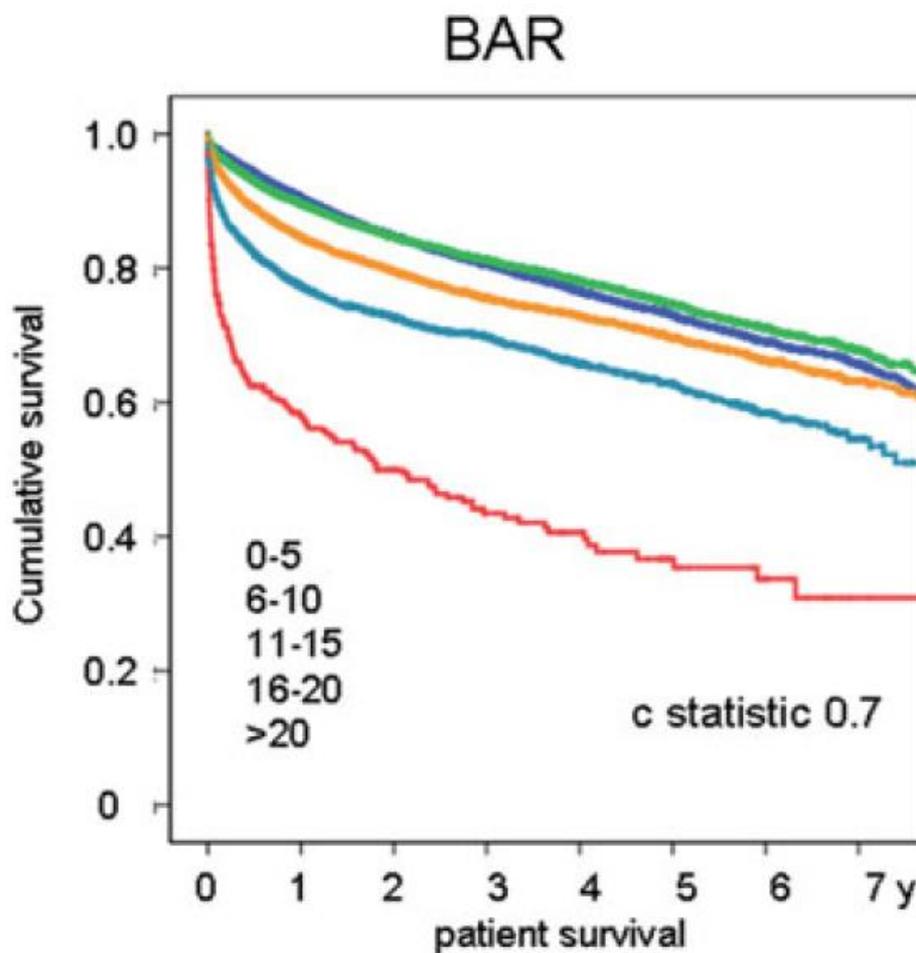
TABLE 3. Development of the Prediction Score Based on a Logistic Regression Analysis

Predictor	Category	Regression Coefficient β	<i>P</i>	Reference Value W_i (Midpoint)	$B \times (W_{ij} - W_{ireference})$	Risk score $(B \times [W_i - W_{ireference}] / B \ddagger)$
Recipient age	≤ 40 y	0.021	<0.001	35.5 ($W_{1reference}$)	0	0
	>40–60 y			50.5	0.315	1
	>60 y			70.5	0.735	3
MELD score at transplantation	6–15	0.155	<0.001	0.5 ($W_{2reference}$)	0	0
	>15–25			20.5	1.550	5
	>25–35			30.5	3.100	10
	>35			40.5	4.650	14
Retransplantation	No	1.052	<0.001	0 ($W_{3reference}$)	0	0
	Yes			1	1.052	4
Life support pretransplant	No	0.800	<0.001	0 ($W_{4reference}$)	0	0
	Yes			1	0.800	3
Cold ischemia	0–6 h	0.042	<0.001	3.0 ($W_{5reference}$)	0	0
	>6–12 h			9.5	0.273	1
	>12 h			15	0.504	2
Donor age	≤ 40 y	0.008	<0.001	35.5 ($W_{6reference}$)	0	0
	>40–60 y			50.5	0.120	1
	>60 y			70.5	0.280	1

*Constant B corresponds to an important change of 8 hrs in cold ischemia, which is equivalent to a coefficient $8 \times 0.042 = 0.338$. Points rounded to the next integer. Shrinkage coefficient: 0.9945

Are There Better Guidelines for Allocation in Liver Transplantation?

A Novel Score Targeting Justice and Utility in the Model for End-Stage Liver Disease Era



Are There Better Guidelines for Allocation in Liver Transplantation?

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In summary, BAR score seems highly suitable to identify in a fast, easy and reproducible manner, poor donor/recipient matches, which may guide for allocation of a specific organ for a specific recipient. Thus, informed decision can be made to optimize the survival rate/resource utilization ratio and maximize the benefit from the limited resource of donor livers. On line calculation of BAR score provided by barscore.org/.

Are There Better Guidelines for Allocation in Liver Transplantation?

A Novel Score Targeting Justice and Utility in the Model for End-Stage Liver Disease Era

Bar Score points and post transplantation survival:

Points (0 - 27):	1 year - survival	3 year - survival	5 year - survival
0 - 4:	91 ± 1 %	81 ± 1 %	74 ± 1 %
5 - 8:	90 ± 1 %	81 ± 1 %	75 ± 1 %
9 - 13:	86 ± 1 %	76 ± 1 %	69 ± 1 %
14 - 18:	80 ± 1 %	71 ± 1 %	66 ± 1 %
> 18:	66 ± 2 %	56 ± 2 %	47 ± 3 %

Online BAR Score Calculation

Please use the form below to calculate the BAR Score:
(proceed)

Abdominal organ procurement in the Netherlands – an analysis of quality and clinical impact

Jacob D. de Boer^{1,2}, Wouter H. Kopp¹, Kirsten Ooms², Bernadette J. Haase-Kromwijk², Christina Krikke³, Jeroen de Jonge⁴, L.W. Ernst van Heurn⁵, Andre G. Baranski¹, J. Adam van der Vliet⁶ & Andries E. Braat¹

Transplant International 2017,

- Analysis of quality in organ procurement in Netherlands
- Procurement program: “multi organ procurement training” for surgeons since 2005
- Procurement teams: surgeons, scrub nurses, anesthesiologists, instruments

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Transplant International 2017,

PREVIOUS DATA

- Injuries in procured livers = 10-34%
- Clinically relevant = 6.6%-23%
- Pancreas = 8%-13% of procured pancreata were discarded form transplantation for surgical injury
- Kidney injuries = 7-21%

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Transplant International 2017,

- 754 organs from 2012 to 2013
- 133 livers, 38 pancreas, 420 kidneys
- Injuries = 25%

Table 1. Quality Form scoring system.

Category	Definition	Example
A	No abnormalities found by procurement surgeon and transplant surgeon	
B	Any differences on definitions or concerning anatomy	
C1	 Possibly preventable injury, organ transplanted	Injured artery, vena or artery without patch
C2	 Possibly preventable injury, organ not transplanted	Arterial or capsular injury or organ not properly flushed
D1	Abnormalities or nonprocurement-related damage, organ transplanted	Aneurysms, arterial stenosis
D2	Abnormalities or nonprocurement-related damage, organ not transplanted	Tumours, haematoma caused by initial trauma
E	Other remarks	Issues concerning packaging, number of bags, leakage

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Transplant International 2017,

- Organ discarded for injuries = 2%

Table 2. Scores per organ and as percentage of the number of organs. (significant differences in bold)

	Kidney (n)	%	Liver (n)	%	Pancreas (n)	%	Significance (P)
A	270	64	76	57	28	74	0.152
B	93	22	30	23	10	26	0.946
C1	96	23	35	26	5	13	0.134
C2 ←	6	1	1	1	5	13	<0.001 ←
D1	11	3	14	11	0	0	0.001
D2	5	1	2	2	1	3	0.600
E	15	4	4	3	1	3	0.710
Number of organs*	420		133		38		

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Transplant International 2017,

- BMI for renal procurement
- DCD donation for livers

Table 3. Odds ratios risk factors on injury per organ and for all abdominal organs combined. (significantly higher odds ratios in bold)

	Kidney OR (95% CI)	Liver OR (95% CI)	Pancreas OR (95% CI)	Abdominal organs OR (95% CI)
BMI	1.059* (1.007–1.114)	1.065 (0.944–1.201)	1.207 (0.940–1.548)	1.06** (1.014–1.109)
Age	0.996 (0.981–1.011)	0.999 (0.975–1.024)	1.002 (0.950–1.058)	0.997 (0.985–1.009)
Sex (F)	0.972 (0.617–1.531)	0.598 (0.274–1.304)	2.588 (0.461–14.529)	0.926 (0.636–1.348)
DCD donor	1.434 (0.797–2.015)	2.316*** (1.063–5.045)	1.179 (0.392–26.917)	1.434 (0.983–2.091)

* $P = 0.02$; ** $P = 0.011$; *** $P = 0.034$.

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Transplant International 2017,

- Center volume = less kidney and pancreas injuries

Table 4. Volume and injury percentage (C1 + C2). (significant correlations in bold)

Center*	All organs		Liver		Pancreas		Kidney	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
I	161	16	37	22	14	7	110	15
II	137	26	29	31	8	25	100	24
III	115	24	30	30	7	43	78	21
IV	97	25	15	40	5	40	77	21
V	76	45	22	23	4	50	50	54
VI	5	60					5	60
		<i>r</i> = -0.469 <i>P</i> = 0.067		<i>r</i> = -0.672 <i>P</i> = 0.214		<i>r</i> = -0.950 <i>P</i> = 0.013		<i>r</i> = -0.910 <i>P</i> = 0.012

*The procurement teams (ZUTs) are based and related to their own centre and are referred to as (procurement) centre. The procurement team of centre VI performed their last procurement in 2012.

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Transplant International 2017,

Outcomes of transplantation

- Organs with repaired injuries have the same survival that non-injured organs

DONOR

Age

Steatosis

Infections

Ischemia



RECIPIENT

MELD

Age

BMI

PV Thrombosis

CHC