

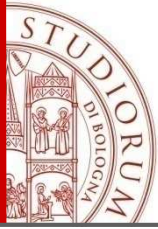
# Use of extended criteria donors in liver transplant

Matteo Cescon

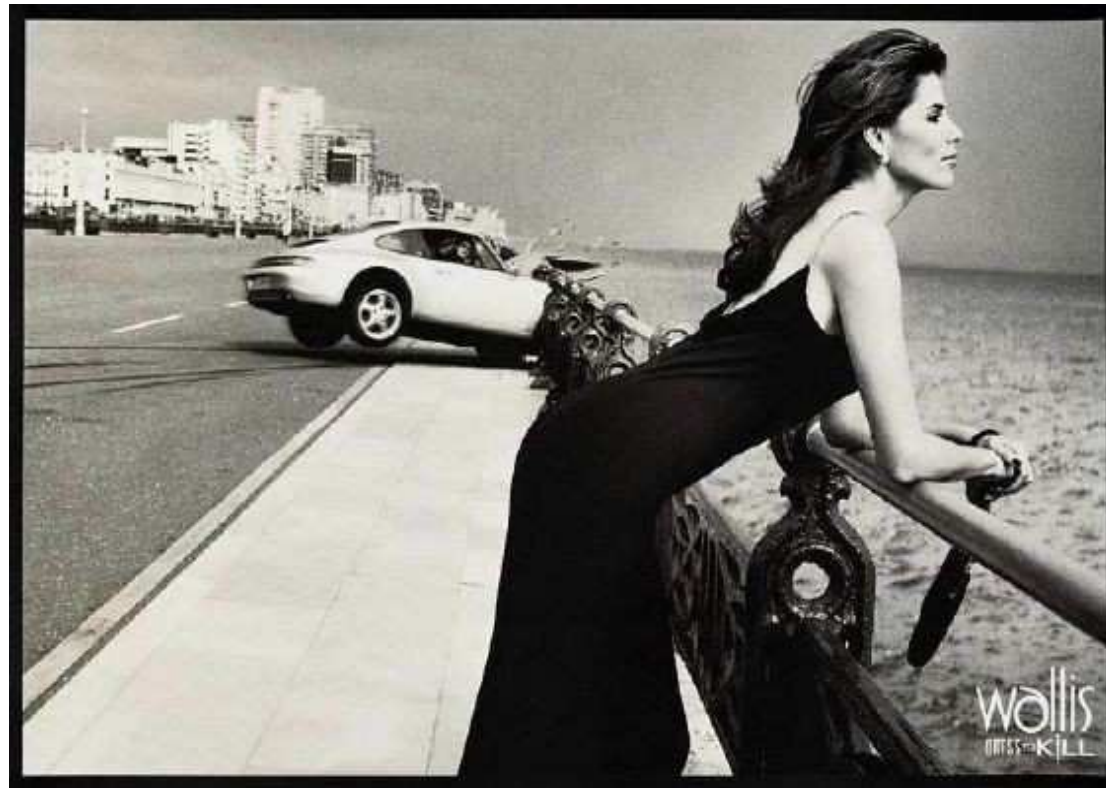
*General Surgery and Transplantation Unit*

*Policlinico Sant'Orsola-Malpighi*

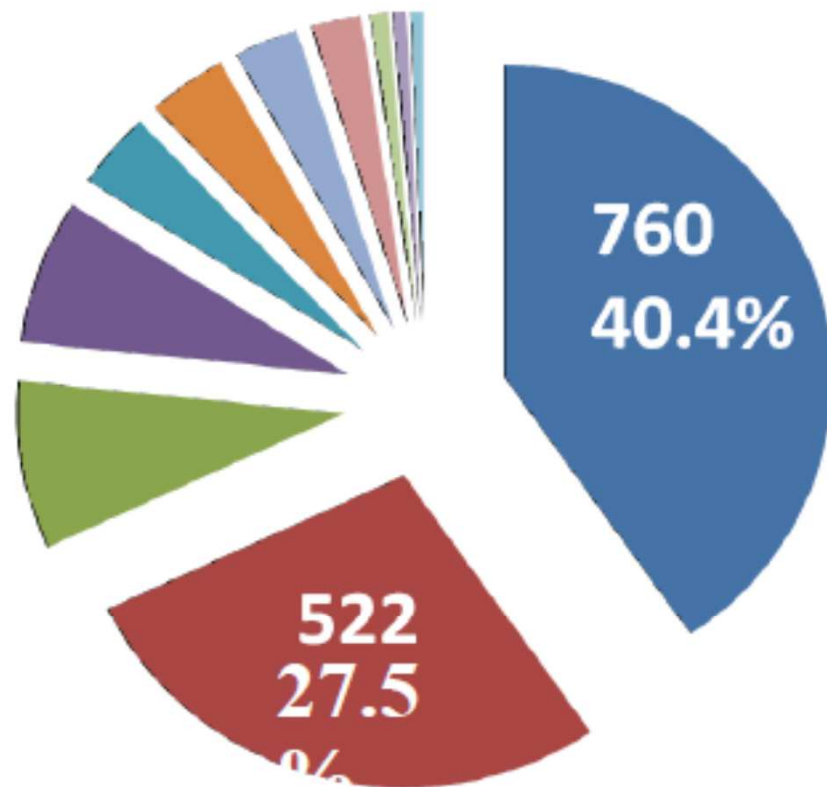
*University of Bologna, Italy*



## Liver transplantation as a trip for patients...

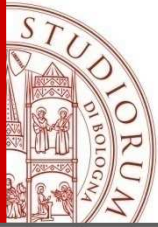


# 1900 Liver transplantations at University of Bologna (1986-2016)



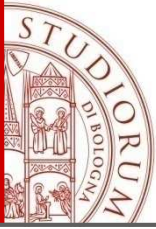
- Viral cirrhosis
- HCC on cirrhosis
- Retransplantations
- Alcoholic cirrhosis
- Primary biliary cirrhosis
- Fulminant hepatitis
- Sclerosant colangitis
- Amiloidosis
- Wilson disease
- Metabolic disease
- Others





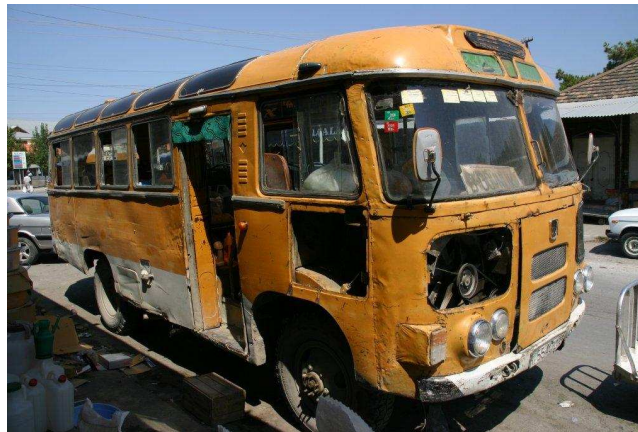
Problems: to many passengers...



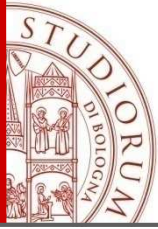


## Extended criteria donors

Graft with an increased risk of early failure  
or inferior graft and patient survival resulting  
from per-transplant factors



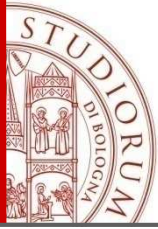
Extended Criteria Donor/Graft = ECD



## Extended criteria donors

---

- ✓ Older donors
- ✓ Steatotic grafts
- ✓ Seropositive Donors
- ✓ Split Grafts
- ✓ Living Donors

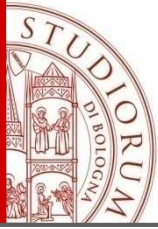


## Extended criteria donors

---

- ✓ Older donors
- ✓ Steatotic grafts
- ✓ Seropositive Donors
- ✓ Split Grafts
- ✓ Living Donors





## “Liberal” allocation of older donors under a low liver damage strategy (2003 – ongoing)

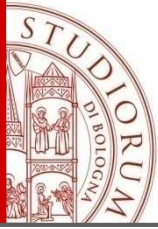
- Routine graft biopsy before donor aorta cross-clamping in donors  $\geq 60$  years
- Histology available before donor aorta cross-clamping
- Recipient entering OT after donor histology evaluation

- Absolute contraindications:
  - Cirrhosis, steatohepatitis
  - Fibrosis stage  $>2 \pm$  severe portal inflammation
  - Necrosis

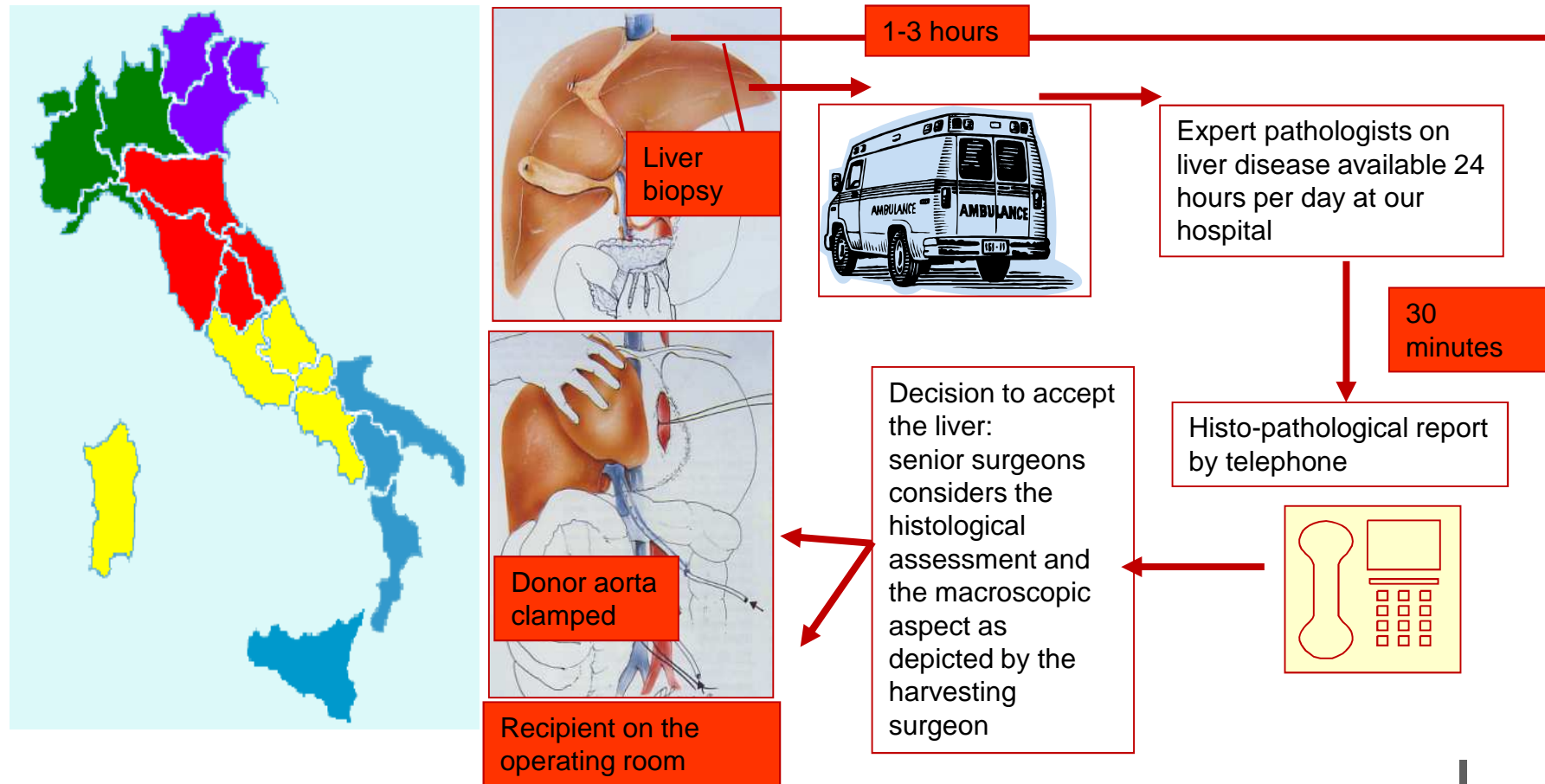
- Relative contraindications:
  - Macrosteatosis  $> 30\%$

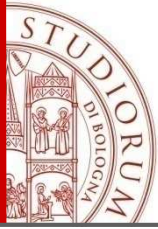
*Ravaioli et al, Transpl Int 2008*



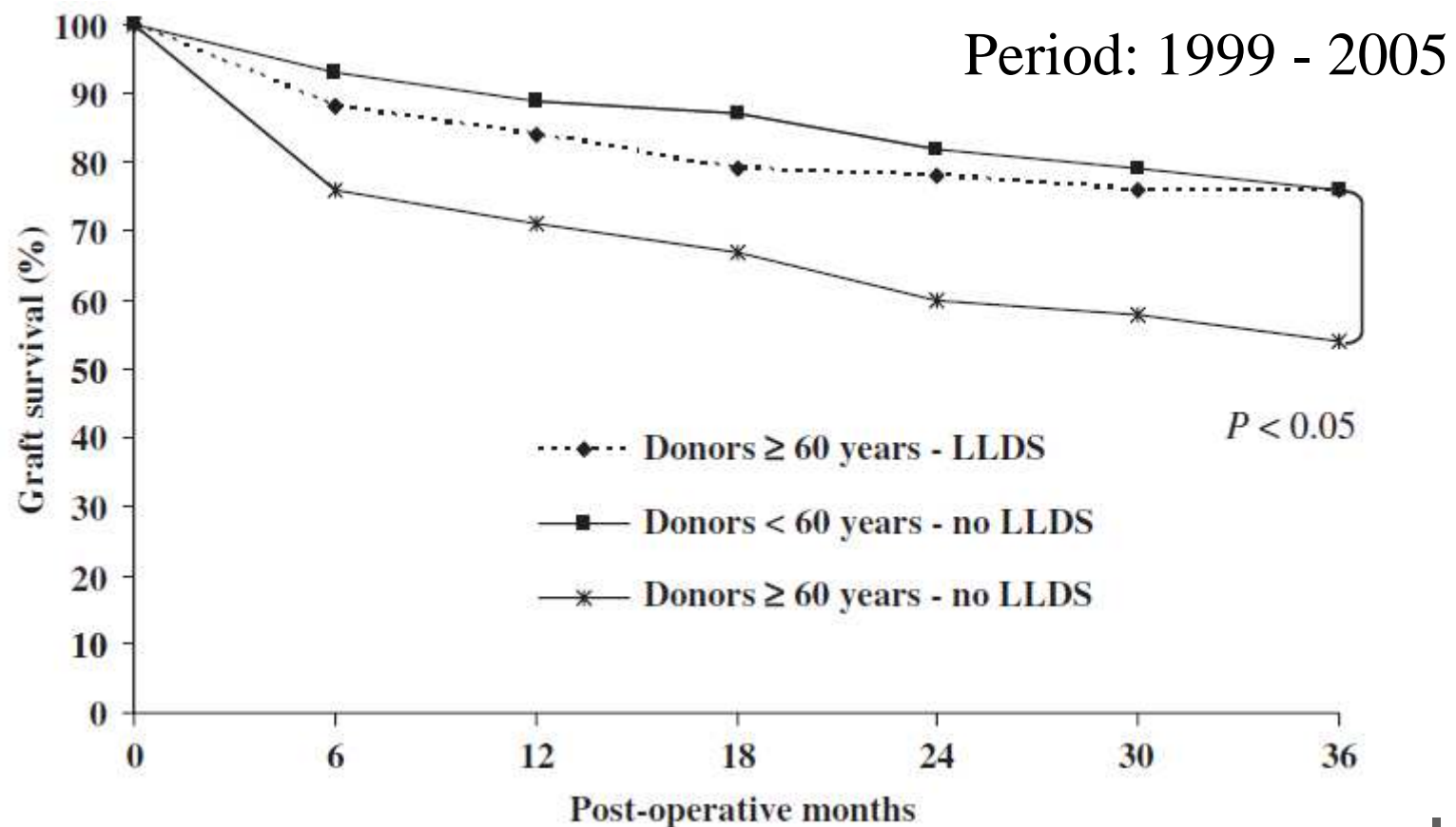


## “Liberal” allocation of older donors under a low liver damage strategy (2003 – ongoing)

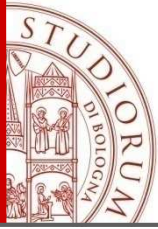




## “Liberal” allocation of older donors under a low liver damage strategy (2003 – ongoing)



*Ravaioli et al, Transpl Int 2008*



# *935 liver transplants in Bologna (1998-2008)*

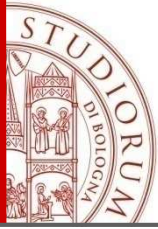
## *Donors characteristics*

	Donor < 70 y (N=713)	Donor ≥ 70 y (N=222)	p
<b>Donor gender (M/F)</b>	<b>408/286</b>	<b>101/114</b>	<b>0.002</b>
Donor anti-HCV positivity	20 (2.8%)	11 (5.0%)	0.092
<b>Donor anti-HBc positivity</b>	<b>104 (14.6%)</b>	<b>45 (20.3%)</b>	<b>0.030</b>
Donor HBsAg positivity	6 (0.8%)	2 (0.9%)	0.933
Donor cause of death			
<b>Cerebral stroke</b>	<b>406 (56.9%)</b>	<b>178 (80.2%)</b>	<b>&lt; 0.001</b>
<b>Trauma</b>	<b>254 (35.6%)</b>	<b>37 (12.7%)</b>	<b>&lt; 0.001</b>
Post-anoxic encephalopathy	19 (2.7%)	2 (2.3%)	0.478

Median follow-up = 96 months



Bertuzzo et al, Ann Surg 2017

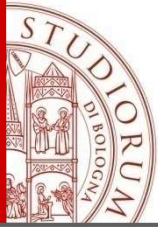


# 935 liver transplants in Bologna (1998-2008)

## Patients characteristics

	Donor < 70 y (N=713)	Donor ≥ 70 y (N=222)	p
Recipient gender (M/F)	523/190	159/63	0.335
Recipient age ≥ 60 years	153 (21.5%)	60 (27.0%)	0.052
<b>Recipient BMI ≥ 25 kg/m<sup>2</sup></b>	<b>293 (42.5%)</b>	<b>107 (49.3%)</b>	<b>0.047</b>
<b>Combined transplant</b>	<b>37 (5.2%)</b>	<b>1 (0.5%)</b>	<b>0.001</b>
Recipient HCV infection	368 (51.6%)	114 (51.4 %)	0.503
Recipient HBV infection	160 (22.4%)	51 (23.0%)	0.467
Recipient HIV positivity	14 (2.0%)	5 (2.3%)	0.484
<b>HCC on cirrhosis</b>	<b>162 (22.7%)</b>	<b>68 (30.6%)</b>	<b>0.012</b>
Alcoholic cirrhosis	56 (7.9%)	17 (7.7%)	0.528
PSC	19 (2.7%)	7 (3.2%)	0.424
<b>PBC</b>	<b>14 (2.0%)</b>	<b>11 (5.0%)</b>	<b>0.019</b>
Acute liver failure	16 (2.2%)	2 (0.9%)	0.203
Re-OLT	65 (9.1%)	26 (11.7%)	0.104
<b>Median natural MELD score</b>	<b>18 (6 - 48)</b>	<b>20 (6 - 45)</b>	<b>0.014</b>
<b>Median D-MELD</b>	<b>832 (104 – 2640)</b>	<b>1445 (444 - 3420)</b>	<b>&lt; 0.001</b>





# *935 liver transplants in Bologna (1998-2008)*

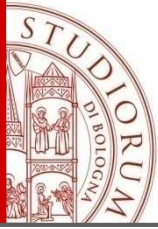
## *Results*

Causes of death	Donor < 70 y (N=713)	Donor ≥ 70 y (N=222)	p
HCV recurrence	55 (8.7%)	25 (11.8%)	0.116
Infection	42 (5.9%)	17 (7.7%)	0.213
Multi-organ failure	31 (4.9%)	9 (4.3%)	0.432
HCC recurrence	25 (3.5%)	9 (4.1%)	0.418
De-novo tumour	17 (2.4%)	11 (5.0%)	0.066



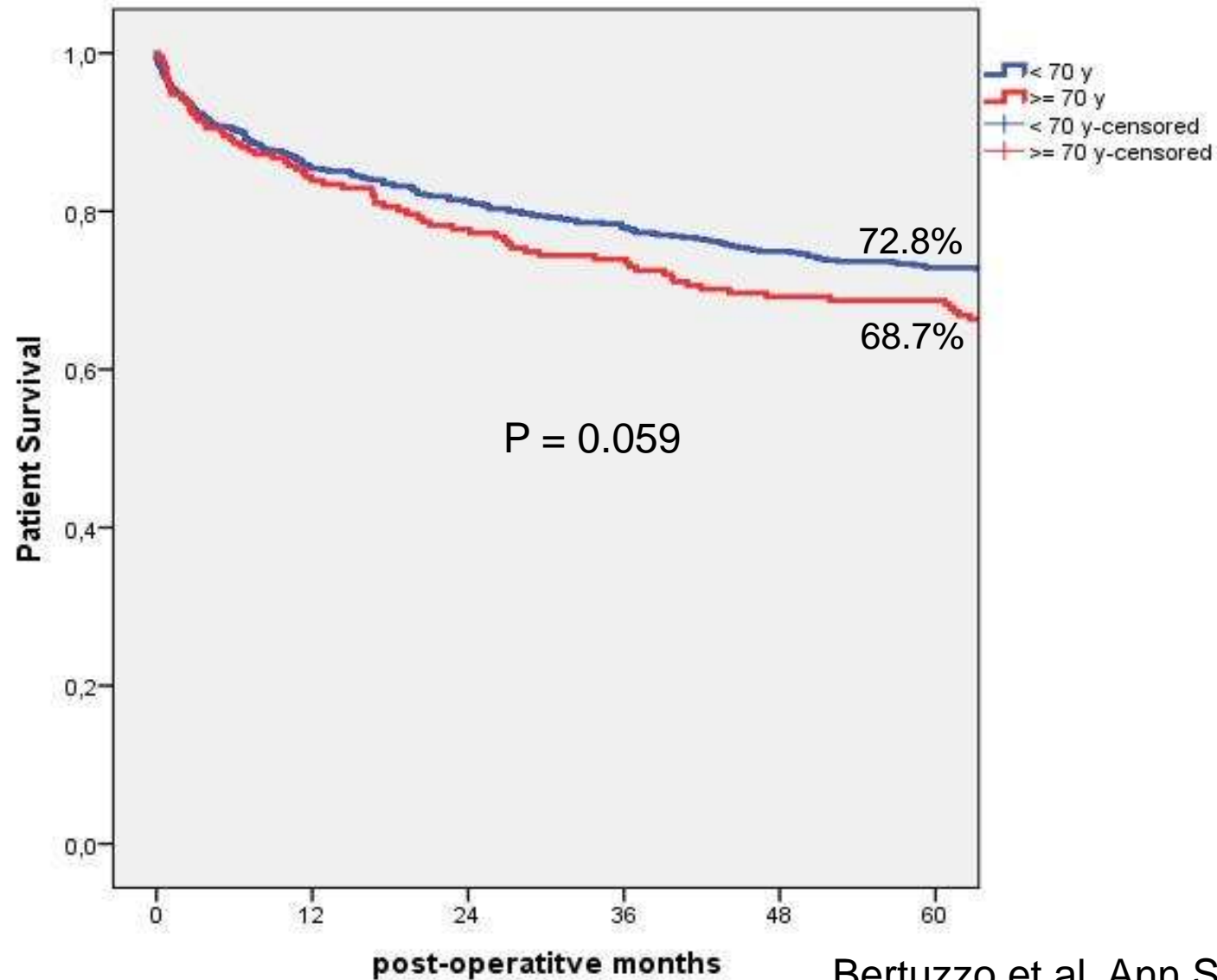
Bertuzzo et al, Ann Surg 2017

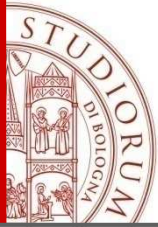




# 935 liver transplants in Bologna (1998-2008)

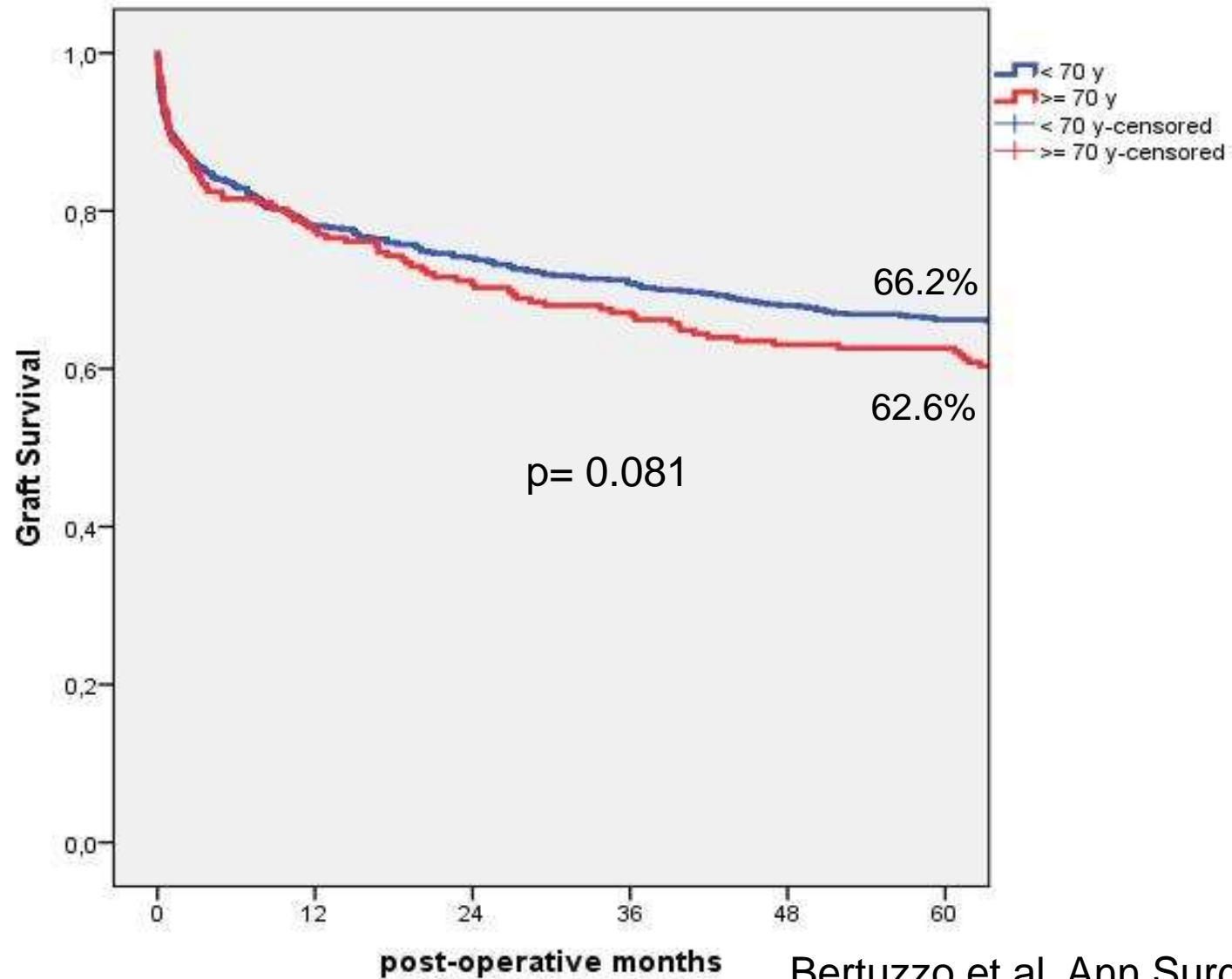
## Results





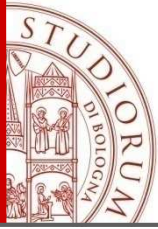
# 935 liver transplants in Bologna (1998-2008)

## Results



Bertuzzo et al, Ann Surg 2017





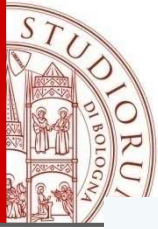
# *946 liver transplants in Bologna (1998-2008)*

## *Comparison between periods - Donors*

	1998-2003 (N=494)	2004-2008 (N=452)	p
Donor gender (M/F)	274/208	236/192	0.326
<b>Donor age</b>	<b>55 (8-87)</b>	<b>60 (19-95)</b>	<b>&lt; 0.001</b>
Donor anti-HCV positivity	8 (1.6%)	23 (5.1%)	0.002
<b>Donor anti-HBc positivity</b>	<b>57 (11.5%)</b>	<b>92 (20.4%)</b>	<b>&lt; 0.001</b>
<b>Donor HBsAg positivity</b>	<b>0</b>	<b>8 (1.8%)</b>	<b>0.003</b>
Donor cause of death			
Cerebral stroke	300 (60.7%)	291 (64.4%)	0.138
<b>Trauma</b>	<b>176 (35.6%)</b>	<b>119 (26.3%)</b>	<b>0.001</b>
Post-anoxic encephalopathy	13 (2.6%)	11 (2.4%)	0.507

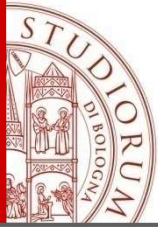


Bertuzzo et al, Ann Surg 2017



# *946 liver transplants in Bologna (1998-2008)* *Comparison between periods – Recipients (1)*

	1998-2003 (N=494)	2004-2008 (N=452)	p
Recipient gender (M/F)	354/140	336/116	0.197
<b>Recipient age ≥ 60 years</b>	<b>78 (15.8%)</b>	<b>138 (30.5%)</b>	<b>&lt; 0.001</b>
Recipient BMI < 25 kg/m <sup>2</sup>	265 (56.1%)	244 (54.8%)	0.369
<b>Combined transplant</b>	<b>7 (1.4%)</b>	<b>34 (7.5%)</b>	<b>&lt; 0.001</b>
Recipient HCV infection	260 (52.6%)	232 (51.3%)	0.368
<b>Recipient HBV infection</b>	<b>129 (26.1%)</b>	<b>83 (18.4%)</b>	<b>0.003</b>
<b>Recipient HIV positivity</b>	<b>0</b>	<b>19 (4.2%)</b>	<b>&lt; 0.001</b>
<b>HCC on cirrhosis</b>	<b>76 (15.4%)</b>	<b>154 (34.1%)</b>	<b>&lt; 0.001</b>
Alcoholic cirrhosis	41 (8.3%)	33 (7.3%)	0.532
PSC	9 (1.8%)	17 (3.8%)	0.052
PBC	13 (2.6%)	12 (2.7%)	0.570
Acute liver failure	13 (2.6%)	5 (1.1%)	0.068
<b>Pre-OLT MELD score ≥ 25</b>	<b>36 (10.3%)</b>	<b>101 (31.0%)</b>	<b>&lt; 0.001</b>
<b>D-MELD ≥ 1628</b>	<b>28 (8.0%)</b>	<b>80 (24.5%)</b>	<b>&lt; 0.001</b>
<b>Pre-OLT MELD-score</b>	<b>17 (6 - 40)</b>	<b>20 (6 - 48)</b>	<b>&lt; 0.001</b>
<b>D-MELD</b>	<b>880 (104 - 2442)</b>	<b>1080 (108 - 3420)</b>	<b>&lt; 0.001</b>



# *946 liver transplants in Bologna (1998-2008)*

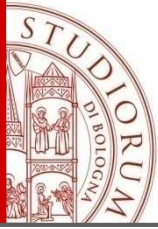
## *Comparison between periods – Recipients (2)*

	1998-2003 (N=494)	2004-2008 (N=452)	p
<b>Re-OLT</b>	<b>35 (36.8%)</b>	<b>60 (12.1%)</b>	<b>0.016</b>
PGNF	20 (4.0%)	17 (3.8%)	0.477
<b>Vascular complications</b>	<b>27 (5.5%)</b>	<b>12 (2.7%)</b>	<b>0.021</b>
<b>HCV recurrence</b>	<b>10 (2.0%)</b>	<b>1 (0.2%)</b>	<b>0.010</b>
Chronic rejection	3 (0.6%)	1 (0.2%)	0.361
PSC recurrence	1 (0.2%)	0	0.522



Bertuzzo et al, Ann Surg 2017





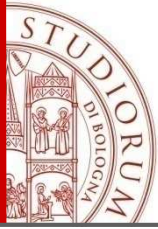
# *946 liver transplants in Bologna (1998-2008)*

## *Comparison between periods - Results*

Causes of death	1998-2003 (N=494)	2004-2008 (N=452)	p
<b>HCV recurrence</b>	<b>53 (12.2%)</b>	<b>27 (6.5%)</b>	<b>0.003</b>
Infection	27 (6.2%)	24 (5.8%)	0.444
Multi-organ failure	25 (5.8%)	15 (3.6%)	0.092
<b>HCC recurrence</b>	<b>8 (1.8%)</b>	<b>25 (6.0%)</b>	<b>0.001</b>
De-novo tumour	10 (2.3%)	18 (4.3%)	0.073
<b>Follow-up (mo)</b>	<b>138 (0 - 198)</b>	<b>82 (0 - 125)</b>	<b>&lt; 0.001</b>

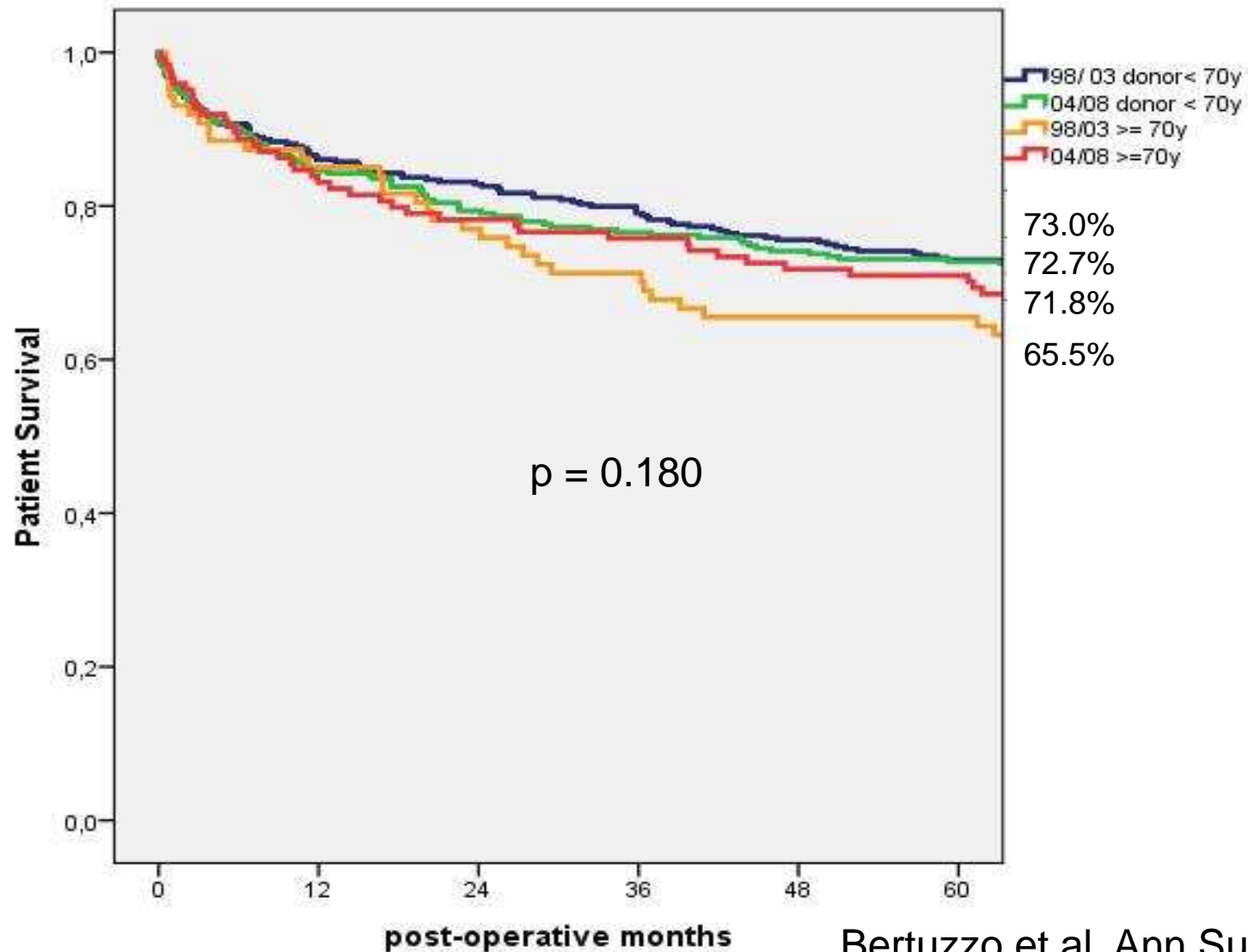


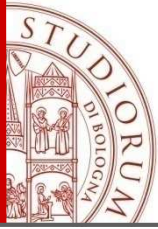
Bertuzzo et al, Ann Surg 2017



# 946 liver transplants in Bologna (1998-2008)

## Results





# *946 liver transplants in Bologna (1998-2008)*

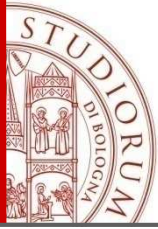
## *Results*

---

### Factors affecting survival

- **LT performed before 2004** (CI=1.164–1.743; Exp[B]=1.424; P=0.001)
- **Recipient HCV-positive serology** (CI=0.554–0.848; Exp[B]=0.686; P=0.001)
- **BAR score >18** (CI=0.140–0.670; Exp[B]=0.306; P=0.003)
- **Pre-LT need for CVVH/HD** (CI=0.351–0.921; Exp[B]=0.568; P=0.022)

Bertuzzo et al, Ann Surg 2017



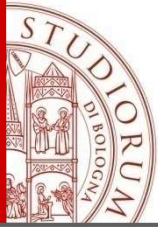
## Inflow problems: hepatic artery and old donors

### Increased Risk of Graft Loss from Hepatic Artery Thrombosis After Liver Transplantation with Older Donors

Zoe A. Stewart, Jayme E. Locke, Dorry L. Segev, Nabil N. Dagher, Andrew L. Singer, Robert A. Montgomery, and Andrew M. Cameron

*Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD*

Donor Age (years)	Relative Risk	95% Confidence Interval	P Value
<40	Reference		
40-49	1.07	0.92, 1.25	0.37
50-59	1.35	1.17, 1.57	<0.001
60-69	1.52	1.28, 1.82	<0.001
≥70	1.61	1.26, 2.06	<0.001



# Inflow problems: hepatic artery and old donors

## Impact of Very Advanced Donor Age on Hepatic Artery Thrombosis After Liver Transplantation

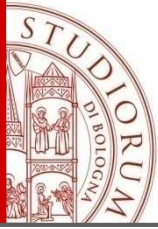
*Matteo Cescon, Matteo Zanello, Gian Luca Grazi, Alessandro Cucchetti, Matteo Ravaioli, Giorgio Ercolani, Massimo Del Gaudio, Augusto Lauro, Maria Cristina Morelli, and Antonio Daniele Pinna*

	<i>P</i>	Exp (B)	95% confidence interval
Hepatic artery anatomical variations	0.005	9.40	1.94–45.59
Jumping graft	0.004	12.36	2.21–68.96
Complex reconstruction(s)	0.63	1.95	0.11–32.09
Study group (A vs. B)	0.01	9.20	1.59–53.21

Reduced incidence of HAT in the period 2003-2008 (B) (1.5%) compared to 1998-2002 (A) (8.8%) mainly related to a more appropriate technical management

TRANSPLANTATION 2011

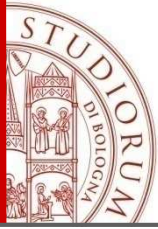




## *Use of octogenarian donors for liver transplantation - Recipients*

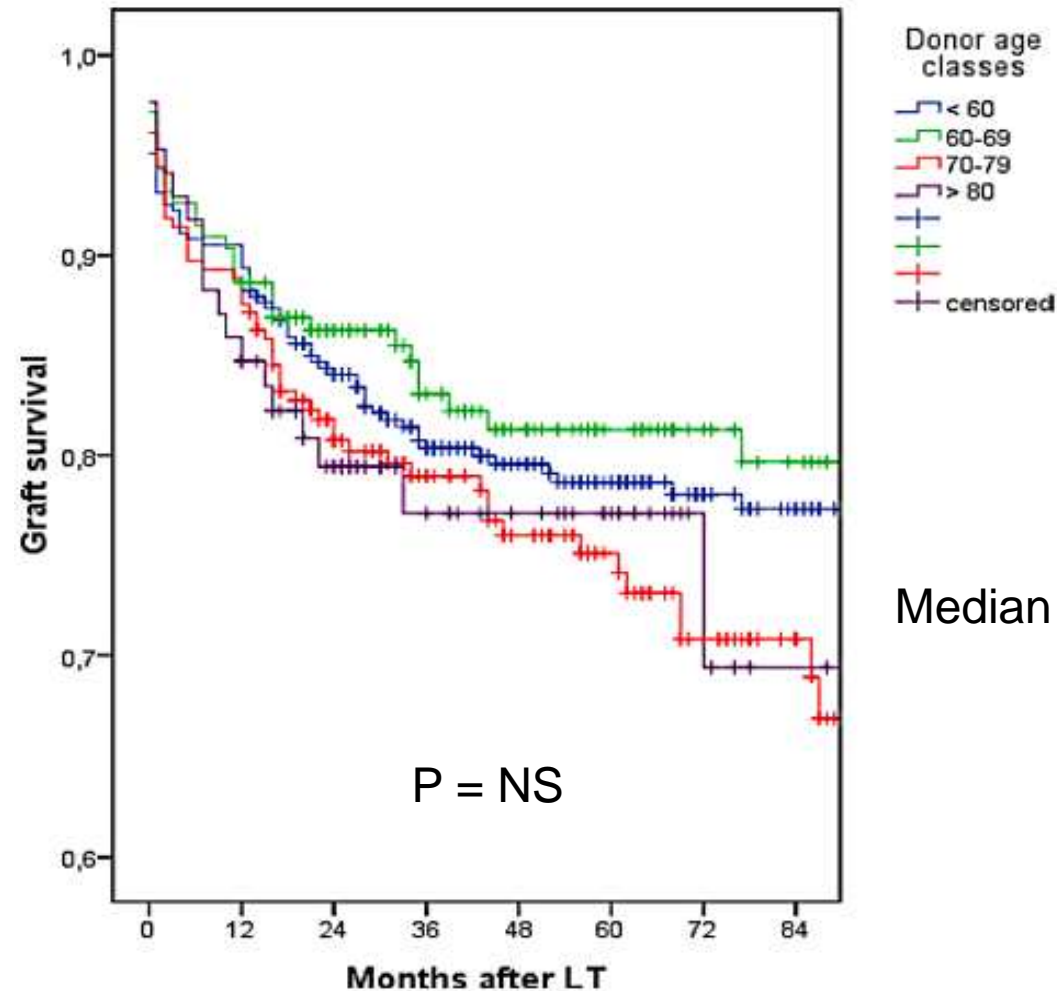
Ghinolfi et al, AJT 2014

	<60 years (n=348)	60-69 years (n=176)	70-79 years (n=233)	≥80 years (n=85)	p
Gender M/F (n, %)	253/95 (73/27)	145/31 (82/18)	180/53 (77/23)	67/18 (79/21)	0.09
Age years, mean ± SD	47.3 ± 0.6	52.7 ± 0.6	54.7 ± 0.4	56.3 ± 0.8	<0.001
Primary indication to OLT (n, %)					<0.001
HCV	147 (42.2)	75 (42.6)	107 (45.9)	31 (36.5)	
HBV	78 (22.4)	32 (18.2)	52 (22.3)	19 (22.4)	
Alcoholic (ALD)	24 (6.9)	37 (21.0)	24 (10.3)	10 (11.8)	
Autoimmune	6 (1.7)	2 (1.1)	3 (1.3)	1 (1.2)	
Cholestatic	35 (10.0)	3 (1.7)	7 (3.0)	4 (4.7)	
Other	58 (16.7)	27 (15.3)	40 (17.2)	20 (23.5)	
HCC (n, %)	91 (26.1)	77 (43.8)	120 (51.5)	47 (55.3)	<0.001
HCV (n, %)	160 (46.0)	84 (47.7)	122 (52.4)	36 (42.4)	0.22
Pre-LT calculated MELD (mean ± SD)	13.9 ± 0.3	13.0 ± 0.4	12.3 ± 0.3	12.2 ± 0.5	0.001
Non-HCC patients pre-LT calculated MELD (mean ± SD)	14.6 ± 5.6	14.4 ± 5.7	13.8 ± 4.2	13.5 ± 5.0	0.38
D-MELD (mean ± SD)	560 ± 16	838 ± 27	911 ± 20	1000 ± 45	<0.001
Platelets (n × 10 <sup>3</sup> /mm <sup>3</sup> ) (median, range)	71 (10-621)	77 (17-408)	73 (20-572)	85 (25-247)	0.84
Creatinine serum level (mg/dL) (mean ± SD)	0.8 ± 0.5	0.82 ± 0.2	0.79 ± 0.2	0.83 ± 0.3	0.803
Albumin serum level (g/L) (mean ± SD)	3.5 ± 0.1	3.7 ± 0.1	3.6 ± 0.1	3.6 ± 0.1	0.13
Post-LT hospital stay (days) (mean ± SD)	22.3 ± 0.9	22.1 ± 1.6	23.7 ± 1.6	20.7 ± 1.9	0.65



## *Use of octogenarian donors for liver transplantation - Survivals*

Ghinolfi et al, AJT 2014



Median follow-up = 4.5 yrs

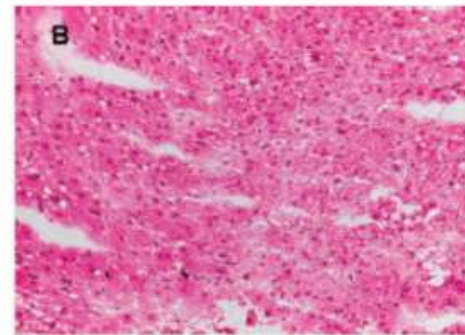
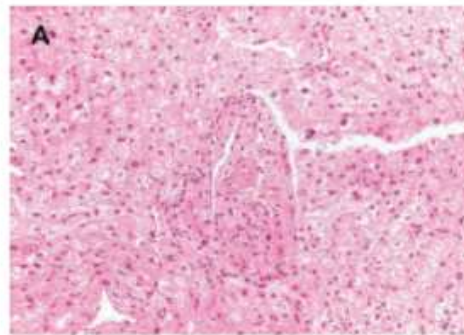


American Journal of Transplantation 2008; 8: 725–726  
Blackwell Munksgaard

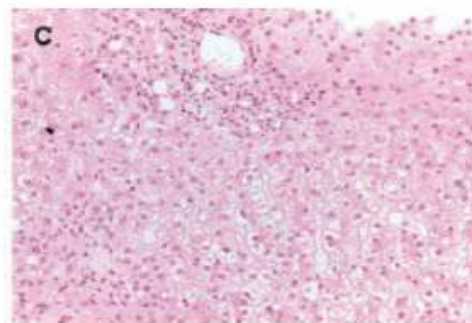
© 2008 The Authors  
Journal compilation © 2008 The American Society of  
Transplantation and the American Society of Transplant Surgeons  
doi: 10.1111/j.1600-6143.2007.02114.x

## Letter to the Editor

# Successful Liver Transplantation from a 95-Year-Old Donor to a Patient with MELD Score 36 and Delayed Graft Arterialization

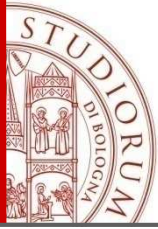


Donor Liver  
biopsy  
at the harvesting



14days after liver transplantation

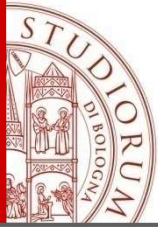
*Grazi GL. et al, Am J Transpl  
2008*



## Extended criteria donors

---

- ✓ Older donors
- ✓ Steatotic grafts
- ✓ Seropositive Donors
- ✓ Split Grafts
- ✓ Living Donors



## Extended criteria donors

Retrospective, single center study:

- Considered only biopsy proven macrovescicular fat (120 donors, 27% of total)

S0 = no fat                      N = 323

S1 = mild < 30%              N = 72

S2 = mod 30-60%            N = 25

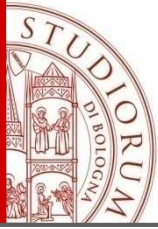
S3 = severe > 60%          N = 23

Findings:

- Increased graft loss with mod and severe macro steatosis
- Higher recurrence in HCV patients with mod and severe macro steatosis
- Graft loss at 6 months due to HCV 17% vs. 2% ( $p < 0.058$ )

*Verran D et al, Liver Transplantation 2003*

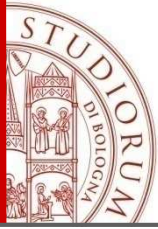




## Extended criteria donors

---

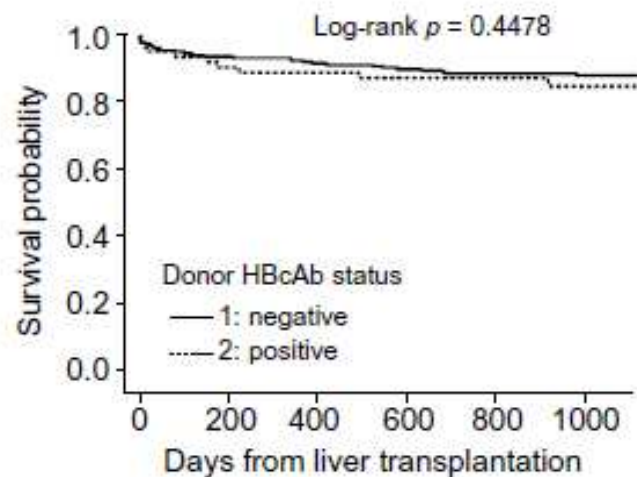
- ✓ Older donors
- ✓ Steatotic grafts
- ✓ Seropositive Donors
- ✓ Split Grafts
- ✓ Living Donors



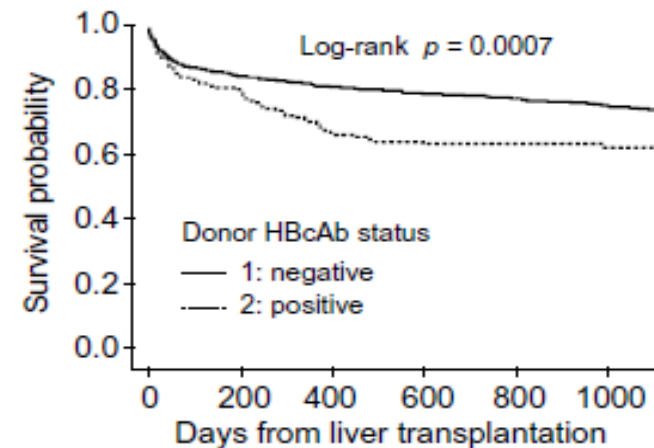
# Hepatitis B-core antibody positive donors

*Angelico et al, J Hepatol 2013*

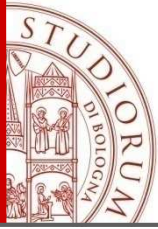
Variable	Hazard Ratio	95% CI		p value
MELD at LT	1.300 (per 10 units)	1.134	1.491	0.0002
Recipient HBsAg status (positive vs. negative)	0.426	0.304	0.597	<0.0001
Portal vein thrombosis (yes vs. no)	1.988	1.139	3.496	0.0156
Donor HBcAb status (positive vs. negative)	1.555	1.184	2.042	0.0015
DRI	1.406 (per unit)	1.029	1.921	0.0325



HBsAg-pos recipients

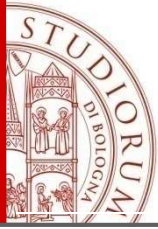


HBsAg-neg recipients

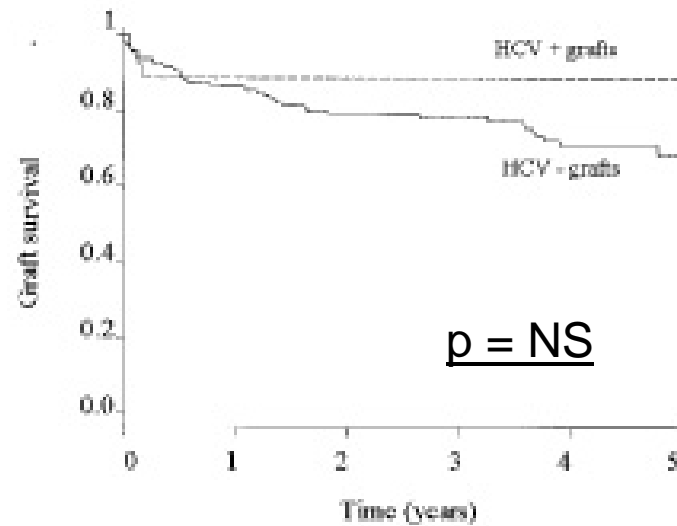
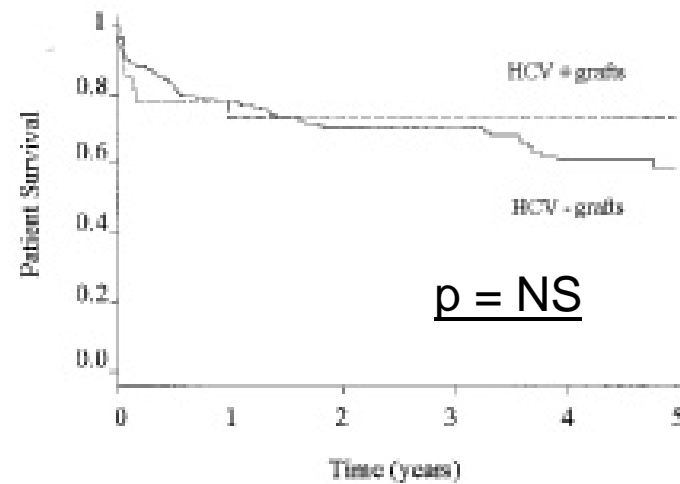


## Bologna experience of LT with MELD >30 (93 cases) *HBcAb related to 90 days mortality*

Variables		90d-M
Pre-OLT creatinine (mg/dL)	< 1.22	2.6%
Donor HBcAb	neg	
Pre-OLT creatinine (mg/dL)	< 1.22	21.3%
Donor HBcAb	pos	
Pre-OLT creatinine (mg/dL)	≥ 1.22	44.4%
Donor HBcAb	yes	



# HCV positive donors



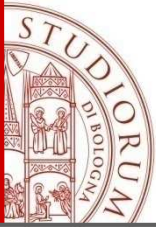
*Saab S, Liver Transplantation 2003*

# Liver grafts from hepatitis B surface antigen-positive donors: A review of the literature

Elisabetta Loggi, Fabio Conti, Alessandro Cucchetti, Giorgio Ercolani, Antonio Daniele Pinna, Pietro Andreone

**Table 1 Published studies with liver transplantation using hepatitis B surface antigen (+) positive donors in hepatitis B surface antigen (+) recipients**

Ref.	Patient No.	Prophylaxis		Outcome at the last FU			Median FU (mo)
		Nucleos(t)ide Analogue	HBIG	HBV disease	HBsAg	HBV-DNA	
Franchello <i>et al</i> <sup>[13]</sup>	3	LMV LMV + ADV ( <i>n</i> = 1)	Yes	No ( <i>n</i> = 1) Yes (HDV = 2)	Persistence	Negative HDVRNA +	19
Ho <i>et al</i> <sup>[17]</sup>	1	LMV + ADV	No	No	Persistence	Negative	24
Hwang <i>et al</i> <sup>[16]</sup>	1	LMV + ADV	Yes	Mild	Persistence	Negative	64
Soejima <i>et al</i> <sup>[15]</sup>	1	LMV	Yes	No	Persistence	Negative	48
Jiao <i>et al</i> <sup>[24]</sup>	2	LMV	Yes	Mild	Persistence	Negative	48
Jang <i>et al</i> <sup>[25]</sup>	6	LMV + ADV	Yes	No	Persistence	Negative	22.5
Bahde <i>et al</i> <sup>[14]</sup>	1	LMV + ADV	Yes	HDV cirrhosis	Persistence	Negative HDVRNA +	50
Loggi <i>et al</i> <sup>[25]</sup>	6	LMV + ADV LMV + TDF	Yes	No	Persistence	Negative	42
Choi <i>et al</i> <sup>[26]</sup>	8	LMV ( <i>n</i> = 2) ETV ( <i>n</i> = 6)	Yes	No	Persistence ( <i>n</i> = 6) Loss ( <i>n</i> = 2)	Negative	25.5
Ju <i>et al</i> <sup>[27]</sup>	23	ETV	Yes	No	Persistence ( <i>n</i> = 17) Loss ( <i>n</i> = 1)	Negative	NA
Saidi <i>et al</i> <sup>[28]</sup>	68	NA	NA	NA	NA	NA	NA
Li <i>et al</i> <sup>[29]</sup>	15	NA	NA	NA	NA	NA	NA
Yu <i>et al</i> <sup>[31]</sup>	38	Not specified	Yes	No	Persistence	Negative	NA
Jeng <i>et al</i> <sup>[32]</sup>	13	ETV	No	No	Persistence	Negative	46

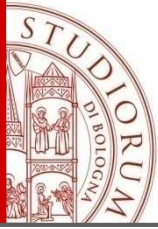


## Extended criteria donors

---

- ✓ Older donors
- ✓ Steatotic grafts
- ✓ Seropositive Donors
- ✓ Split Grafts
- ✓ Living Donors

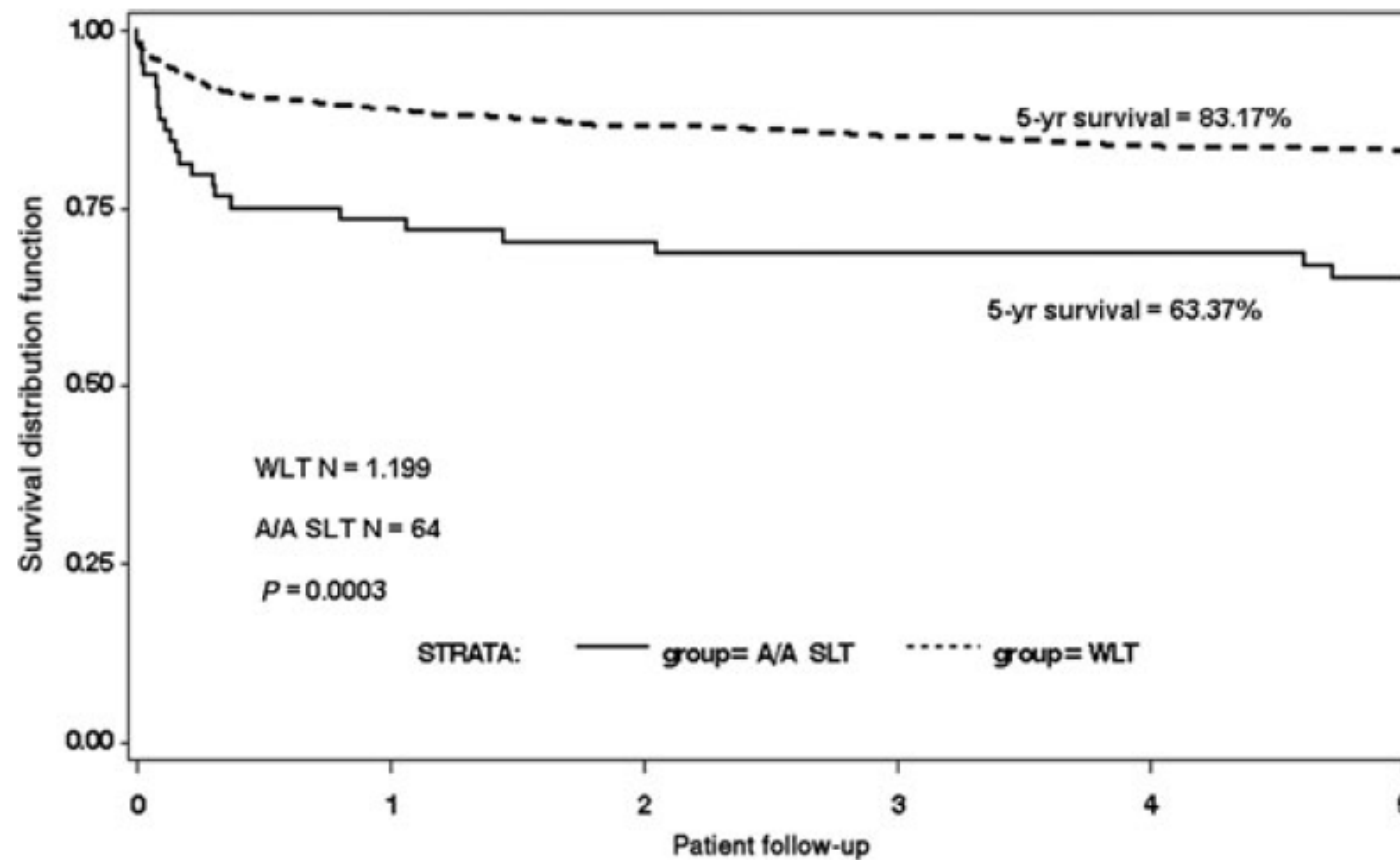




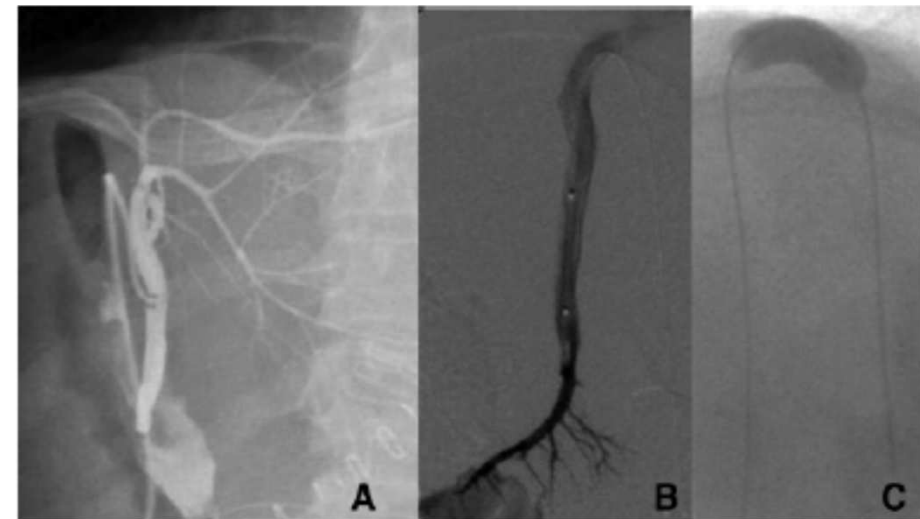
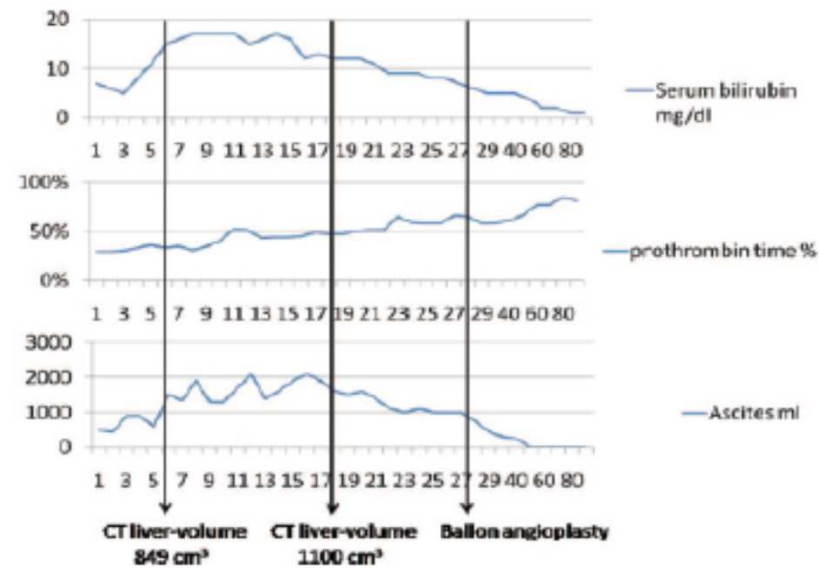
# A Prospective Policy Development to Increase Split-Liver Transplantation for 2 Adult Recipients

*Results of a 12-Year Multicenter Collaborative Study*

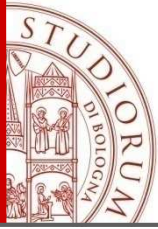
*(Ann Surg 2014;259:157–165)*



## Liver Transplantation With Left Lateral Segments in Adults: A Risk or a Possibility?



Ravaioli M. et al., Transplantation 2009



# Estimates of Early Death, Acute Liver Failure, and Long-term Mortality Among Live Liver Donors

---

4111 live liver donors in the United States between April 1994 and March 2011 for a mean of 7.6 years

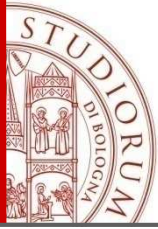
## **Seven donors had early deaths**

risk of death did not vary with age of the liver recipient or portion of liver donated

Long-term mortality of live liver donors was comparable to that of live kidney donors and NHANES participants (1.2%, 1.2%, and 1.4% at 11 years, respectively;  $P = .9$ ).

**The risk of early death among live liver donors in the United States is 1.7 per 1000 donors. Mortality of live liver donors does not differ from that of healthy, matched individuals over a mean of 7.6 years.**

*Gastroenterology 2012*



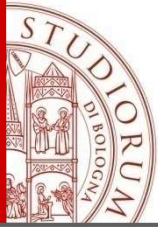
# What happen without risks in liver transplantation

Centers that received low performance evaluations (LP) had an average decrease of 39.9 transplants ( $p < 0.01$ ) and 67.3 candidates ( $p < 0.01$ ).

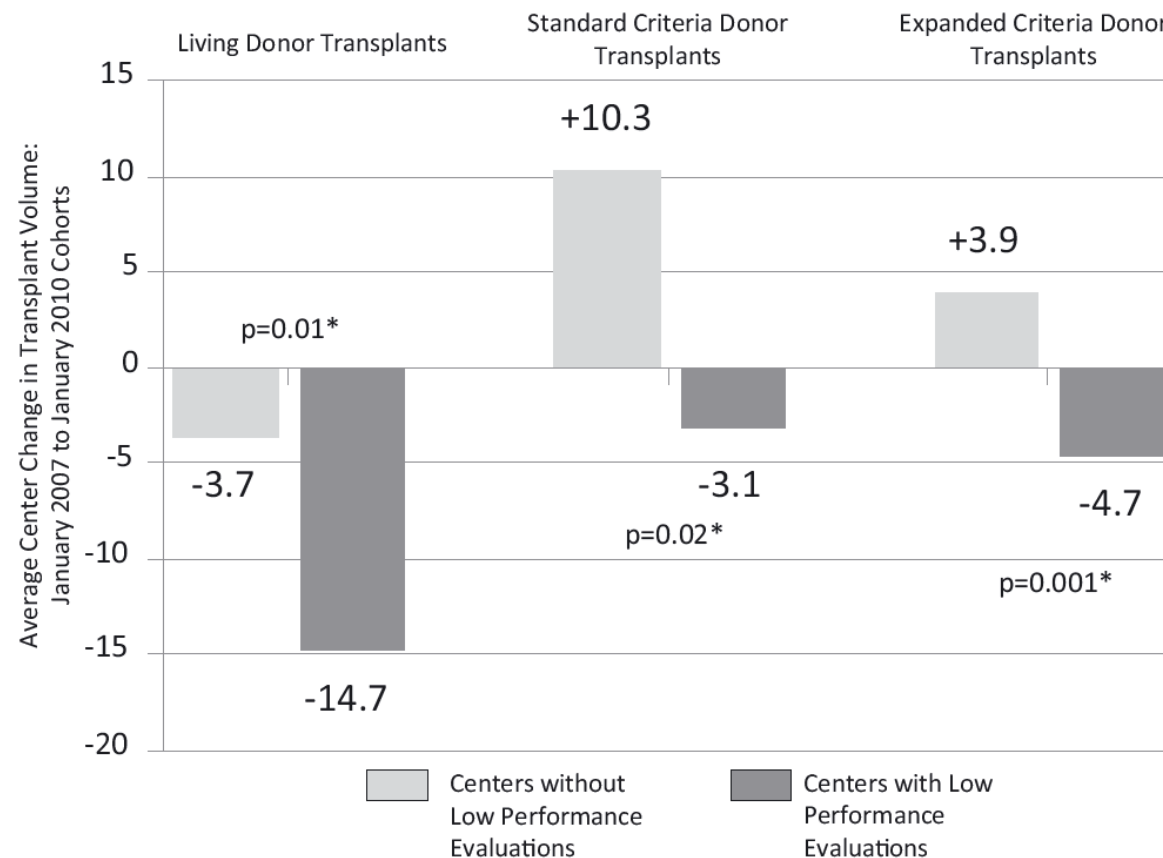
*LP centers reduced the use of older donors, donations with longer cold ischemia, and donations after cardiac death (p-values  $< 0.01$ ).*

Transplant characteristics	Low performing centers (n = 15 478)	Average or high performing centers (n = 34 369)	p-Value
Recipient age: mean (SD)	+2.1 (2.1)	+2.7 (1.8)	0.14
<b>Donor age: mean (SD)</b>	<b>-0.6 (2.9)</b>	<b>+1.8 (4.1)</b>	<b>0.008</b>
Recipient creatinine: mean (SD)	+0.4 (0.3)	+0.4 (0.2)	0.93
<b>Cold ischemia hours: mean (SD)</b>	<b>-1.6 (1.5)</b>	<b>-0.3 (1.6)</b>	<b>0.001</b>
Albumin: mean (SD)	+0.06 (0.22)	+0.11 (0.26)	0.39
INR: mean (SD)	+0.06 (0.31)	+0.04 (0.35)	0.77
MELD at listing: mean (SD)	+0.73 (1.76)	+0.67 (1.88)	0.88
MELD prior to transplant: mean (SD)	+0.85 (2.49)	+1.01 (2.42)	0.78
Donor risk index: mean (SD)	+0.02 (0.08)	+0.02 (0.08)	0.45
Length of stay: mean (SD)	-0.02 (0.21)	-0.02 (0.29)	0.99
Distance to center (miles): mean (SD)	-7.1 (39.7)	+4.9 (57.0)	0.32
HCV (%)	+7%	+3%	0.12
<b>DCD (%)</b>	<b>-1%</b>	<b>+3%</b>	<b>0.001</b>

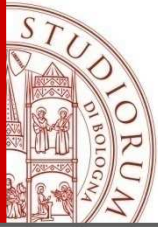
*Buccini et al. American journal of Transplantation 2014*



# What happen without risks in kidney transplantation



*Schold et al. American journal of Transplantation 2013*



# Patients Benefit ? MELD >30

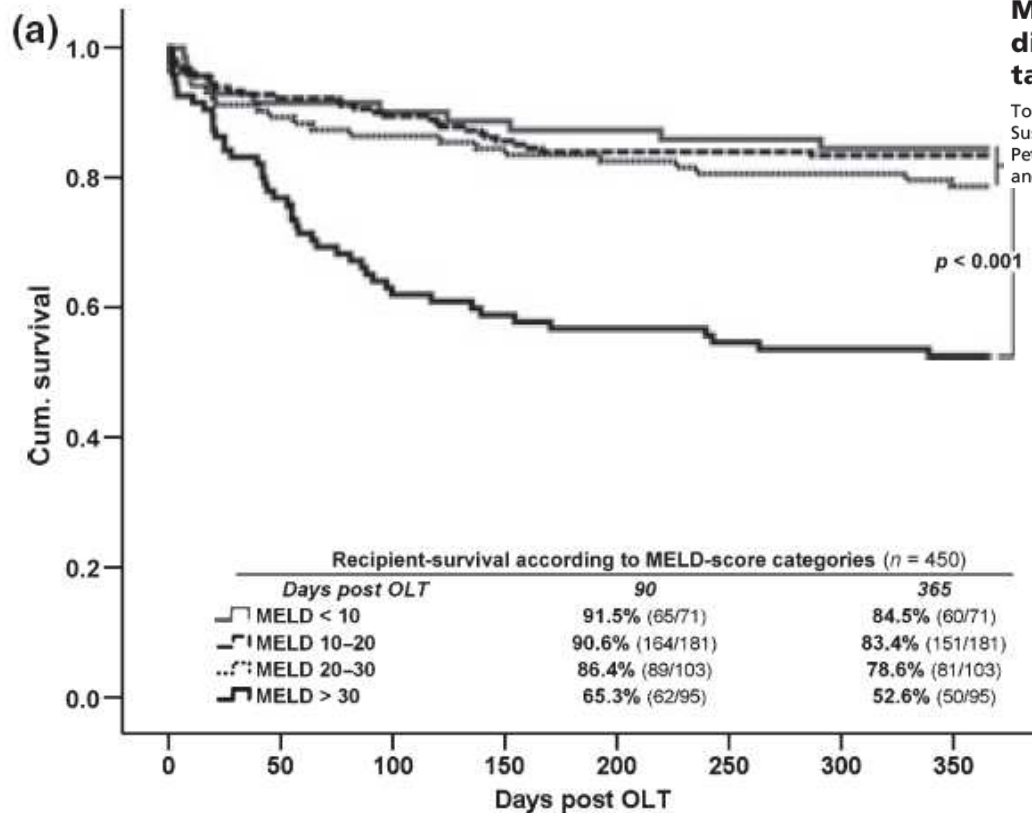
Transplant International

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

## Multicentric evaluation of model for end-stage liver disease-based allocation and survival after liver transplantation in Germany – limitations of the 'sickest first'-concept

Tobias J. Weismüller,<sup>1,2</sup> Panagiotis Fikatas,<sup>3</sup> Jan Schmidt,<sup>4</sup> Ana P. Barreiros,<sup>5</sup> Gerd Otto,<sup>5</sup> Susanne Beckebaum,<sup>6,7</sup> Andreas Paul,<sup>7</sup> Markus N. Scherer,<sup>8</sup> Hartmut H. Schmidt,<sup>9</sup> Hans J. Schlitt,<sup>8</sup> Peter Neuhaus,<sup>3</sup> Jürgen Klempnauer,<sup>2,10</sup> Johann Pratschke,<sup>3</sup> Michael P. Manns<sup>1,2</sup> and Christian P. Strassburg<sup>1,2</sup>



*we would not  
generally recommend  
to restrict OLT to pts  
with MELD <30*

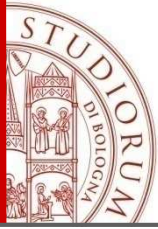




But common principles among different organ allocation policies...

---

- Equity
- Clear and common rules
- Patients benefit



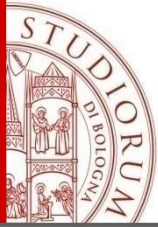
# Liver transplantation begun with this indication

*Although now non HCC malignancies represent borderline indications to LT, the history of this procedure is founded on these cases*

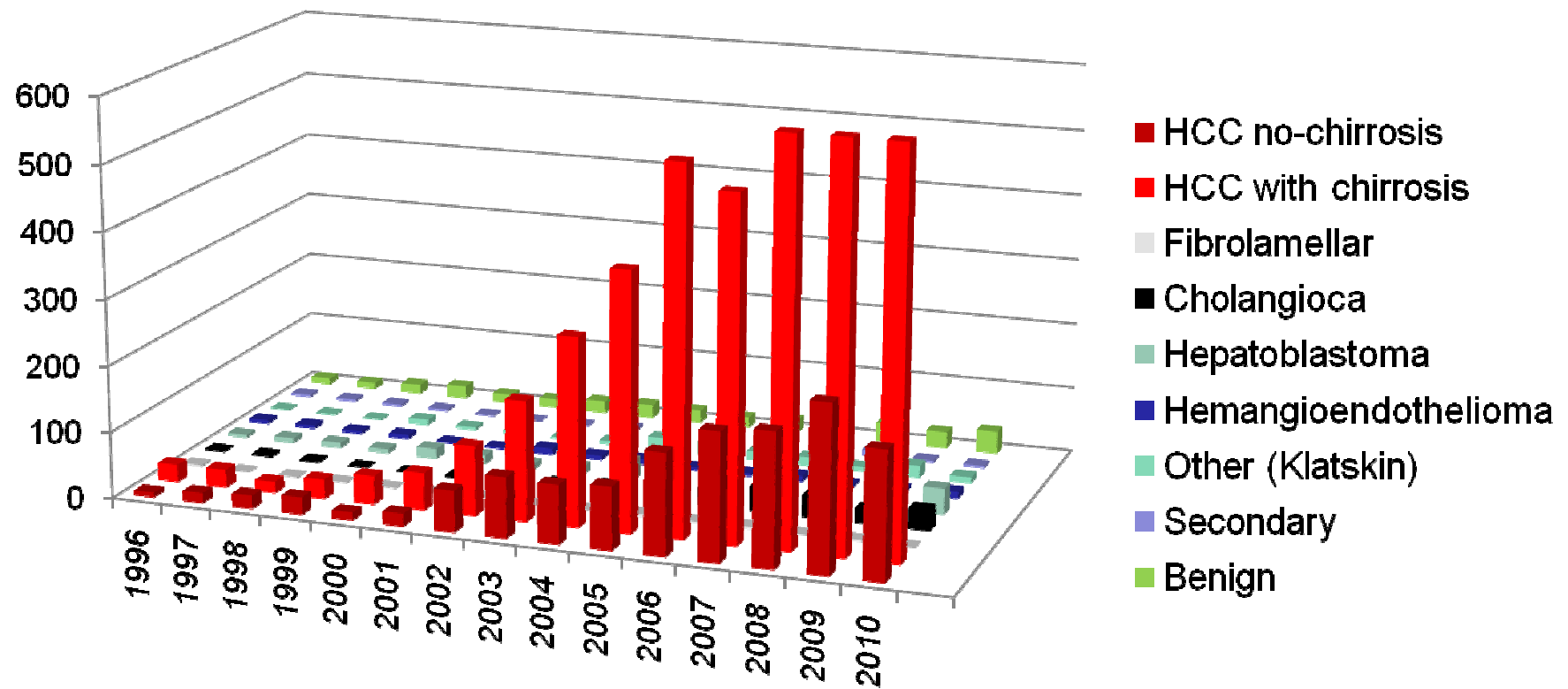
Table 3. The First Seven Human Liver Recipients

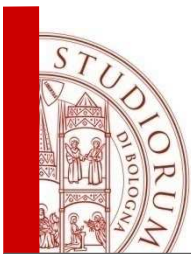
Age (y)	Date	City (ref)	Liver disease	Survival (d)	Main cause of death
3	3-1-63	Denver (60)	Biliary atresia	0	Intraoperative bleeding
48	5-5-63	Denver (60)	Hepatoma, cirrhosis	22	Pulmonary emboli, sepsis
68	6-3-63	Denver (60)	Duct cell carcinoma	7.5	Pulmonary emboli
52	7-10-63	Denver (64)	Hepatoma, cirrhosis	6.5	Gastrointestinal bleeding, pulmonary emboli/edema, liver failure
58	9-16-63	Boston (65)	Colon metastases	11	Pneumonitis, hepatic abscesses, failure
29	10-4-63	Denver (64)	Hepatoma	23	Sepsis, bile peritonitis, pulmonary emboli
75	1-?-64	Paris (66)	Colon metastases	0	Intraoperative hemorrhage

*Starzl et al. J Am Coll Surg 2002*

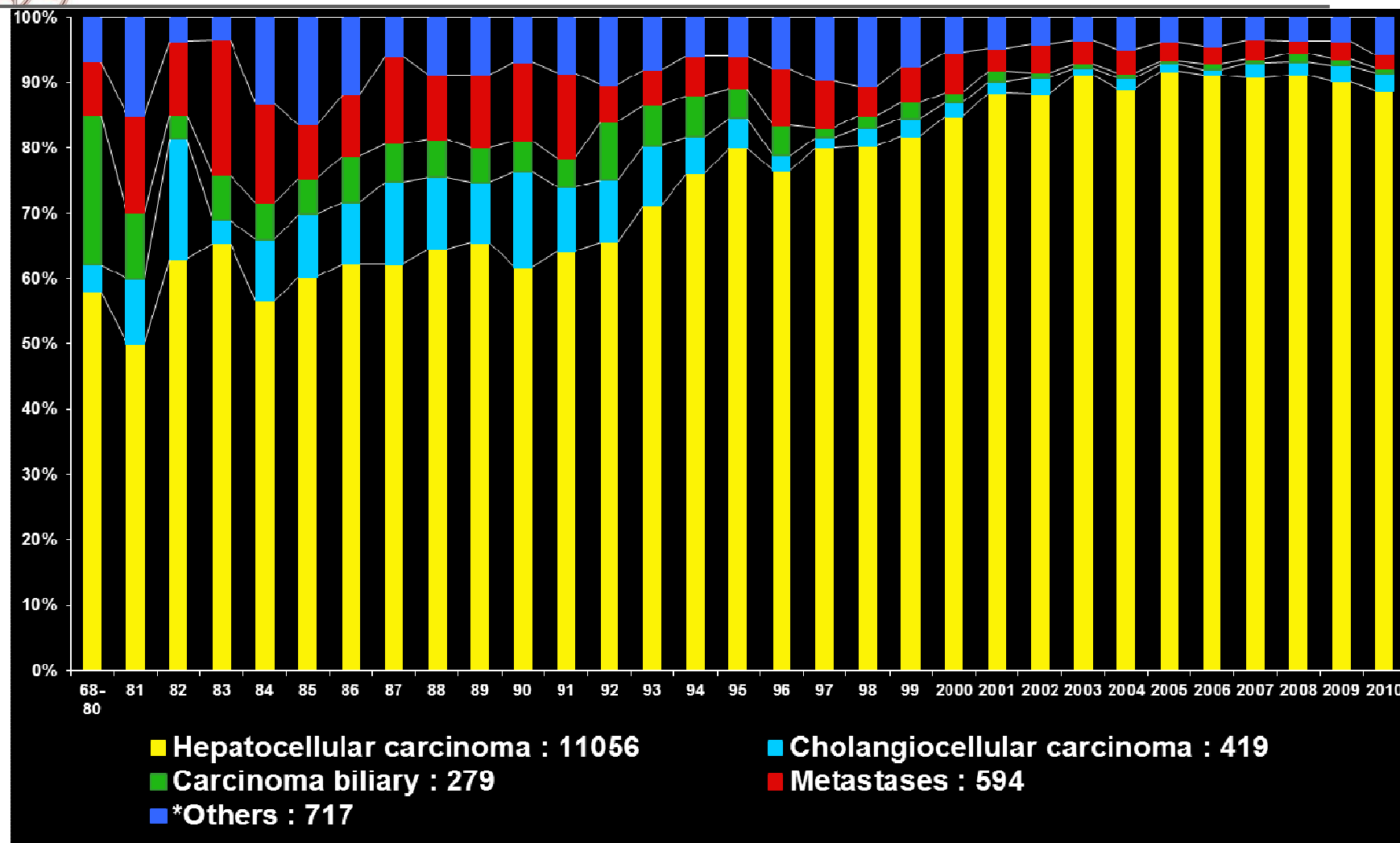


# UNOS data



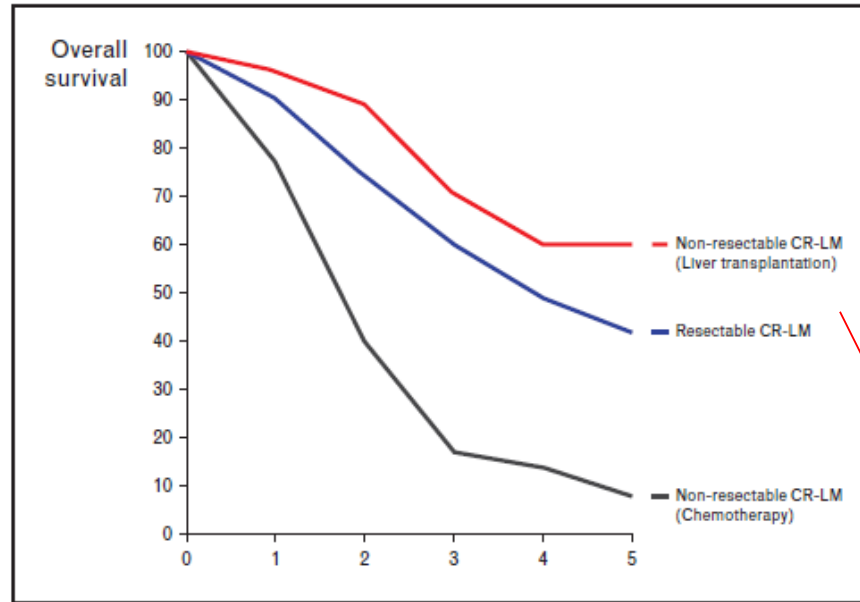


## ELTR data





# LT for metastases from colorectal cancer



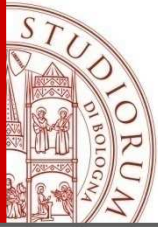
**FIGURE 1.** Overall survival of CR-LM patients. Red line: Liver transplantation in patients with nonresectable liver metastases (data from the SECA study). Blue line: Resectable liver metastases (data from [13]). Grey line: Nonresectable patients treated with chemotherapy (FOLFOXIRI) (Data from [2]).

- 2006-2011 period
- 21 patients transplanted
- median n° of liver metastasis  
= 8 (range 2-40)
- median size of largest lesion  
= 4.5 cm (range 2.8-13)

1-year survival: 96%  
3-years survival: 70%  
5-years survival: 60%

...but...

- patient cohort is small
- control arm lacking
- 90% patients experienced recurrence (> lung → pulmonary resection)



# ECD, other strategies to improve the outcome?

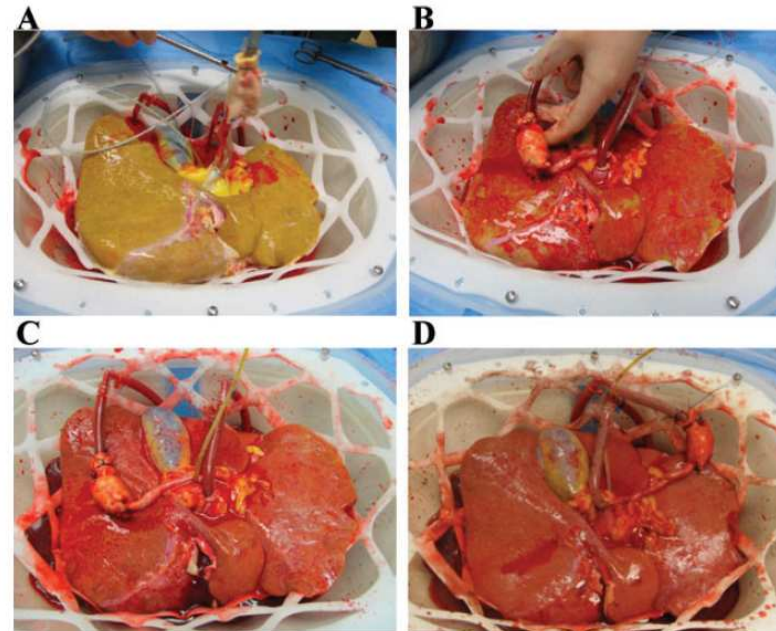
## ***Ex vivo* Normothermic Machine Perfusion and Viability Testing of Discarded Human Donor Livers**

*American Journal of Transplantation 2013; 13: 1327–1335*

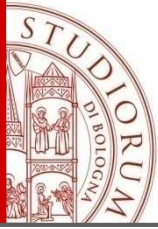
S. op den Dries<sup>a,b</sup>, N. Karimian<sup>a,b</sup>,  
M. E. Sutton<sup>a,b</sup>, A. C. Westerkamp<sup>a,b</sup>,  
M. W. N. Nijsten<sup>c</sup>, A. S. H. Gouw<sup>d</sup>,  
J. Wiersema-Buist<sup>b</sup>, T. Lisman<sup>a,b</sup>,  
H. G. D. Leuvenink<sup>b</sup> and R. J. Porte<sup>a,\*</sup>

<sup>a</sup>Section of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery; <sup>b</sup>Surgical Research Laboratory; <sup>c</sup>Department of Critical Care and <sup>d</sup>Department of Pathology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

\*Corresponding author: Robert J. Porte,  
r.j.porte@umcg.nl







## ECD, other strategies to improve the outcome?

# Hypothermic Machine Preservation in Human Liver Transplantation: The First Clinical Series

*American Journal of Transplantation 2010; 10: 372–381*

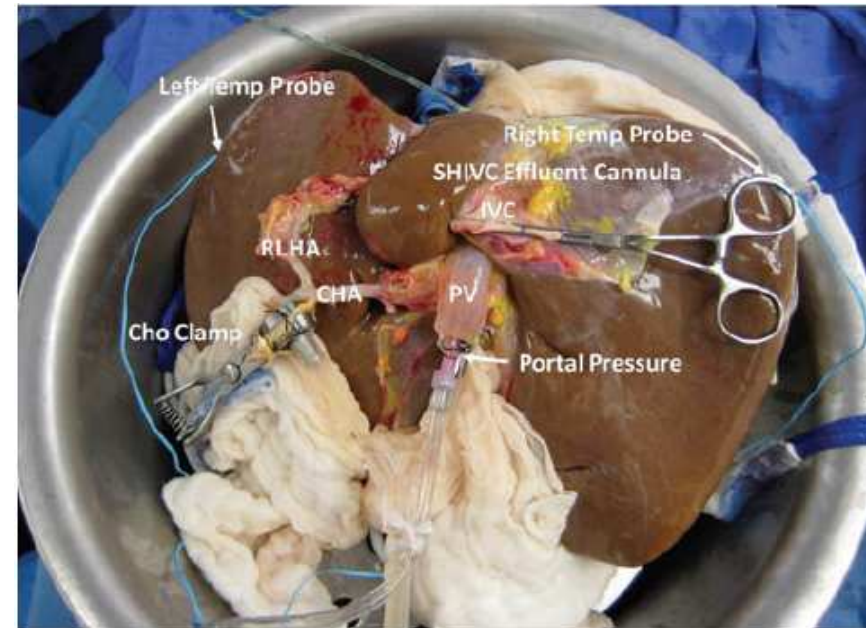
J. V. Guarrera<sup>a,\*</sup>, S. D. Henry<sup>a</sup>, B. Samstein<sup>a</sup>,  
R. Odeh-Ramadan<sup>a</sup>, M. Kinkhabwala<sup>d</sup>,  
M. J. Goldstein<sup>a</sup>, L. E. Ratner<sup>a</sup>, J. F. Renz<sup>c</sup>,  
H. T. Lee<sup>b</sup>, R. S. Brown, Jr.<sup>a</sup> and J. C. Emond<sup>a</sup>

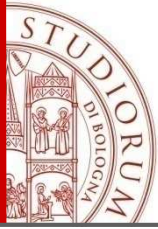
<sup>a</sup>Center for Liver Disease and Transplantation,  
Department of Surgery and <sup>b</sup>Department of  
Anesthesiology, Columbia University Medical Center,  
New York, NY

<sup>c</sup>Division of Transplantation, University of Arizona,  
Tucson, AZ

<sup>d</sup>Division of Transplantation, Montefiore Medical Center,  
Bronx, New York, NY

\*Corresponding author: James V. Guarrera,  
jjg46@columbia.edu or liverpreservation@gmail.com





# ECD, other strategies to improve the outcome?

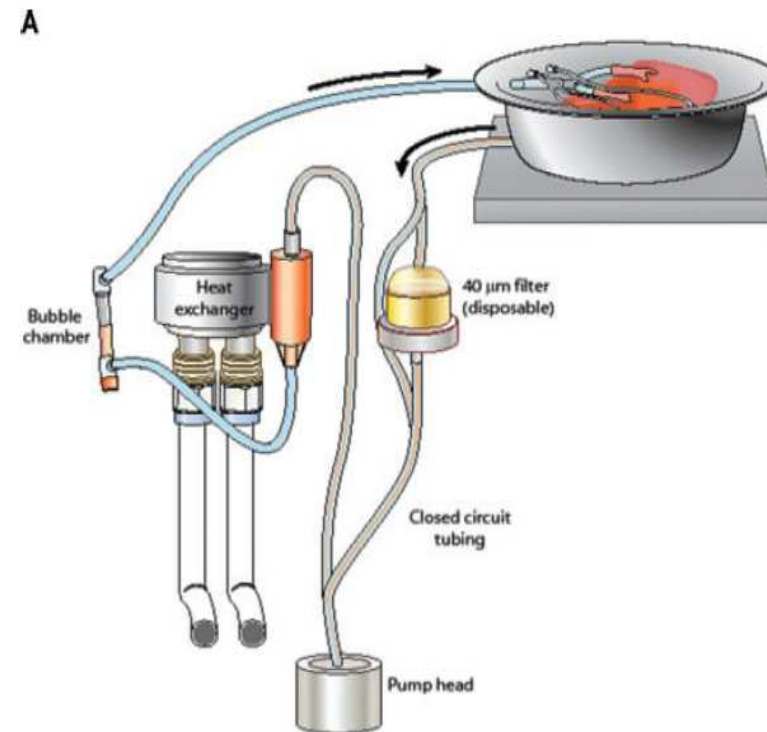
20 LTs HMP preserved vs. 20 a matched group transplanted with CS livers

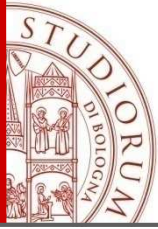
	Machine perfusion (HMP)	Cold storage (CS)
Primary nonfunction	0	0
Early allograft dysfunction	1* (5%) <sup>1</sup>	5 (25%)
Vascular complications (total)	0	1
Hepatic artery stenosis		1
Biliary complications (total)	2	4
Early bile leak	1	1
Biliary stricture	1	3
Hospital length of stay (days)	10.9 ± 4.7 <sup>2</sup>	15.3 ± 4.9
Actual graft and patient survival	18/20 (90%)	18/20 (90%)
Deaths with fuctional grafts	2	2
	Cardiovascular death at 1 month	Recurrent cancer at 5 months
	Pneumonia and sepsis at 3 months	Recurrent HCV and sepsis at 7 months

<sup>1</sup>p = 0.08, <sup>2</sup>p = 0.006.

\*Technically met criteria but occurred in the setting of early acute cellular rejection.

**Early allograft dysfunction**  
**Rates were 5% in the HMP group**  
**versus 25% in controls**  
**(p = 0.08)**





# ECD, other strategies to improve the outcome?

## Liver Transplant Using Donors After Unexpected Cardiac Death: Novel Preservation Protocol and Acceptance Criteria

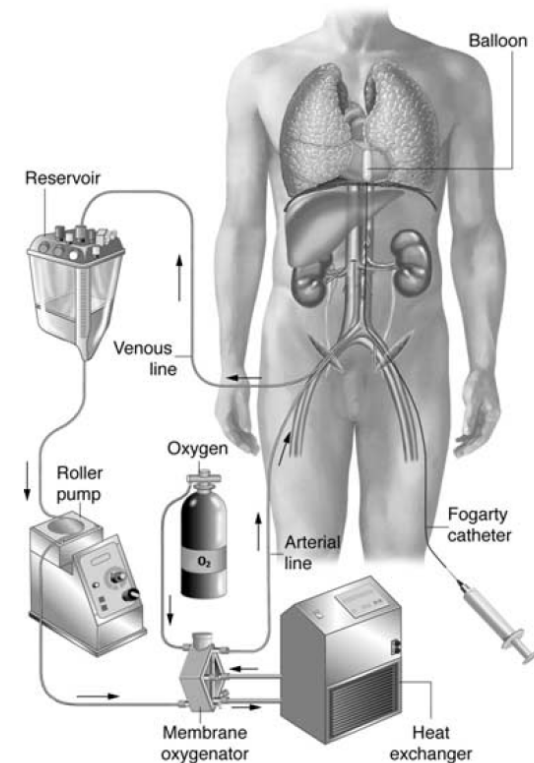
*American Journal of Transplantation 2007; 7: 1849–1855*

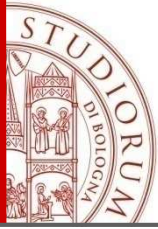
C. Fondevila<sup>a,\*</sup>, A. J. Hessheimer<sup>a</sup>, A. Ruiz<sup>b</sup>,  
D. Calatayud<sup>a</sup>, J. Ferrer<sup>a</sup>, R. Charco<sup>a</sup>, J. Fuster<sup>a</sup>,  
M. Navasa<sup>c</sup>, A. Rimola<sup>c</sup>, P. Taurá<sup>d</sup>, P. Ginés<sup>c</sup>,  
M. Manyalich<sup>b</sup> and J. C. García-Valdecasas<sup>a</sup>

<sup>a</sup>Departments of Surgery, <sup>b</sup>Transplant Coordination,  
<sup>c</sup>Gastroenterology and <sup>d</sup>Anesthesia, Institut de Malalties  
Digestives, Hospital Clínic, Institut d'Investigacions  
Biomèdiques August Pi I Sunyer (IDIBAPS), University  
of Barcelona, 08036 Barcelona, Spain

\*Corresponding author: Constantino Fondevila,  
cfonde@clinic.ub.es

**Donors after cardiac death (DCD) maintain with  
normothermic extracorporeal membrane  
oxygenation (NECMO)**





# ECD, other strategies to improve the outcome?

## One Hour Hypothermic Oxygenated Perfusion (HOPE) Protects Nonviable Liver Allografts Donated After Cardiac Death

*Olivier de Rougemont, MD,\* Stefan Breitenstein, MD,\* Boris Leskosek,\* Achim Weber, MD,† Rolf Graf, PhD,\*  
Pierre-Alain Clavien, MD, PhD,\* and Philipp Dutkowski, MD\**

*(Ann Surg 2009;250: 674–683)*

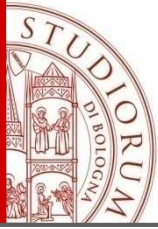
### DCD group

60 min WI	7 h CI	OLT (termination after 6 h)	study I (n = 6)
60 min WI	7 h CI	OLT + survival	study II (n = 5)

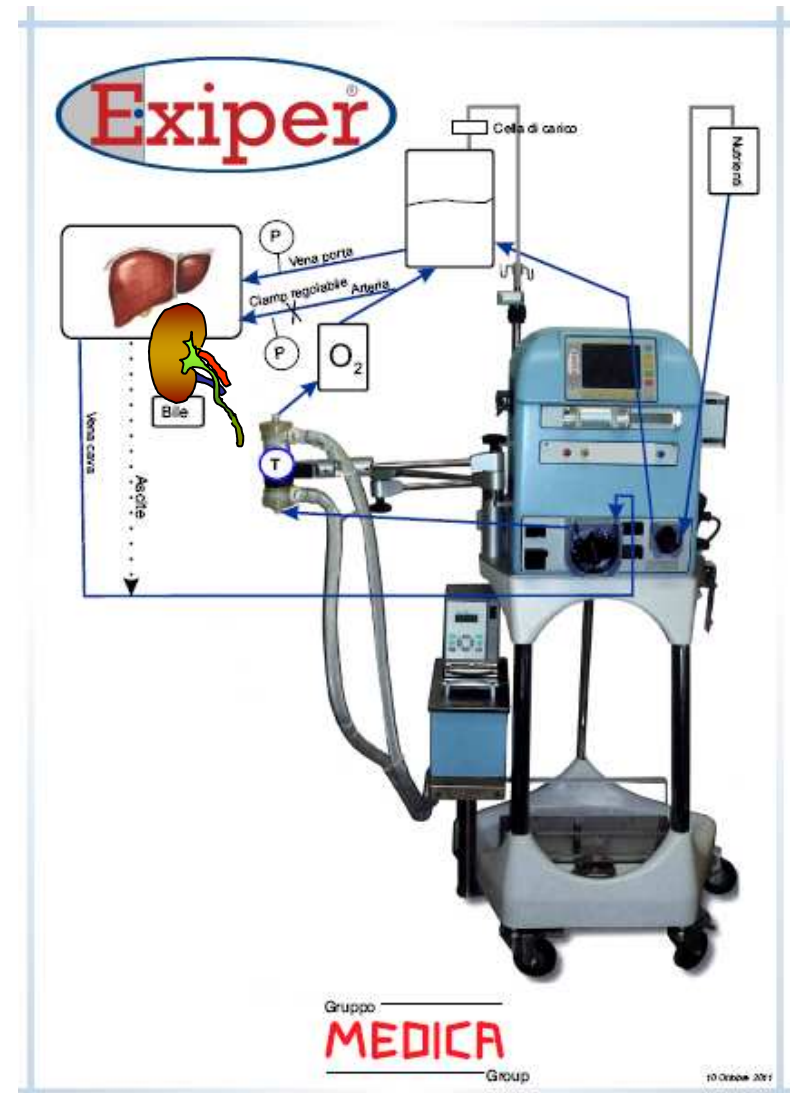
### HOPE group

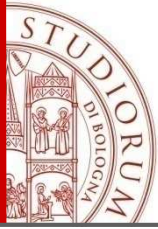
60 min WI	6 h CI	1 h HOPE	OLT (termination after 6h)	study I (n = 6)
60 min WI	6 h CI	1 h HOPE	OLT + survival	study II (n = 5)





## ECD, other strategies... Bologna researches..





*Conclusions: centers can choose their transport but do not forget any passengers*





