12/2013

Compared efficacy of preservation Solutions in liver transplantation:

a long-term graft outcome study from the European Liver Transplant Registry.

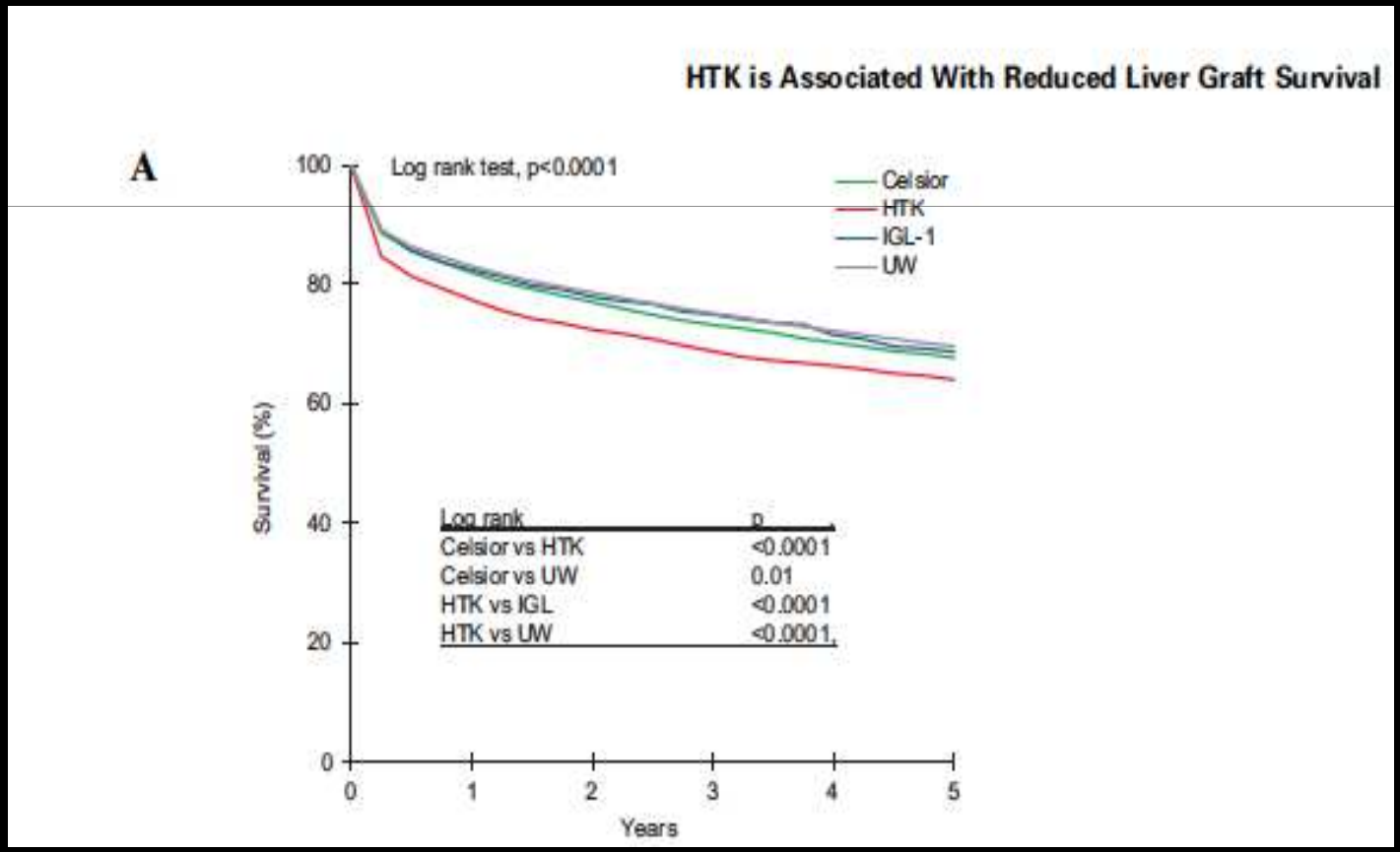
René ADAM, Valérie DELVART, Vincent KARAM, Christian DUCERF, Francis NAVARRO, Christian LETOUBLON, Jacques BELGHITI, Denis PEZET, Denis CASTAING, Yves Patrice Le TREUT, Jean GUGENHEIM, Philippe BACHELLIER, Paolo MUIESAN

and all the ELTR contributing centres www.eltr.org

and the European Liver and Intestine Transplant Association (ELITA).

Compared Efficacy of Preservation Solutions in Liver Transplantation: A Long-Term Graft Outcome Study From the European Liver Transplant Registry

American Journal of Transplantation 2015; 15: 395–406



Adam et al, AJT 2015

DISCUSSION

The first time since UW that a study demonstrate a difference between preservation solutions…

1.Are the results reliable ?

- Multicentric data on more than 42,000 LT...
- Data valid excluding the potential bias of more LRLT in the HTK group...
- Multivariate analysis

→ Propensity score matching analysis

Propensity score matching

- To control for differences in baseline characteristics between groups
- Patients were paired on a 1:2 ratio [HTK (n=4964):Others (n=9928)] according to similar pre-defined characteristics
  - All unmatched patients were excluded from the analysis

Recipient gender
Period (2003-2007 vs 2008-2012)
Recipient_HIV status
Recipage >= 60 yrs
Urgency
Hepatocellular carcinoma in dis1 or dis2
Donor age >= 55 yrs
Cadaveric full size graft
ABO Blood group compatibility
Cold schemia time >= 6hrs
Centers performing more than 10 living donors

- Univariate, multivariate and Kaplan–Meier analyses were repeated using these matched patients

Multivariate analysis - Cox Model
Before Propensity matching (n= 31,129)

Risk Factors	p	Risk ratio	95% CI
LT1 unos1	<.0001	1.78	[1.65;1.92]
HIV pos	<.0001	1.42	[1.21;1.65]
Rec antiHCV pos	<.0001	1.39	[1.32;1.46]
LT1 ischemia time ≥ 12 hrs	<.0001	1.34	[1.25;1.43]
LT1 HTK	**<.0001**	**1.28**	**[1.21;1.35]**
LT1 donor age ≥ 65 yrs	<.0001	1.28	[1.22;1.36]
HBsAg neg	<.0001	1.26	[1.16;1.35]
Not Cadaveric Full size	<.0001	1.25	[1.16;1.35]
LT1 recip age ≥ 60 yrs	<.0001	1.22	[1.16;1.28]
LT1 non Iso blood group	0.0092	1.12	[1.03;1.22]
Rec Male	<.0001	1.11	[1.05;1.16]
Main dis not Cirrhosis	0.0014	1.08	[1.03;1.13]
No Pts center < 500	0.0106	1.08	[1.02;1.14]

Multivariate analysis - Cox Model

Before Propensity matching (n= 34,520)

- Stratified by Center -

Risk Factors	p	Risk ratio	95% CI
HIV pos	<.0001	1.50	[1.28;1.75]
Rec antiHCV pos	<.0001	1.41	[1.34;1.47]
ACHF as main disease	<.0001	1.34	[1.22;1.47]
LT1 donor age ≥ 65 yrs	<.0001	1.32	[1.24;1.39]
LT1 Red or Split	<.0001	1.30	[1.16;1.44]
HBsAg neg	<.0001	1.24	[1.15;1.33]
LT1 non Iso blood group	<.0001	1.23	[1.14;1.34]
LT1 recip age ≥ 60 yrs	<.0001	1.23	[1.17;1.28]
LT1 ischemia time ≥ 12 hrs	<.0001	1.19	[1.11;1.27]
LT1 HTK	**0.02**	**1.11**	**[1.02;1.20]**
Rec Male	0.0001	1.10	[1.05;1.15]
Main dis not Cirrhosis	0.0003	1.09	[1.04;1.14]
interaction HTK Age D	0.01	0.84	[0.74;0.96]

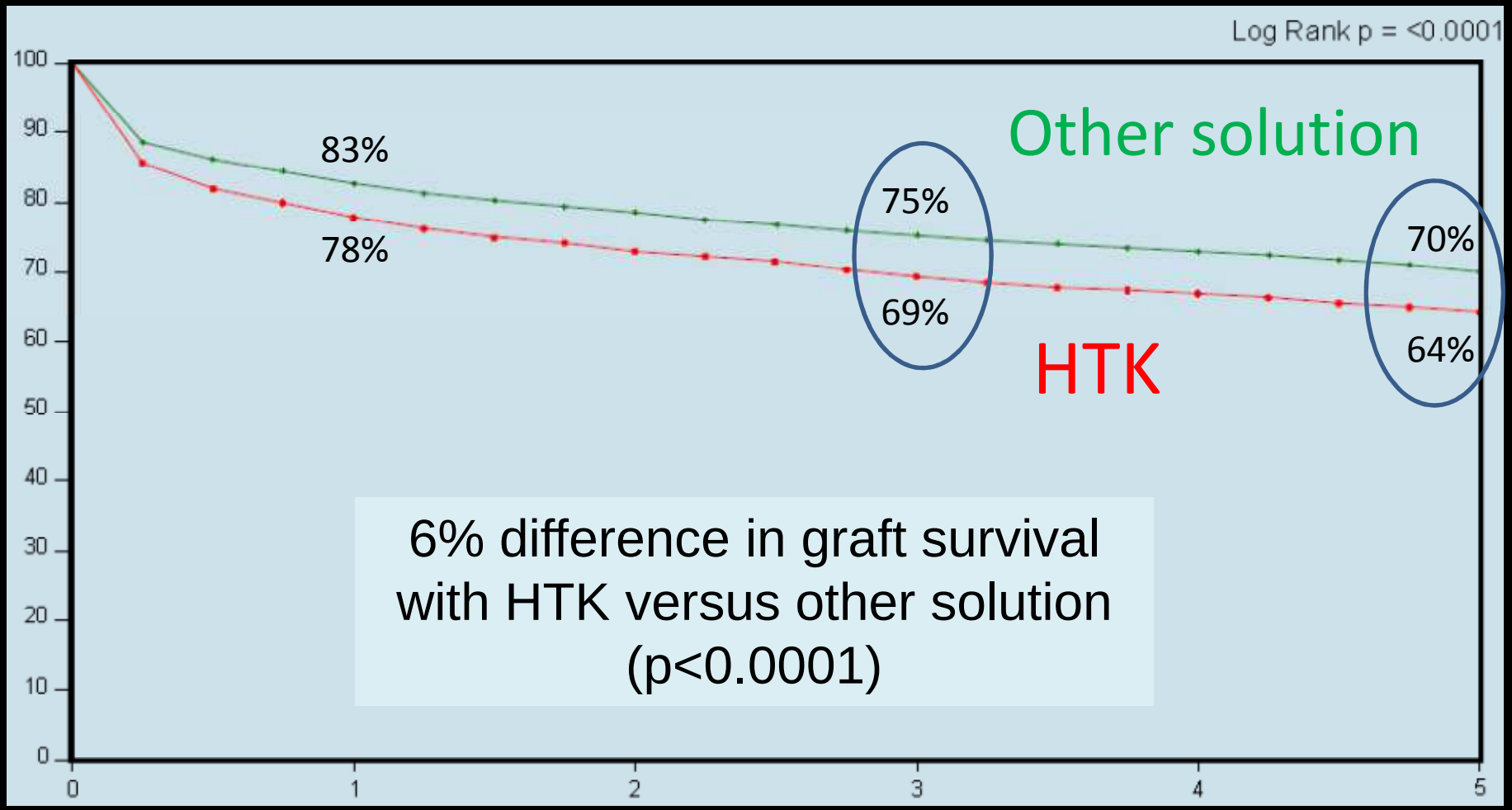
Multivariate analysis - Cox Model
After Propensity matching (n= 12,809)

Facteur de risque	p	Risk ratio	95% CI
LT1 Unos1	<.0001	1.66	[1.48;1.87]
Rec antiHCV pos	<.0001	1.42	[1.32;1.54]
LT1 ischemia time ≥ 12 hrs	<.0001	1.37	[1.25;1.50]
LT1 donor age ≥ 65 yrs	<.0001	1.34	[1.23;1.46]
Not Cadaveric Full size	0.0007	1.29	[1.12;1.50]
LT1 HTK	**<.0001**	**1.28**	**[1.19;1.38]**
HBsAg neg	0.0020	1.22	[1.08;1.39]
LT1 recip age ≥ 60 yrs	<.0001	1.21	[1.12;1.31]
LT1 non Iso blood group	0.0067	1.19	[1.05;1.36]
Rec Male	0.0061	1.11	[1.03;1.20]
Main dis not Cirrhosis	0.0144	1.09	[1.02;1.17]

Multivariate analysis - Cox Model
After Propensity matching (n= 31,925)
- Stratified by Center -

Facteur de risque	p	Risk ratio	95% CI
Rec antiHCV pos	<.0001	1.43	[1.32;1.54]
ACHF as main disease	<.0001	1.35	[1.18;1.54]
HBsAg neg	0.0001	1.28	[1.13;1.45]
LT1 recip age ≥ 60 yrs	<.0001	1.24	[1.15;1.33]
LT1 nonIsogr blood gp	0.001	1.23	[1.09;1.40]
LT1 ischemia_time ≥ 12 hrs	<.0001	1.23	[1.12;1.35]
LT1 donor age ≥ 65 yrs	<.0001	1.23	[1.13;1.34]
LT1 reduced or split	0.04	1.22	[1.01;1.47]
LT1 HTK	0.05	1.10	[1.00;1.22]
Main dis not Cirrhosis	0.01	1.10	[1.02;1.19]
Rec Male	0.03	1.09	[1.01;1.17]

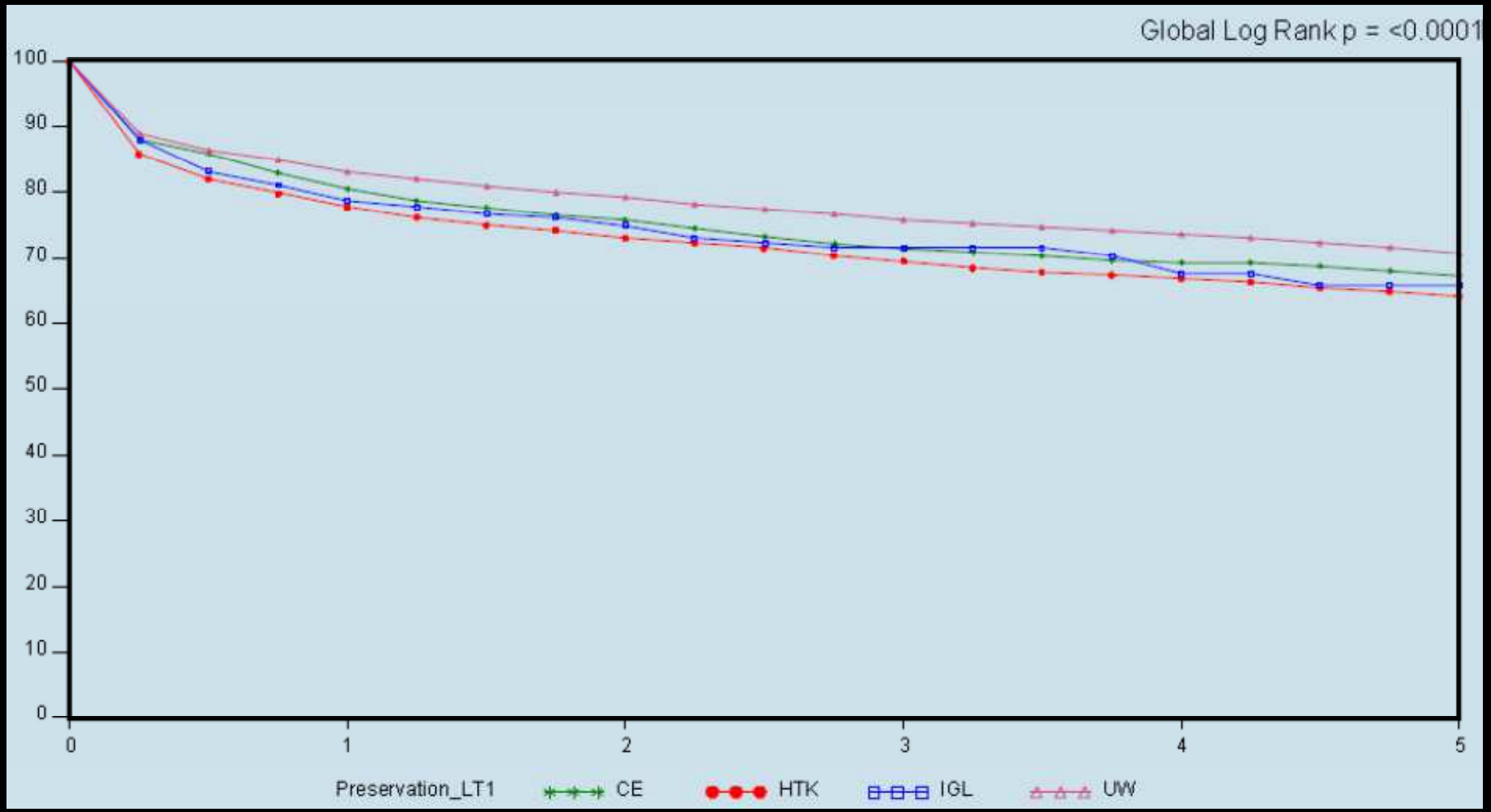
Graft Survival
After Propensity matching



Graft Survival

After Propensity matching

- Detail of Other solution -



DISCUSSION

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1.Are the results reliable ?

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2. Did these results are confirmed by other studies ?

12/2013

Histidine–Tryptophan–Ketoglutarate (HTK) Is Associated with Reduced Graft Survival in Deceased Donor Livers, Especially Those Donated After Cardiac Death

Z. A. Stewart, A. M. Cameron, A. L. Singer, R. A. Montgomery and D. L. Segev*

American Journal of Transplantation 2009; 9: 286–293

UNOS Database (2004-2008)
HTK (n= 4755) versus UW (n= 12673)

« After adjusting for donors, recipient and graft factors that affect graft survival, HTK preservation was associated with an increased risk of graft loss (HR 1.44, p= 0.002) especially with DCD allografts and those with cold ischemia time over 8 hours…
Furthermore HTK preservation was associated with a 1.2-fold higher odds of early (< 30 days) graft loss compared to UW »

12/2013

Histidine-Tryptophan-Ketoglutarate (HTK) Is Associated with Reduced Graft Survival in Pancreas Transplantation

Z. A. Stewart, A. M. Cameron, A. L. Singer, N. N. Dagher, R. A. Montgomery and D. L. Segev*

American Journal of Transplantation 2009; 9: 217–221

Histidine-Tryptophan-Ketoglutarate (HTK) Is Associated with Reduced Graft Survival of Deceased Donor Kidney Transplants

Z. A. Stewart, B. E. Lonze, D. S. Warren, N. N. Dagher, A. L. Singer, R. A. Montgomery and D. L. Segev*

American Journal of Transplantation 2009; 9: 1048–1054

Conclusion

12/2013

1- Comparison of preservation solutions used in Europe in a recent 9-year period demonstrate similar results for UW, IGL and Celsior but worst results for HTK

2- 1- and 3-yr Graft survival is 5 and 6% lower with HTK compared to all the other solutions

3- The mechanisms involved in these results are still unknown but PNF and Graft Dysfunction are significantly more frequently involved in Graft Loss after HTK use

4- These data confirmed by propensity score analysis share the 1.2 fold higher risk of graft loss demonstrated by a UNOS study

Adam et al, Am J Transplantation 2015

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