Advanced Donor Age and Recipient Age Do Not Interact to Influence Long-Term Outcomes after Liver Transplantation

Table S1. Results from a multivariate Cox regression for patient survival after stepwise backward selection of the final set of covariates and extension of the model with stratification of the risk associated with recipient age.

Variable	HR (95%CI)	p-value
Donor age ≥ 70 years (ref.: no)	0.79 (0.53-1.17)	0.23
Recipient age (ref.: <50 years)	1	<0.001
50-59	1.09 (0.75-1.59)	0.65
60-69	1.995 (1.40-2.85)	<0.0001
≥70	2.001 (1.10-2.66)	0.02
Donor of thoracic organs (ref.: no)	0.57 (0.43-0.77)	<0.0001
Re-transplantation (no. of transplant)	1.72 (1.23-2.41)	0.002
UNOS (ref.: home)	1	<0.0001
ICU	3.45 (2.23-5.31)	<0.0001
Ward	1.95 (1.30-2.93)	0.001
Continuous care	1.41 (0.99-2.00)	0.053
HCC (ref.: no)	1.79 (1.29-2.48)	<0.0001
Cold ischemia time (hour)	1.1 (1.03-1.17)	0.004

Results based on 224 events in 763 subjects.

Abbreviations: HCC, hepatocellular carcinoma; UNOS, united network for organ sharing score.

N. Gilbo et al.

Table S2. Univariate and multivariate Cox regression for patient survival at six months and one year after liver transplantation.

Characteristic	Patient survival at 6 months				Patient survival at 1 year			
	Univariate		Multivariate[a]		Univariate		Multivariate[b]	
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
Donor age ≥ 70 years (ref.: no)	0.37 (0.002-583)	0.79	0.17 (0.0002-211)	0.63	5.64 (0.04-820)	0.50	2.93 (0.02-384)	0.67
Recipient age (year)	1.04 (1.02-1.07)	0.001	1.06 (1.03-1.09)	0.00008	1.04 (1.02-1.07)	0.001	1.06 (1.03-10.9)	0.00003
Age interaction	1.001 (0.89-1.12)	0.98	1.01 (0.91-1.13)	0.81	0.97 (0.89-1.05)	0.38	0.98 (0.90-1.06)	0.53
Donor gender (ref.: male)	1.47 (0.91-2.38)	0.12	-	-	1.27 (0.83-1.95)	0.27	-	-
DCD (ref.: no)	0.84 (0.39-1.86)	0.68	-	-	1.10 (0.59-1.23)	0.31	-	-
Total warm ischemia[c] (min)	1 (0.96-1.03)	0.77	-	-	1.01 (0.98-1.03)	0.71	-	-
Functional warm ischemia[d] (min)	0.97 (0.91-10.4)	0.44	-	-	1 (0.95-1.05)	0.96	-	-
Asystolic warm ischemia[e] (min)	0.95 (0.86-1.05)	0.95	-	-	0.98 (0.91-10.6)	0.63	-	-
Donor ICU hospitalization (day)	0.99 (0.95-1.03)	0.60	-	-	0.98 (0.94-1.03)	0.42	-	-
Donor BMI	0.98 (0.91-1.05)	0.53	-	-	0.99 (0.93-1.06)	0.78	-	-
Donor height (cm)	0.99 (0.96-1.02)	0.38	-	-	0.99 (0.97-1.01)	0.44	-	-
Donor highest AST (IU/L)	1 (0.99-1.002)	0.59	-	-	1 (0.99-1.001)	0.46	-	-
Donor highest ALT (IU/L)	1 (0.99-1.002)	0.64	-	-	1 (0.99-1.002)	0.40	-	-
Donor hepatitis C virus positivity	6.35 (1.55-25.99)	0.01	-	-	5.35 (1.31-21.81)	0.02	-	-
Donor history of arterial hypertension (ref.: no)	1.57 (0.91-2.74)	0.11	-	-	1.53 (0.94-2.50)	0.09	-	-
Donor history of diabetes (ref.: no)	1.19 (0.37-3.86)	0.78	-	-	1.42 (0.56-3.55)	0.50	-	-
Donor cause of death (ref.: others)	1	0.51	-	-	1	0.45	-	-
Trauma	0.48 (0.19-1.23)	0.13	-	-	0.57 (0.24-1.35)	0.20	-	-
Cerebrovascular accident	0.59 (0.25-1.40)	0.23	-	-	0.62 (0.28-1.38)	0.24	-	-
Cardiac arrest	0.81 (0.23-2.88)	0.75	-	-	0.87 (0.28-2.76)	0.82	-	-
Hypoxia	0.40 (0.11-1.42)	0.16	-	-	0.34 (0.1.-1.17)	0.09	-	-
Procurement team (ref.: local)	1	0.11	-	-	1	0.32	-	-
Regional	1.27 (0.70-2.29)	0.44	-	-	1.33 (0.80-2.21)	0.27	-	-
Interregional	1.83 (1-04-3.22)	0.04	-	-	1.45 (0.85-2.46)	0.17	-	-

N. Gilbo et al.

Donor of thoracic organ(s)[f] (ref.: no)	1.11 (0.68-1.83)	0.68	-	-	0.80 (0.52-1.23)	0.31	-	-
HTK preservation solution (ref.: no)	2.08 (1.26-3.42)	0.004	1.84 (1.07-3.15)	0.03	1.64 (1.03-2.59)	0.04	-	-
Cold ischemia time[g] (hour)	1.11 (0.99-1.24)	0.05	-	-	1.10 (1.003-1.22)	0.04	-	-
Duration of transplantation (hour)	1.09 (0.95-1.25)	0.08	-	-	1.07 (0.94-1.21)	0.31	-	-
Recipient gender (ref.: male)	0.99 (0.60-1.62)	0.96	-	-	1.02 (0.66-1.58)	0.93	-	-
Recipient BMI	1.02 (0.97-1.07)	0.4	-	-	1.02 (0.98-1.07)	0.30	-	-
Recipient lab MELD score (point)	1.05 (1.02-1.07)	<0.0001	-	-	1.05 (1.03-1.07)	<0.0001	1.02 (0.99-1.05)	0.10
Recipient UNOS score (ref.: home)	1	0.004	1	0.0001	1	<0.0001	1	0.005
ICU	4.49 (2.16-9.32)	0.0001	5.37 (2.47-11.67)	0.00002	4.48 (2.42-8.31)	<0.0001	3.43 (1.48-7.95)	0.004
Ward	1.91 (0.87-4.18)	0.12	1.82 (0.80-3.91)	0.15	1.56 (0.78-3.12)	0.21	1.06 (0.49-2.32)	0.88
Continuous care	1.55 (0.73-3.32)	0.26	1.79 (0.82-3.91)	0.15	1.32 (0.68-2.56)	0.42	1.20 (0.61-2.36)	0.60
Recipient history of arterial hypertension (ref.: no)	0.97 (0.59-1.58)	0.90	-	-	1.11 (0.72-1.71)	0.65	-	-
Recipient history of diabetes (ref.: no)	1.40 (0.83-2.37)	0.21	-	-	1.47 (0.92-2.34)	0.11	-	-
Recipient renal replacement therapy (ref.: no)	1.93 (0.70-5.33)	0.21	-	-	1.91 (0.77-4.75)	0.16	-	-
Recipient portal vein thrombosis (ref.: no)	0.57 (0.75-3.29)	0.23	-	-	1.57 (0.81-3.04)	0.18	-	-
Indication			-	-			-	-
Post-ethyl cirrhosis	0.59 (0.29-1.19)	0.14	-	-	0.57 (0.30-1.07)	0.08	-	-
Post-hepatitis B cirrhosis	1.23 (0.39-3.92)	0.73	-	-	1.32 (0.48-3.59)	0.59	-	-
Post-hepatitis C cirrhosis	0.93 (0.29-2.97)	0.91	-	-	0.73 (0.23-2.32)	0.60	-	-
NASH	1.15 (0.42-3.17)	0.78	-	-	1.41 (0.62-3.24)	0.41	-	-
HCC	0.97 (0.58-1.64)	0.91	-	-	1.05 (0.53-2.05)	0.89	-	-
Re-transplantation (no. of transplant)	2.04 (1.28-3.23)	0.002	2.21 (1.27-3.86)	0.005	1.90 (1.23-2.93)	0.004	1.87 (1.09-3.19)	0.02

Abbreviations: ALT, alanine transferase; AST, aspartate transferase; BMI, body mass index; DCD, donation after circulatory death; HCC, hepatocellular carcinoma; HTK, histidine-tryptophan-ketoglutarate preservation solution; ICU, intensive care unit; MELD, model for end-stage liver disease score; NASH, non-alcoholic steatohepatitis; UNOS: united network for organ sharing score.

[a] Results from a multivariate model predicting six months patient survival based on 57 events in 758 subjects. Covariates were retained in the final multivariate model after backwards stepwise selection; donor ≥ 70 years, recipient age, and their interaction product were introduced in the model irrespectively from their performance at univariate analysis.

[b] Results from a multivariable model predicting one year patient survival based on 73 events in 764 subjects. Covariates were retained in the final multivariate model after backwards stepwise selection; donor ≥ 70 years, recipient age, and their interaction product were introduced in the model irrespectively from their performance at univariate analysis.

[c] Total warm ischemia was defined as the time between withdrawal of therapy and initiation of the cold flush *in situ* during organ procurement.

[d] Functional warm ischemia was defined as the time between the drop of systemic blood pressure below 60 mmHg and initiation of cold flush *in situ* during organ procurement.

[e] Asystolic warm ischemia was defined as the time between the occurrence of circulatory arrest and initiation of cold flush in situ during organ procurement.

[f] Donors were considered also donors of thoracic organ(s) when either heart, lungs, heart and lungs were procured.

[g] Cold ischemia was defined as the time between the initiation of the cold flush *in situ* during organ procurement and the liver graft being placed in the recipient abdomen.

N. Gilbo et al.

Table S1. Results from an additive multivariate Cox regression predicting the risk of patient's death in the subgroup of recipients ≥ 60 years.

Variable	HR (95% CI)	*P* value
Donor age ≥ 70 years (ref.: no)	0.66 (0.39-1.11)	0.12
Donor of thoracic organs (ref.: no)	0.45 (0.30-0.68)	0.0002
UNOS (ref.: home)	1	0.01
ICU	2.91 (1.53-5.52)	0.001
Ward	1.57 (0.91-2.73)	0.11
Continuous care	1.42 (0.89-2.28)	0.15
HTK preservation solution (ref.: no)	1.44 (0.96-2.17)	0.08

Results based on 111 events in 335 subjects. Covariates were retained in the final multivariate model after backwards stepwise selection; donor age ≥ 70 years was introduced in the model irrespectively from its performance in univariate analysis.

Abbreviations: HTK, histidine-tryptophan-ketoglutarate preservation solution; UNOS, united network for organ sharing score.

N. Gilbo et al.

Table S2. Results from a multivariate Cox regression predicting the risk of patient's death after stepwise backwards selection of the final set of covariates and extension of the model with different donor-recipient age matches (D<70/R<70, D<70/R≥70, D≥70/R<70, D≥70/R≥70).

Variable	HR (95%CI)	p-value
Donor age[a] (year)	1.003 (0.99-1.01)	0.52
Recipient age (year)	1.03 (1.02-1.05)	<0.0001
Age match (ref.: D<70/R<70)	1	0.39
D<70/R≥70	1.29 (0.74-2.25)	0.37
D≥70/R<70	0.75 (0.46-1.23)	0.26
D≥70/R≥70	0.64 (0.27-1.60)	0.34
Donor of thoracic organs (ref.: no)	0.60 (0.44-0.81)	0.001
Re-transplantation (no. of transplant)	1.76 (1.26-2.47)	0.001
UNOS (ref.: home)		<0.0001
ICU	3.46 (2.25-5.34)	<0.0001
Ward	1.89 (1.26-2.84)	0.002
Continuous care	1.42 (1.001-2.01)	0.049
HCC (ref.: no)	1.74 (1.26-2.41)	0.001
Cold ischemia time (hour)	1.10 (1.04-1.17)	0.002

Results based on 224 events in 763 subjects.

Abbreviations: HCC, hepatocellular carcinoma; UNOS, united network for organ sharing score.

[a] "Donor age ≥70 years" has been replaced to avoid excessive collinearity with the covariate "age match."

N. Gilbo et al.

Table S5. Results from a multivariate Cox regression predicting the risk of death in recipients of donation after brain-death liver transplant after stepwise backward selection of the final set of covariates.

Variable	HR (95%CI)	p-value
Donor age ≥ 70 years (ref.: no)	1.42 (0.09-23.12)	0.81
Recipient age (ref.: <50 years)	1.03 (1.01-1.04)	<0.0001
Age interaction	0.99 (0.95-1.04)	0.69
Donor of thoracic organs (ref.: no)	0.57 (0.42-0.79)	0.001
Re-transplantation (no. of transplant)	1.78 (1.26-2.50)	0.001
UNOS (ref.: home)	1	<0.0001
ICU	3.87 (2.45-6.11)	<0.0001
Ward	1.97 (1.26-3.06)	0.003
Continuous care	1.49 (1.02-2.16)	0.04
HCC (ref.: no)	1.94 (1.38-2.73)	<0.0001
Cold ischemia time (hour)	1.12 (1.05-1.20)	0.001

Results based on 202 events in 662 subjects.

Abbreviations: HCC, hepatocellular carcinoma; UNOS, united network for organ sharing score.
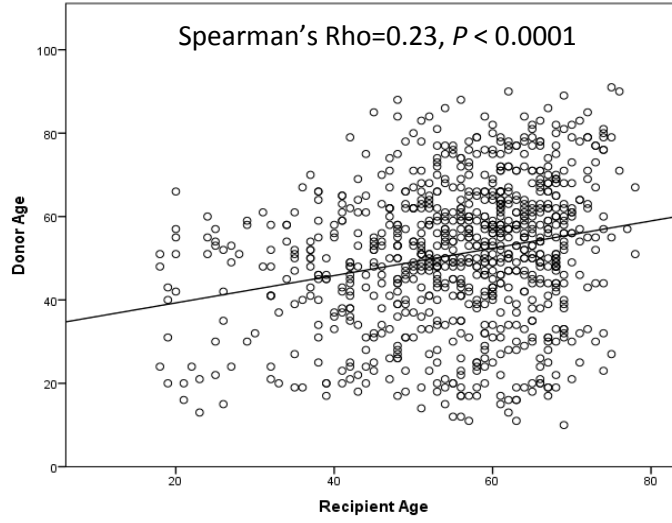
N. Gilbo et al.

Figure S1. Correlation between donor and recipient age: a significant tendency towards matching older donors with older recipients was observed in our center (Spearman's Rho: 0.23, *P* < 0.0001).

N. Gilbo et al.