Predictors of Patient and Graft Survival Following Paediatric Liver Transplantation: Long-Term Analysis of more than 300 Cases From Single Centre

Amr Alnagar[1,2], Khaled Daradka[1], Eirini Kyrana[1], Marumbo Methga[1], Karthikeyan Palaniswamy[1], Suzanne Davison[1], Patricia Mcclean[1], Sanjay Rajwal[1], Moira O'Meara[1], Jamila Mulla[1], Abdul Hakeem[1], Vivek Upasani[1], Vijayanand Dhakshinamoorthy[1], Raj Prasad[1], Magdy Attia[1]

[1]The Leads Teaching Hospitals NHS Trust, UK, [2]General Surgery Department, Faculty of Medicine, Alexandria University, Egypt

BACKGROUND

- As a result of improved outcomes, referral to paediatric liver transplant (PLT) services has gradually increased but unfortunately graft pool did not show similar expansion resulting in graft shortage. Identifying of pre-transplant predictors of patient and graft survival can help in more effective graft allocation and can be crucial in guiding medical care and re-listing decisions.

AIM OF THE WORK

- Identifying the pre-transplant factors that can by itself or in combination predict post-transplant patient and graft survival.

METHODS

- This is a retrospective review of PLT episodes in Leeds Teaching Hospitals NHS trust from 2000 to 2020. Univariate and Multivariate analysis of pretransplant factors were used to identify predictors of patient and graft survival. We classified aetiology of liver disease into 6 broad categories: End stage chronic liver disease (ESCLD), Acute liver failure (ALF), acute on top of ESCLD, metabolic liver disease, tumours, and re-transplantation. Grafts used were divided into whole and technical variant grafts where technical variant grafts include all split and reduced grafts, technical variant grafts were further divided into grafts from cadaveric or living donors (LD).

RESULTS

- 276 patients in our centre received 320 LTs. In terms of indications for LT, ESCLD was the main indication (60.6%) followed by re-transplantation (13.7%), ALF (10.3%), tumours (8.8%), metabolic (5.3%) and acute on top of ESCLD (1.3%). Source of liver grafts were DBD donors in 271 (84.7%) transplant episodes while 49 grafts (15.3%) were from living donors. Number of grafts per patient was one graft in 276 patients (86.2%), two grafts in 39 patients (12.2%) and three grafts in 5 (1.6%) patients.

- Most common cause of graft loss was hepatic artery thrombosis (HAT) in 13 re-transplants (29.6%). At the end of study, 239(86.6%) recipients survived while 37 (13.4%) died. Most common cause of death was sepsis. Univariate analysis for patient survival showed that following variables had a significant (p<0.05) impact on overall patient survival: patient age, patient weight, patient height, graft type, category, era of transplant and invasive ventilation. Univariate analysis for graft survival showed that the following variables had a significant (p<0.05) impact on graft survival: patient age, patient weight, patient height, category, and era of transplant. Multivariate statistical analysis of Patient and graft Survival showed that the only significant factor for graft and patient survival is the era of transplant where patients transplanted after 2010 has significantly higher recipient and graft survival.

Univariate cox regression analysis of risk factors for death and graft loss after PLT

	Patient death		Graft Loss	
	p	HR (95%C.I)	p	HR (95%C.I)
Age				
0 – 5 months	0.538	1.471 (0.430 –5.025)	0.138	2.075 (0.790 –5.446)
6 – 11 months	0.002*	0.095 (0.022 – 0.411)	0.056	0.525 (0.272 –1.016)
1 – 4 year	0.002*	0.246 (0.102 – 0.593)	0.004*	0.398 (0.212 – 0.750)
5 – 12 year	0.040*	0.415 (0.179 – 0.962)	0.229	0.683 (0.367 –1.272)
≥13 year(reference)		1.000		1.000
Gender/Female	0.805	1.085 (0.569 –2.067)	0.785	1.064 (0.681 –1.664)
Graft type				
Whole(reference)		1.000		1.000
Technical variant	0.003*	0.355 (0.179 – 0.704)	0.081	0.642 (0.390 –1.057)
Technical variant LD	0.115	0.413 (0.138 –1.239)	0.240	0.631 (0.293 –1.360)
Category				
ESCLD (reference)		1.000		1.000
ALF	0.003*	3.361 (1.492 –7.569)	0.049*	1.867 (1.003 –3.476)
ALF on top of ESCLD	0.986	–	0.619	1.654 (0.227 –12.034)
Tumor	0.096	2.339 (0.861 –6.351)	0.990	0.995 (0.424 –2.335)
Metabolic	0.972	–	0.425	0.562 (0.136 –2.318)
Re-transplantation	0.261	1.706 (0.672 –4.330)	0.674	1.153 (0.595 –2.233)
Weight (kg)				
<5	0.032*	3.812 (1.125 –12.912)	0.024*	3.340 (1.174 –9.502)
≥5 – 10	0.001*	0.140 (0.042 – 0.471)	0.072	0.589 (0.330 –1.049)
≥10 – 20	0.077	0.479 (0.212 –1.083)	0.174	0.665 (0.369 –1.198)
>20 (reference)		1.000		1.000
Height				
≤Mean	0.001*	0.223 (0.096 – 0.519)	0.042*	0.594 (0.360 – 0.982)
>Mean (reference)		1.000		1.000
Warm ischemia time (min)	0.427	1.014 (0.980 –1.049)	0.163	1.018 (0.993 –1.043)
Cold ischemia time	0.821	1.014 (0.899 –1.144)	0.871	1.007 (0.927 –1.093)
Year of surgery				
Before 2005 (reference)		1.000		1.000
2005 – 2010	0.295	0.674 (0.322 –1.411)	0.242	0.726 (0.425 –1.242)
After 2010	0.004*	0.254 (0.101 – 0.638)	0.001*	0.381 (0.211 – 0.687)
Invasive ventilation	0.012*	2.899 (1.268 –6.631)	0.061	1.894 (0.972 –3.691)

Multivariate cox regression analysis of risk factors for death and graft loss after PLT

	Patient death		Graft Loss	
	p	HR (95%C.I)	p	HR (95%C.I)
Age in years				
0 – 5 months	0.943	6541.074 (0.0 – 1.8×10108)	0.239	5.143 (0.336 –78.712)
6 – 11 months	0.949	2555.491 (0.0 – 7.0×10107)	0.622	1.693 (0.209 –13.731)
1 – 4 year	0.204	0.273 (0.037 –2.023)	0.484	0.591 (0.135 –2.581)
5 – 12 year	0.088	0.370 (0.118 –1.160)	0.439	0.733 (0.334 –1.609)
≥13 year (reference)		1.000		1.000
Graft type				
Whole (reference)		1.000		-
Technical variant	0.705	1.229 (0.423 –3.573)		-
Technical variant LD	0.085	4.663 (0.810 –26.858)		-
Category				
CLD (reference)		1.000		1.000
ALF	0.639	0.709 (0.168 –2.985)	0.400	0.618 (0.202 –1.895)
ALF on top of CLD	0.984	0.000 (-)	0.976	0.000 (–)
Tumor	0.160	2.477 (0.700 –8.769)	0.929	1.044 (0.404 –2.697)
Metabolic	0.948	0.000 (0.0 – 2.7×10130)	0.391	0.415 (0.056 –3.100)
Re-transplantation	0.853	1.128 (0.315 –4.044)	0.131	0.467 (0.173 –1.255)
Weight(kg)				
<5	0.951	0.001 (0.0 – 1.582×10101)	0.778	0.627 (0.024 –16.179)
≥5 – 10	0.932	0.001 (0.0 – 7.352×1099)	0.567	0.581 (0.090 –3.739)
≥10 – 20	0.965	1.037 (0.208 –5.172)	0.425	1.524 (0.542 –4.287)
>20 (reference)		1.000		1.000
Height				
≤Mean	0.847	0.838 (0.140 –5.019)	0.552	0.656 (0.163 –2.634)
>Mean (reference)		1.000		1.000
Year of surgery				
Before 2005 (reference)		1.000		1.000
2005 – 2010	0.430	0.695 (0.281 –1.716)	0.619	0.855 (0.461 –1.585)
After 2010	0.003*	0.112 (0.027 – 0.471)	0.015*	0.397 (0.188 – 0.836)
Invasive ventilation	0.492	1.637 (0.402 –6.672)	0.237	1.877 (0.662 –5.324)
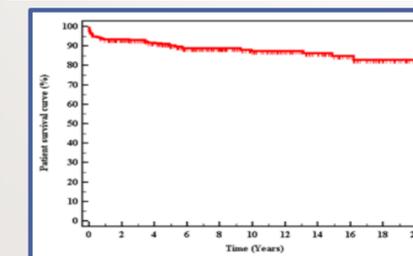
Figure(1): Patient Kaplan-Meier survival curve
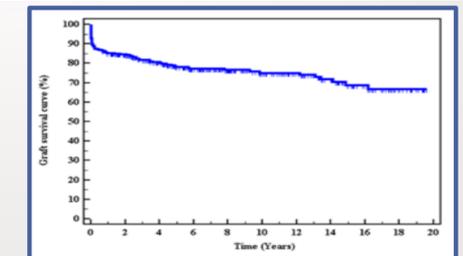
Figure(2): Graft Kaplan-Meier survival curve

SUMMARY

- This study, spanning over about 20 years, represents one of the biggest UK based PLT single centre reports. Only significant factor for patient and graft survival was era of transplant with PLT after 2010 has significantly better patient and graft survival.

CONCLUSION

- Traditional view of worse outcomes of smaller candidates should be changed especially in high volume centres with prolonged experience.