

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

LIVER SPLITTING ACTIVITY REPORT

SUMMARY

BACKGROUND

- 1 Donors after brain death (DBD) aged < 40 years, weighing > 50kg and known to have spent < five days in an intensive care unit meet the criteria for liver splitting. If a donated liver is split it can be used to transplant two patients; typically one adult and one paediatric. This paper reports on the outcome of livers from DBD who donated their liver in a recent time period and who met the criteria for liver splitting. It also reports on survival outcomes of patients who received split liver transplants.

DATA ANALYSIS

- 2 There were 75 livers donated between 1 October 2013 and 31 March 2014 from donors who met the criteria for liver splitting (18% fewer than previous six months, Apr-Sep 2013). Of these, 52 (69%) were available for splitting for elective recipients, having not been used in super-urgent, hepatoblastoma, intestinal or multi-organ recipients. Of these, 24 (46%) were offered for splitting and 13 (54% of the 24) were actually split (41% fewer than previous six months, Apr-Sep 2013). In just over half of the 28 cases where the liver was available for splitting but was not offered for splitting, abnormal or raised liver function tests were cited as the reason for not considering splitting. Eleven livers were offered for splitting but instead used whole or reduced. Common reasons for not splitting these livers were the fattiness of the organ or a lack of suitable paediatric patients for the left lateral segment.
- 3 Analyses of transplant survival following split liver transplantation in paediatric and adult patients showed no evidence of an impact on transplant survival up to five years depending on whether the split liver was retained or imported for paediatric patients, but for adult patients there was some evidence of superior survival for retained split livers ($p=0.08$). There was no difference found between the survival of livers split by adult unit surgeons and livers split by paediatric unit surgeons.

ACTION

- 4 Members are asked to note that this report now includes longer-term survival rates than were previously reported and donor AST level has been reported for livers not offered for splitting, as requested.
- 5 A "paired survival analysis" would be required to account for lack of independence in survival times of patients receiving a split liver from the same donor. If this is requested by the LAG then variables to adjust for in such an analysis would need to be discussed and agreed with a clinical lead.
- 6 Members are reminded that completion of the Split Liver Information form is the most reliable way of recording data on where liver splitting is performed and by whom on the UK Transplant Registry to inform analyses (currently the return rate is approximately 80%).
- 7 A review within ODT of the process for recording reasons for not splitting livers from donors who meet the liver splitting criteria was carried out and improvements to the process, in terms of efficiency and level of detail of reasons, were implemented.

Sally Rushton
May 2014

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

LIVER SPLITTING ACTIVITY REPORT

INTRODUCTION

- 1 If a liver from a deceased donor is split it can be used to transplant two patients; typically an adult patient receives the right liver lobe and a paediatric patient receives the left lobe or the left lateral segment. This paper reports on the outcome of livers from donors after brain death (DBD) who donated their liver between 1 October 2013 and 31 March 2014 and who met the criteria for liver splitting.
- 2 The paper also reports on a comparison of survival outcomes for patients who received a split liver transplant using livers from DBD donors, between 1 April 2006 and 31 March 2013, where the split liver was retained by the centre where the splitting was performed versus those where the split liver was imported from another centre. A comparative analysis was also performed between split livers that were split by adult unit surgeons versus those that were split by paediatric unit surgeons. Finally, a comparison of the unadjusted survival of whole versus split livers transplanted into adult patients is also shown.

LIVER SPLITTING ACTIVITY

Data and methods

- 3 Data were obtained from the UK Transplant Registry (UKTR) on the 75 UK DBD donors whose liver was donated between 1 October 2013 and 31 March 2014 and who met the criteria for liver splitting. These were donors under 40 years of age, weighing more than 50kg and were known to have spent less than five days in an intensive care unit (ICU). The time in ICU was calculated as the time lapse between start of ventilation and time of second test for brainstem death. These livers were transplanted in the UK or the Republic of Ireland.
- 4 For comparison, data were also obtained on the 91 UK DBD whose liver was donated between 1 April and 30 September 2013 and who met the criteria for liver splitting. These livers were also transplanted in the UK or the Republic of Ireland.
- 5 Donated livers were classed as split livers when they were used to transplant two patients and as reduced livers when cut down and used for one patient. Consequently reduced livers were not classed as split livers.
- 6 Livers were classed as offered for splitting if there was a record in the UKTR stating that part of the liver had been offered to a centre (offers that were withdrawn were discounted), as recorded by the ODT Duty Office.

Results

- 7 The status of each liver that was transplanted is shown in **Table 1** for October 2013 to March 2014, with April to September 2013 figures for comparison. Between 1 October 2013 and 31 March 2014, of the 75 DBD donors meeting the splitting criteria (91 between 1 April and 30 September 2013), 52 (69%) livers were available for splitting (63 (69%) between April and September 2013). Of these 52 livers, 24 (46%) were offered for splitting (37 of the 63 (59%) between April and September 2013). Of the 24 livers offered for splitting, 13 (54%) were actually split (22 of the 37 (59%) were split between April and September 2013).

Table 1 Donors meeting criteria for liver splitting, by donor allocation zone, 1 October 2013 to 31 March 2014 (1 April to 30 September 2013)

Donor allocation zone	Total meeting liver splitting criteria and transplanted		Super-urgent liver or intestinal/hepatoblastoma recipients		Elective intestinal/multi-organ recipients		Available for splitting		Offered for splitting		Split		Whole		Reduced					
	N		N _{P1}		N _{P2}		N _A		N _O		N _S		N _W		N _R					
									% of available		% of offered									
Birmingham	13	(16)	4	(5)	1	(1)	8	(10)	2	(5)	25	(50)	1	(2)	50	(40)	1	(3)	0	(0)
Cambridge	6	(6)	4	(2)	0	(0)	2	(4)	1	(0)	50	(0)	0	(0)	-	-	1	(0)	0	(0)
Edinburgh	9	(17)	2	(3)	2	(0)	5	(14)	5	(8)	100	(57)	1	(4)	20	(50)	3	(3)	1	(1)
King's College	17	(19)	2	(7)	1	(1)	14	(11)	5	(9)	36	(82)	4	(7)	80	(78)	1	(2)	0	(0)
Leeds	16	(18)	2	(3)	0	(1)	14	(14)	7	(11)	50	(79)	5	(6)	71	(55)	2	(5)	0	(0)
Newcastle	6	(4)	2	(0)	0	(0)	4	(4)	3	(2)	75	(50)	1	(1)	33	(50)	2	(1)	0	(0)
Royal Free	8	(11)	3	(5)	0	(0)	5	(6)	1	(2)	20	(33)	1	(2)	100	(100)	0	(0)	0	(0)
TOTAL	75	(91)	19¹	(25²)	4³	(3⁴)	52	(63)	24	(37)	46	(59)	13	(22)	54	(59)	10	(14)	1	(1)

¹ Four of these livers were split and used to transplant one super-urgent/ hepatoblastoma recipient and one elective liver only recipient

² Six of these livers were split: one liver was used to transplant one super-urgent recipient and one hepatoblastoma patient and each of the other five livers were used to transplant one super-urgent/ hepatoblastoma recipient and one elective liver only recipient

³ Two of these livers were split and used to transplant one multi-organ/ elective intestinal recipient and one elective liver only recipient

⁴ Two of these livers were split and used to transplant one multi-organ recipient and one elective liver only recipient

Note: Due to small numbers the percentages presented must be viewed with caution

Livers were not necessarily transplanted by the centre that resides in the donor allocation zone

$N = N_{P1} + N_{P2} + N_A$; $N_O = N_S + N_W + N_R$

- 8 These 75 livers resulted in 93 transplants, of which 19 (20%) were performed in paediatric patients (the 91 livers between April and September 2013 resulted in 121 transplants, 31 (26%) of which were performed in paediatric patients).
- 9 **Table 2** details the reasons given by the transplanting centre or noted by the ODT Duty Office for 28 livers not being offered for splitting (72% of the 39 livers available for splitting that were not split). In 15 cases there were concerns over liver function tests. The donor AST level, reported on the Core Donor Data Form, is presented in the table but it was only reported for 50% of donors.

Table 2 Reasons given for why 28 livers from donors meeting the liver splitting criteria, between 1 October 2013 and 31 March 2014, were not offered for splitting

Donor	Donor allocation zone	Transplanting centre	Reason for liver not being offered for splitting	AST (iu/l)
Donor reasons				
1	Birmingham	Birmingham	Donor past medical history, labile blood pressure and raised liver function tests	28
2	Birmingham	Birmingham	Not splittable - fatty and donor history	
3	Birmingham	Birmingham	Donor history and raised liver function tests	
4	Birmingham	Birmingham	Raised liver function tests	
5	Birmingham	Birmingham	Size of donor - BMI 37 kg/m ²	
6	Cambridge	Cambridge	Raised liver function tests	69
7	King's College	King's College	Not splittable - raised liver function tests	
8	King's College	King's College	Donor past medical history, CPR ruptured and damaged segment 1 & 4	634
9	King's College	King's College	Obese donor, fatty liver and HCV indeterminate	11
10	King's College	King's College	Donor had brain tumour and classed as too high risk for a paediatric recipient	77
11	King's College	King's College	Deranged liver function tests	321
12	King's College	King's College	Abnormal liver function tests, BMI of 35 kg/m ² and liver weighed 2.2 kg	
13	King's College	King's College	Abnormal liver function tests	744
14	King's College	King's College	Abnormal liver function tests	96
15	Leeds	Cambridge	Fatty liver	26
16	Leeds	Leeds	Abnormal liver function tests	
17	Leeds	Leeds	Virology	296
18	Leeds	Leeds	Laceration to the left lobe	
19	Leeds	Leeds	Deranged liver function tests	
20	Leeds	Royal Free	Abnormal liver function tests and donor history	96
21	Royal Free	Birmingham	All other centres declined whole liver on donor history	599
22	Royal Free	Birmingham	Raised liver function tests	
23	Royal Free	Royal Free	Abnormal liver function tests	25
Other reasons				
24	Birmingham	Birmingham	Late decline for super-urgent recipients, too late to consider splitting as organ was already retrieved	
25	King's College	King's College	Warm ischemic time too long and raised donor sodium levels	55
26	Leeds	Birmingham	Not identified as meeting liver splitting criteria at time of organ offering	
27	Newcastle	Royal Free	Not identified as meeting liver splitting criteria at time of organ offering	
28	Royal Free	Royal Free	Warm ischemic time too long and raised liver function tests	

- 10 The reasons given for not splitting the remaining 11 livers that were offered for splitting but were not split (28% of the 39 livers available for splitting that were not split) are detailed in **Table 3**.

Table 3 Reasons given for why 11 livers from donors meeting the split liver criteria, between 1 October 2013 and 31 March 2014, that were offered for splitting were not split			
Donor	Donor allocation zone	Transplanting centre	Details of why liver was not split
Donor reasons			
1	Birmingham	Cambridge	Retrieval surgeon decided too fatty for splitting
2	Edinburgh	Edinburgh	Organ fatty
3	King's College	King's College	All paediatric centres declined left lateral segment due to history
4	Newcastle	Leeds	Organ fatty
5	Newcastle	Newcastle	All paediatric centres declined left lateral segment due to function
Recipient reasons			
6	Edinburgh	Cambridge	Paediatric centres had no suitable recipients
7	Leeds	Leeds	All paediatric centres declined left lateral segment as no suitable recipients
Other reasons			
8	Cambridge	Edinburgh	All paediatric centres declined left lateral segment due to no suitable recipients and size
9	Edinburgh	Birmingham	Liver was split but right lobe not placed so left lobe only transplanted. Edinburgh declined right lobe due to problem with bile duct and other centres declined on cold ischaemic time, already transplanting or not able to get recipient into centre
10	Edinburgh	Edinburgh	All paediatric centres declined left lateral segment due to size and no suitable recipients
11	Leeds	Leeds	All paediatric centres declined left lateral segment due to function and no ITU beds

TRANSPLANT SURVIVAL

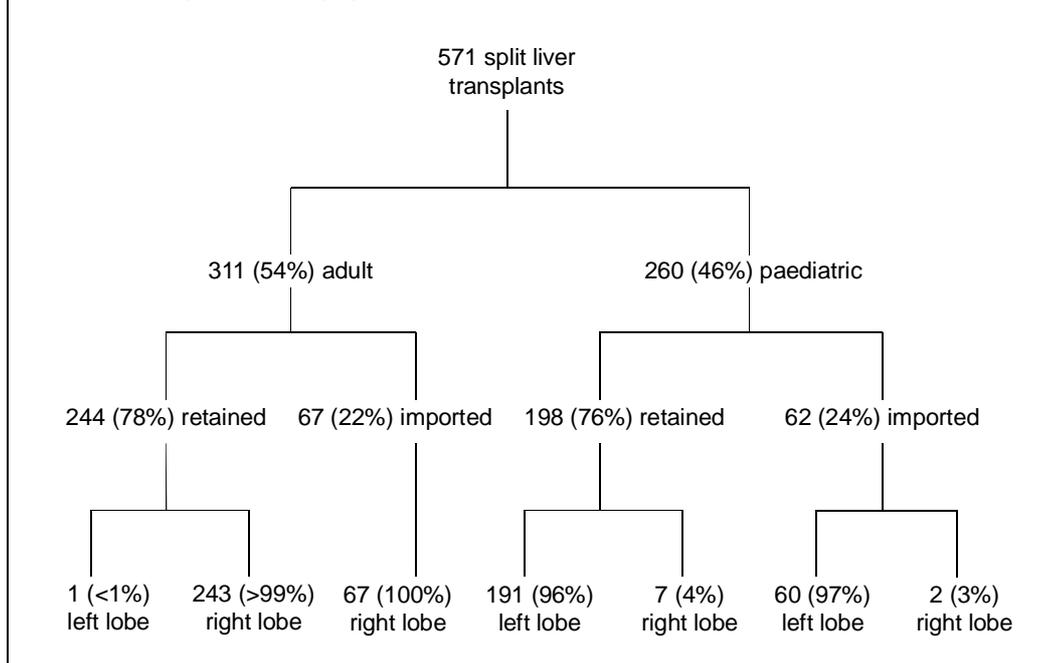
Data and methods

- 11 Data on 571 NHS group 1 first elective split liver only transplants in the UK using livers from DBD donors between 1 April 2006 and 31 March 2013 were analysed. Heterotopic, auxiliary and intestinal transplants were excluded from this cohort as were regrafts. Follow-up data were as recorded on the UKTR on 8 May 2014.
- 12 Each split liver was categorised into “retained”/ “imported” and “split by adult unit surgeon”/ “split by paediatric unit surgeon” (where surgeons from Birmingham, King’s College and Leeds are classed as paediatric unit surgeons). Data returned via the Split Liver Information form was the primary source for categorising split livers into these groups. “Retained”/ “imported” was determined using the centre where the splitting was performed, which was reported in 48% of cases, and “split by adult unit surgeon”/ “split by paediatric unit surgeon” was determined by the centre where the splitting surgeon was appointed, which was reported in 50% of cases. The secondary source for finding out this information was the ODT Duty Office notes. If it was not clear from these notes where the liver was split and who performed the split, a judgement call was made (for instance, if the zonal centre was a paediatric centre who retained the left lobe and exported the right lobe, then we assumed that the paediatric centre performed the split in-house if the primary and secondary sources were insufficient).
- 13 Survival up to five years post-split liver transplant was compared for “retained” and “imported” split livers and for “adult unit surgeon” and “paed unit surgeon” split livers, separately for adult and paediatric patients. These analyses were performed using the Kaplan-Meier estimation method and the log-rank test. There was no risk-adjustment made to control for confounding factors. Median cold ischaemic time (CIT) was also compared, for retained and imported split livers, using the Mann-Whitney U test.
- 14 A comparison of the survival of whole and split liver transplants up to five years was also made, for adult recipients only. This analysis included 2,711 NHS group 1 first adult elective patients transplanted in the UK between 1 April 2006 and 31 March 2013. A sub-group analysis was performed on just those transplants performed between 1 April 2009 and 31 March 2013 (N=1,614). Again, heterotopic, auxiliary and multi-organ transplants and regrafts were excluded and follow-up data were as recorded on the UKTR on 8 May 2014.

Results

- 15 **Figure 1** shows a breakdown of the 571 split liver transplants by recipient age group (adult (≥ 17 years), paediatric (< 17 years)) and whether the liver was retained or imported.

Figure 1 Breakdown of NHS group 1 elective split liver only transplants in the UK using livers from donors after brain death, 1 April 2006 and 31 March 2013



16 **Table 4** shows a breakdown of the 571 split liver transplants by recipient age group, transplant centres and whether the liver was retained or imported.

Table 4 NHS group 1 first elective split liver only transplants in the UK using livers from donors after brain death, 1 April 2006 – 31 March 2013

Transplant centre	Retained N	Imported N	Total
Paediatric recipients			
Birmingham	82	15	97
King's College	84	35	119
Leeds	32	12	44
Total	198	62	260
Adult recipients			
Birmingham	103	2	105
Cambridge	13	9	22
Edinburgh	19	30	49
King's College	69	2	71
Leeds	28	5	33
Newcastle	4	7	11
Royal Free	8	12	20
Total	244	67	311
TOTAL	442	129	571

- 17 **Table 5** shows the median and range of CIT, in hours, of retained and imported split livers transplanted in adult and paediatric patients (left lobes transplanted in adult patients and right lobes transplanted in paediatric patients were excluded (N=10)). On average, CIT was 2.5 hours longer for imported left liver lobes compared with retained left liver lobes (Mann-Whitney U test: $p < 0.0001$) and 2.6 hours longer for imported right liver lobes compared with retained right liver lobes (Mann-Whitney U test: $p < 0.0001$).

	N ¹	CIT (hours)	
		Median	Range
Left lobes transplanted in paediatric patients			
Retained	169	9.0	3.6 – 16.2
Imported	52	11.5	1.3 – 16.5
Right lobes transplanted in adult patients			
Retained	231	9.8	3.9 – 17.6
Imported	65	12.4	6.6 – 16.3

¹ CIT was not reported for a total of 44 split livers

Unadjusted survival analysis

- 18 **Figure 2** shows the Kaplan-Meier estimated survival curves up to five years post-transplant (where the outcome event is graft failure or patient death) for paediatric and adult patients, by whether the split liver was retained or imported. The estimated five year transplant survival rates for paediatric patients were very similar for retained and imported split livers, at approximately 82%. The log-rank test showed no statistical difference in the overall survival curves in the paediatric analysis ($p=0.8$). Contrastingly, there was a borderline significant difference between the survival curves in the adult analysis ($p=0.08$). The estimated five year transplant survival rates for imported and split livers were approximately 68% and 80% but there was some overlap in confidence intervals (52%-80% and 74%-85%, respectively).
- 19 **Figure 3** shows the Kaplan-Meier estimated survival curves up to five years post-transplant (where the outcome event is graft failure or patient death) for paediatric and adult patients, by whether the liver was split by an adult unit surgeon or a paediatric unit surgeon. Note that there were only six events in the “split by adult unit surgeon” group in the paediatric analysis and only seven in the adult analysis, so the results should be viewed with caution. There was no statistically significant difference found between these groups in the paediatric or adult analysis. The estimated five year transplant survival rates for livers split by adult unit surgeons and livers split by paediatric unit surgeons were approximately 78% (54%-91%) and 83% (77%-88%), respectively, for paediatric patients and 82% (67%-91%) and 77% (71%-83%), respectively, for adult patients.
- 20 Causes of graft failure or patient death that were reported to the UKTR for the 100 out of 571 split liver transplant recipients who died or whose graft failed within five years following transplant are presented for reference in **Appendix I** by age group, by whether the split liver was retained/ imported and by whether the liver was split by an adult/ paediatric unit surgeon.

Figure 2 Comparison of five year transplant survival of retained and imported split livers transplanted in NHS group 1 elective patients in the UK between 1 April 2006 and 31 March 2013

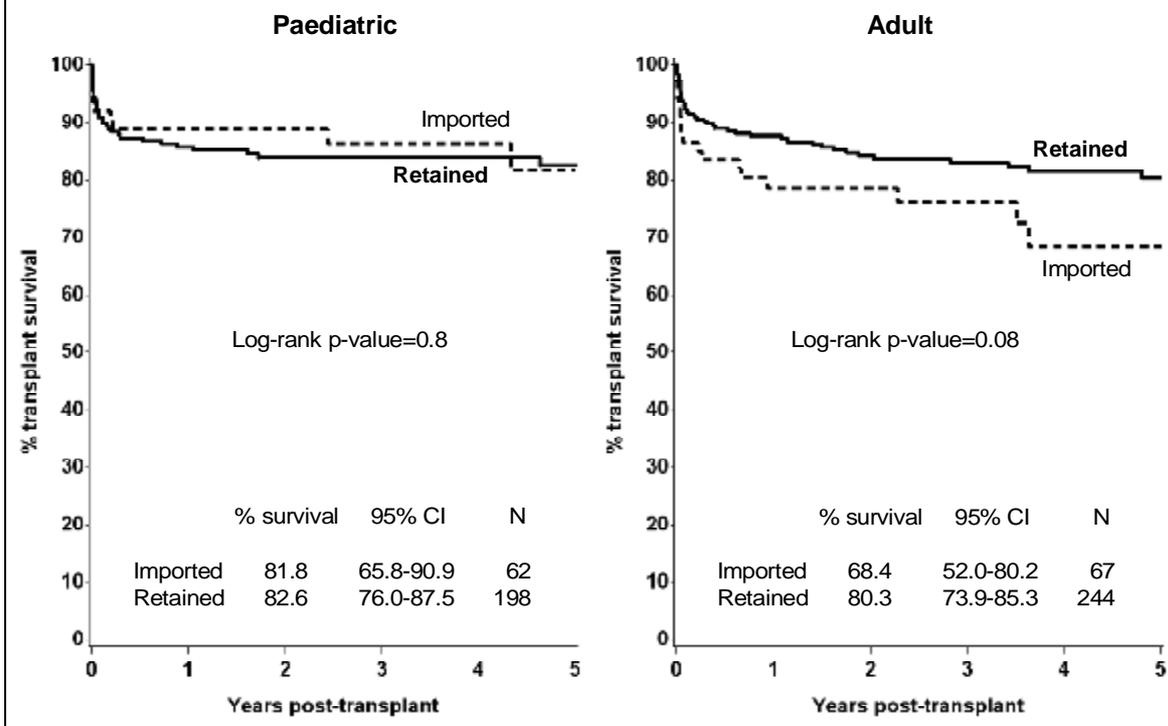
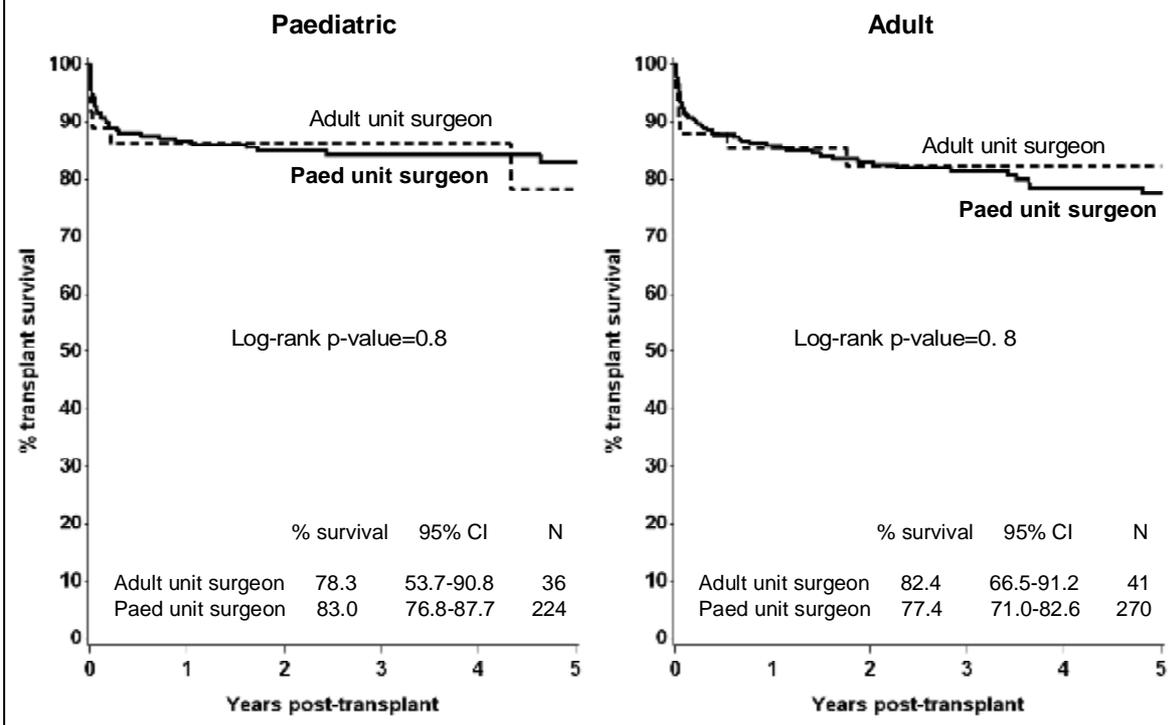
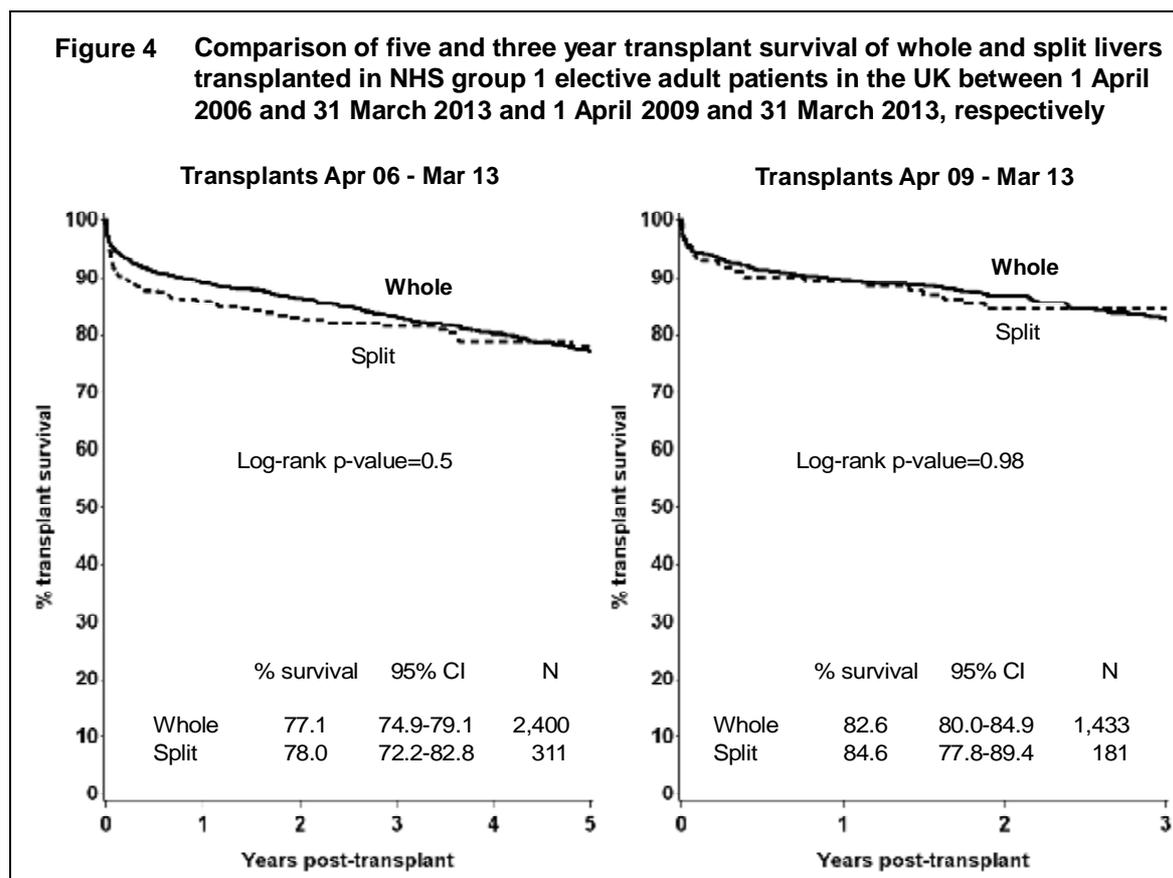


Figure 3 Comparison of five year transplant survival of livers split by adult and paediatric unit surgeons, transplanted in NHS group 1 elective patients in the UK between 1 April 2006 and 31 March 2013



- 21 **Figure 4** shows the Kaplan-Meier estimated survival curves comparing transplant survival (where the outcome event is graft failure or patient death) up to five years for whole and split liver transplants between 1 April 2006 and 31 March 2013 and up to three years for whole and split liver transplants in the reduced cohort of 1 April 2009 to 31 March 2013. For transplants between April 2006 and March 2013, the unadjusted analysis suggests that the long-term survival of whole and split liver transplants is similar; however shorter-term (<2 years) survival appears to be superior for whole liver transplants. For just those transplants carried out more recently, between April 2009 and March 2013, there is no difference in the unadjusted survival curves up to three years (p=0.98).



SUMMARY

- 22 There were 75 livers donated between 1 October 2013 and 31 March 2014 from donors who met the criteria for liver splitting (18% fewer than previous six months, Apr-Sep 2013). Of these, 52 (69%) were available for splitting for elective recipients, having not been used in super-urgent, hepatoblastoma, intestinal or multi-organ recipients. Of these, 24 (46%) were offered for splitting and 13 (54% of the 24) were actually split (41% fewer than previous six months, Apr-Sep 2013). In just over half of the 28 cases where the liver was available for splitting but was not offered for splitting, abnormal or raised liver function tests were cited as the reason for not considering splitting. Eleven livers were offered for splitting but instead used whole or reduced. Common reasons for not splitting these livers were the fattiness of the organ or a lack of suitable paediatric patients for the left lateral segment.

- 23 An unadjusted analysis of survival following split liver transplantation, comparing retained and imported split livers transplanted between 1 April 2006 and 31 March 2013, showed no evidence of an impact on transplant survival up to five years depending on whether the split liver was retained or imported for paediatric patients, but for adult patients there was some evidence of superior survival for retained split livers ($p=0.08$). An unadjusted survival analysis on the same cohort comparing livers that were split by adult unit surgeons and livers that were split by paediatric unit surgeons showed no difference in transplant survival up to five years for paediatric or adult patients.
- 24 A comparison of unadjusted survival estimates following whole and split liver transplantation in adult patients, between 1 April 2006 and 31 March 2013, showed that the long-term survival of whole and split liver transplants is similar; however shorter-term (<2 years) survival appears to be superior for whole liver transplants.

Action

- 25 Members are asked to note that this report now includes longer-term survival rates than were previously reported and donor AST level has been reported for livers not offered for splitting, as requested.
- 26 A “paired survival analysis” would be required to account for lack of independence in survival times of patients receiving a split liver from the same donor. If this is requested by the LAG then variables to adjust for in such an analysis would need to be discussed and agreed with a clinical lead.
- 27 Members are reminded that completion of the Split Liver Information form is the most reliable way of recording data on where liver splitting is performed and by whom on the UKTR to inform analyses (currently the return rate is approximately 80%).
- 28 A review within ODT of the process for recording reasons for not splitting livers from donors who meet the liver splitting criteria was carried out and improvements to the process, in terms of efficiency and level of detail of reasons, were implemented.

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Statistics and Clinical Studies

May 2014

Appendix I Causes of graft failure or patient death for NHS group 1 elective split liver only transplant recipients in the UK between 1 April 2006 and 31 March 2013 who died or whose graft failed within five years following transplant, by age group, whether the split liver was retained/ imported and whether the liver was split by an adult/ paediatric unit surgeon

Causes of graft failure or patient death	Retained split liver	Imported split liver	Liver split by paediatric unit surgeon	Liver split by adult unit surgeon	Total
	N	N	N	N	N
PAEDIATRIC PATIENTS					
<i>Cause of graft failure - patient did not die</i>					
Hepatic artery thrombosis	9	2	9	2	11
Primary non-function	3	2	3	2	5
Chronic rejection	1	1	2	0	2
Other	2	0	2	0	2
Not reported	2	0	2	0	2
Total	17	5	18	4	22
<i>Cause of death</i>					
Multi-system failure	3	1	4	0	4
Septicaemia	2	1	3	0	3
Primary non-function -> multi-system failure	2	0	2	0	2
Recurrent disease	2	0	2	0	2
Other	5	1	5	1	6
Not reported	1	1	1	1	2
Total	15	4	17	2	19
TOTAL	32	9	35	6	41
ADULT PATIENTS					
<i>Cause of graft failure - patient did not die</i>					
Hepatic artery thrombosis	11	3	11	3	14
Other	3	3	6	0	6
Total	14	6	17	3	20
<i>Cause of death</i>					
Multi-organ failure	4	2	5	1	6
Hepatic artery thrombosis -> multi-system failure/myocardial infarction/pulmonary infection	3	2	4	1	5
Non-lymphoid malignant disease	4	0	4	0	4
Recurrent disease	1	3	4	0	4
Non-thrombotic infarction -> multi-system failure/septicaemia	2	0	2	0	2
Cerebro-vascular accident	2	0	2	0	2
Renal failure	2	0	2	0	2
Vascular occlusion -> multi-system failure	2	0	2	0	2
Rejection/primary non-function	1	1	1	1	2
Other	5	2	6	1	7
Not reported	2	1	3	0	3
Total	28	11	35	4	39
TOTAL	42	17	52	7	59