

NHS BLOOD AND TRANSPLANT

BOWEL ADVISORY GROUP

DEVELOPING A RISK-ADJUSTED MODEL FOR PATIENT SURVIVAL FOLLOWING INTESTINAL TRANSPLANTATION

SUMMARY

BACKGROUND

- 1 This paper presents results from a preliminary analysis towards the development of a risk-adjusted model for patient survival following intestinal transplant.

DATA ANALYSIS

- 2 Data were extracted from the UK Transplant Registry (UKTR) as at 21 September 2014 on 108 first intestinal transplants carried out in the UK between 1 April 2008 and 31 March 2014.
- 3 A set of transplant, recipient and donor variables that are used in the National Bowel Allocation Scheme and some variables that are known to affect survival following other types of organ transplantation were considered for model development.
- 4 The effect of each of these variables on one year patient survival was investigated by fitting a Cox proportional hazards model with each variable as an individual explanatory variable. Variables *recipient sex*, *recipient ethnic group*, *primary indication for transplant* and *loss of intravenous line access* showed some degree of explanatory power and should be considered for inclusion in the model. However, the number of transplants is very small, resulting in few or none deaths for some variable levels, which could in turn produce meaningless inferences.

ACTION

- 5 Members are asked to identify a lead clinician to work with NHSBT Statistics and Clinical Studies to further develop this work.
- 6 Since there are relatively few events in the levels of many of the variables considered for inclusion in the model, members are asked to confirm that one year survival is the appropriate outcome measure.
- 7 The robust development of this model requires complete and up to date follow-up data to be submitted to the UKTR.

Sally Rushton and Elisa Allen
Statistics and Clinical Studies

September 2014

NHS BLOOD AND TRANSPLANT

BOWEL ADVISORY GROUP

DEVELOPING A RISK-ADJUSTED MODEL FOR PATIENT SURVIVAL FOLLOWING INTESTINAL TRANSPLANTATION

BACKGROUND

- 1 Intestinal transplantation is a relatively new and evolving procedure. Four UK transplant centres have been commissioned since 2008 to perform transplants involving the small bowel; these are Cambridge and Oxford, who transplant adult patients, and Birmingham and King's College, who transplant paediatric patients. Dedicated intestinal transplant registration and transplant record forms went live on 1 July 2008.
- 2 This paper presents results from a preliminary analysis towards the development of a risk-adjusted model for patient survival following intestinal transplant.

DATA AND METHODS

- 3 Data were extracted from the UK Transplant Registry (UKTR) as at 21 September 2014 on 108 first intestinal transplants carried out in the UK between 1 April 2008 and 31 March 2014.
- 4 The transplant, recipient and donor variables shown in **Table 1** were considered in this preliminary analysis. This list includes some of the variables that are used in the National Bowel Allocation Scheme and some variables that are known to affect survival following other types of organ transplantation.

Table 1 Variables considered in the development of a risk-adjusted model for patient survival following intestinal transplantation

Transplant variables	Recipient variables	Donor variables
Transplant type	Age	Age
Donor-recipient blood group matching	Height	Height
	Weight	Weight
	Sex	Sex
	Ethnic group	Cause of death
	Primary indication for transplant	
	Bilirubin	
	Patient location	
	Previous abdominal surgery	
	Loss of intravenous line access	

- 5 All of these variables were recorded at time of transplant except for *loss of intravenous line access* which was recorded at time of registration, however, missing values were substituted with the patient's most recent registration data if populated (this applied to recipient *height*, *weight*, *primary indication for transplant*, *bilirubin*, *patient location* and *previous abdominal surgery*, where 43%, 22%, 33%, 19%, 18% and 17% of values were previously missing, respectively). These variables were investigated across transplant centres for the 108 transplants in the cohort.

- 6 The first step in model development is to identify a set of explanatory variables, out of those shown in **Table 1**, that have the potential for being included in the risk-adjusted model. The selected set will contain those variables that have been recorded for each individual, but additionally terms corresponding to interactions between variables may be also required.
- 7 The effect of each of these variables on one year patient survival was investigated by fitting a Cox proportional hazards model with each variable as an individual explanatory variable. Likelihood ratio test p-values are presented, which test whether a model including only one of these explanatory variables is significantly better than a model that contains no explanatory variables. A significant p-value indicates that the explanatory variable in question significantly affects the risk of death of patients. If death occurred within one year following transplant, this was considered an event. Patients who survived longer than one year were censored at one year. Patient survival times were available at time of analysis for 81% of the cohort so this part of the analysis could only be conducted on a cohort of 87 observations.
- 8 In selecting variables for inclusion the significance level should not be too small; a level of 20% or less has been considered.

RESULTS

Cohort investigations

- 9 **Table 2** shows a summary of the variables considered in the development of the risk-adjusted model, by transplant centre.

Table 2 Summary data on transplant, recipient and donors factors, across transplant centres, for first intestinal transplants carried out in the UK between 1 April 2008 and 31 March 2014						
Variable	Level	Transplant centre				Total
		Cambridge	Oxford	Birmingham	King's College	
No. transplants		39	25	34	10	108
Transplant factors		N (%)	N (%)	N (%)	N (%)	N (%)
Transplant type	Bowel only	8 (21)	20 (80)	14 (41)	7 (70)	49 (45)
	Bowel and pancreas	0 (-)	0 (-)	0 (-)	1 (10)	1 (1)
	Liver, bowel and pancreas	2 (5)	0 (-)	13 (38)	2 (20)	17 (16)
	Multivisceral	21 (54)	0 (-)	3 (9)	0 (-)	24 (22)
	Modified multivisceral	8 (21)	5 (20)	4 (12)	0 (-)	17 (16)
Donor-recipient blood group matching	Identical	32 (82)	23 (92)	28 (82)	10 (100)	93 (86)
	Compatible, non-identical	7 (18)	2 (8)	6 (18)	0 (-)	15 (14)
Recipient factors						
Age (years)	Median	47	40	2	5	31.5
	Range	18-64	23-73	0-13	0-16	0-73
Height (cm)	Median	168	170	82	103	160
	Range	137-183	155-185	66-147	54-155	54-185
	Missing, N (%)	2 (5)	1 (4)	2 (6)	0 (-)	5 (5)

Weight (kg)	Median Range	60 27-97	66 45-86	12 7-43	16.5 6-57	51 6-97
		N (%)	N (%)	N (%)	N (%)	N (%)
Sex	Male	21 (54)	15 (60)	18 (53)	5 (50)	59 (5)
	Female	18 (46)	10 (40)	16 (47)	5 (50)	49 (45)
Ethnic group	White	35 (90)	23 (92)	27 (79)	9 (90)	94 (87)
	Asian	1 (3)	0 (-)	5 (15)	1 (10)	7 (6)
	Black	2 (5)	2 (8)	0 (-)	0 (-)	4 (4)
	Other/missing	1 (3)	0 (-)	2 (6)	0 (-)	3 (3)
Primary indication for transplant	Short bowel syndrome	20 (51)	13 (52)	18 (53)	5 (50)	56 (52)
	Motility disorders	3 (8)	5 (20)	5 (15)	3 (30)	16 (15)
	Primary mucosal disorders	0 (-)	0 (-)	4 (12)	1 (10)	5 (5)
	Malignancy	3 (8)	2 (8)	0 (-)	0 (-)	5 (5)
	Liver disease	3 (8)	1 (4)	1 (3)	0 (-)	5 (5)
	Other/missing	10 (26)	4 (16)	6 (18)	1 (10)	21 (19)
Bilirubin (µmol/l)	0-99	34 (87)	25 (100)	22 (65)	9 (90)	90 (83)
	100-199	3 (8)	0 (-)	7 (21)	1 (10)	11 (10)
	200+	1 (3)	0 (-)	3 (9)	0 (-)	4 (4)
	Missing	1 (3)	0 (-)	2 (6)	0 (-)	3 (3)
Patient location	Outpatient	28 (72)	24 (96)	28 (82)	8 (80)	88 (81)
	Ward	5 (13)	1 (4)	4 (12)	1 (10)	11 (10)
	ICU/HDU	5 (13)	0 (-)	0 (-)	1 (10)	6 (6)
	Missing	1 (3)	0 (-)	2 (6)	0 (-)	3 (3)
Previous abdominal surgery	No	3 (8)	1 (4)	5 (15)	1 (10)	10 (9)
	Yes	35 (90)	24 (96)	26 (76)	9 (90)	94 (87)
	Missing	1 (3)	0 (-)	3 (9)	0 (-)	4 (4)
Loss of intravenous line access	None patent	3 (8)	0 (-)	2 (6)	1 (10)	6 (6)
	Some non-patent	4 (10)	9 (36)	16 (47)	1 (10)	30 (28)
	All patent	1 (3)	1 (4)	2 (6)	1 (10)	5 (5)
	Missing	31 (79)	15 (60)	14 (41)	7 (70)	67 (62)
Donor factors						
Age (years)	Median Range	34 9-57	25 10-51	4.5 0-36	3.5 0-43	20 0-57
Height (cm)	Median Range	167 144-191	170 139-184	107.5 64-178	103.5 49-175	162 49-191
Weight (kg)	Median Range	60 32-85	65 40-85	18 5-70	17 3-63	55 3-85
		N (%)	N (%)	N (%)	N (%)	N (%)
Sex	Male	12 (31)	14 (56)	17 (50)	7 (70)	50 (46)
	Female	27 (69)	11 (44)	17 (50)	3 (30)	58 (54)
Cause of death	Stroke	21 (54)	11 (44)	8 (24)	3 (30)	43 (40)
	Trauma	6 (15)	11 (44)	7 (21)	2 (20)	26 (24)
	Other	12 (31)	3 (12)	19 (56)	5 (50)	39 (36)

Univariate tests

- 10 **Table 3** shows the results of tests to assess whether or not each of the variables in turn explains the survival experience one year after transplant significantly better than a model without any variable (the null model). Only one variable has been considered at a time and no interaction terms have been tested.
- 11 **Table 3** shows that variables *recipient sex*, *recipient ethnic group*, *primary indication for transplant* and *loss of intravenous line access* have some degree of explanatory power and should be considered for inclusion in the model. In addition, there might be other variables of clinical relevance that, although not statistically significant, may be considered in the development of the model.
- 12 The number of deaths five years after transplantation is also shown in **Table 3** to inform the group when deciding whether one year or five year post-transplant survival should be modelled.

Future work

- 13 **Clinically relevant variables.** Variables that are clinically important for inclusion in the model need to be identified.
- 14 **Multivariate tests.** Further variable selection tests need to be carried out as variables that appear to be important in **Table 3** may cease to be important in the presence of other variables. Similarly, variables that were not important on their own may become important in the presence of others. Interaction terms could be considered.
- 15 **Model checking.** Once a candidate multivariate model has been identified and fitted to the data, checks on the adequacy of the model will be conducted.

ACTION

- 16 Members are asked to identify a lead clinician to work with NHSBT Statistics and Clinical Studies to further develop this work.
- 17 Since there are relatively few events in the levels of many of the variables considered for inclusion in the model, members are asked to confirm that one year survival is the appropriate outcome measure.
- 18 The robust development of this model requires complete and up to date follow-up data to be submitted to the UKTR.

Sally Rushton and Elisa Allen
Statistics and Clinical Studies

September 2014

Table 3 Univariate Cox proportional hazards analysis of the effect of each explanatory variable on patient survival after intestinal transplantation.

Variable		Level	No. txs	One-year outcome		Five-year outcome
				No. deaths at one year	Likelihood ratio test p-value	No. deaths at five years
Transplant factors						
Transplant type	Bowel only	34	5	0.6	9	
	Multivisceral ¹	39	7		13	
	Modified multivisceral ²	14	4		6	
Donor-recipient blood group matching	Identical	76	13	0.3	25	
	Compatible, non-identical	11	3		3	
Recipient factors						
Age (years) category	0-17	24	5	0.5	10	
	18-39	22	2		5	
	40-49	18	5		6	
	50+	23	4		7	
Height (cm)		83	15	0.7	27	
Weight (kg)		87	16	0.6	28	
Sex	Male	47	11	0.2	17	
	Female	40	5		11	
Ethnic group	White	77	12	0.1	22	
	Non-white	10	4		6	
Primary indication for transplant	Short bowel syndrome	47	7	0.1	12	
	Motility disorders	13	2		6	
	Primary mucosal disorders, Malignancy and Liver disease grouped	12	1		4	
	Other/missing	15	6		6	
Log bilirubin (μmol/l)		85	15	0.8	27	
Patient location	In-patient	14	2	0.9	2	
	Out-patient	71	13		25	
	Missing	2	1		1	
Previous abdominal surgery	Yes	78	14	0.8	25	
	No	6	1		2	
	Missing	3	1		1	
Loss of intravenous line access	None patent	4	0	0.08	1	
	Some non-patent	22	2		6	
	All patent	4	0		1	
	Missing	57	14		20	
Donor factors						
Age (years)		87	16	0.6	28	
Height (cm)		87	16	0.9	28	
Weight (kg)		87	16	0.9	28	
Sex	Male	41	9	0.5	15	
	Female	46	7		13	
Cause of death	Stroke	36	8	0.3	10	
	Trauma	21	5		10	
	Other	30	3		8	
¹ Liver, bowel and pancreas only or including one or more of kidney, spleen, stomach, abdominal wall or colon						
² Bowel and pancreas only or including one or more of kidney, spleen, stomach, abdominal wall or colon						