

# NHS BLOOD AND TRANSPLANT

## CARDIOTHORACIC ADVISORY GROUP – HEART

### Review of heart transplant risk model August 2022

#### BACKGROUND

1. In 2015/16, the risk adjustment model for patient survival post heart transplantation was redeveloped by Statistics and Clinical Research, NHSBT, using the previous model developed by the UK Cardiothoracic Transplant Audit as a basis (see **Appendix** for 2015/16 model). This paper presents the 2022 revision of this model.
2. The model presented here was used in the recently published Annual Report on Cardiothoracic Transplantation to calculate risk-adjusted survival rates at 30 days, 90 days, 1 year and 5 years post heart transplant.

#### DATA AND METHODS

3. Thirty-day, 90 day and 1 year survival times were modelled using 926 first time DBD heart only transplants performed in adult patients in the UK between 1 April 2014 and 31 March 2021. Five year survival was modelled using 903 transplants performed between 1 April 2010 and 31 March 2017.
4. Cox proportional hazards models were built separately for each time horizon. These were stratified by centre so as to allow different baseline hazard functions for each centre. A stepwise variable selection method was used, with a significance level of 0.1.
5. The variables in **Table 1** were considered in the modelling, where treatment of missing data is explained in the final column. These were chosen due to their availability on the UK Transplant Registry and their use in other published risk models in this context.
6. The final model contained any factor shown to be significant at any one time horizon. Modelling checking involved assessing standard errors for any poorly fitting variables, checking for influential observations using df betas and the likelihood displacement, and calculating Harrell's concordance statistic for an overall goodness of fit measure.

**Table 1 Candidate variables in the Cox proportional hazards models for survival post adult heart transplantation**

Candidate variable	Possible values	Treatment of missing data
<b>RECIPIENT VARIABLES</b>		
Primary disease	coronary heart disease; cardiomyopathy; congenital heart disease; other/missing	N/A – no missing values
Age	continuous	N/A – no missing values
Age group	<40; 40-49; 50-59; 60+	N/A – no missing values
Age group2	<60 vs 60+ (as per IMPACT score)	N/A – no missing values
Blood group	O; A; B; AB	N/A – no missing values
Sex	male; female	N/A – no missing values
Urgency	non-urgent; urgent/super-urgent	N/A – no missing values
CMV status	positive; negative	1% set to negative
Height	continuous	<1% set to median

Candidate variable	Possible values	Treatment of missing data
Weight	continuous	<1% set to median
BMI	continuous	Height and weight imputed first
BMI group	<25; 25-<30; 30+	Height and weight imputed first
Hospital status	in patient; out patient	<1% set to out patient
Mechanical support	none; long-term VAD; short-term VAD or ECMO	N/A – no missing values
IABP	no; yes	N/A – no missing values
Creatinine	continuous	1% set to median
Creatinine	<75 umol/l; 75 to <100 umol/l; 100 to <125 umol/l; 125 umol/l and above	1% set to 75 to <100 umol/l
Creatinine clearance	continuous	Creatinine and weight imputed first
eGFR	continuous	Creatinine imputed first
eGFR group	Normal: 90ml/min or above; CKD G2: 60 to 89 ml/min; CKD G3a: 45 to 59 ml/min; CKD G3b/4/5: 44 ml/min or below	Creatinine imputed first
Bilirubin (recorded at reg)	Continuous (logged)	3% set to median
Bilirubin group	<1 mg/dL; 1 to <2 mg/dL; 2 mg/dL and above (as per IMPACT score)	3% set to <1 mg/dL
Bilirubin group2	<1 mg/dL; 1-2.5 mg/dL; >2.5 mg/dL (as per Singh et al)	3% set to <1 mg/dL
Recent infection	no; yes	2% set to no
Prior heart surgery (recorded at reg)	none; at least one	3% set to none
Diabetes (recorded at reg)	no; yes	1% set to no
Hypertension requiring treatment (recorded at reg)	no; yes	2% set to no
Cerebrovascular disease (recorded at reg)	no; yes	2% set to no
<b>DONOR VARIABLES</b>		
Age	continuous	N/A – no missing values
Age group	<30; 30-39; 40-49; 50+	N/A – no missing values
Blood group	O; A; B; AB	N/A – no missing values
Sex	male; female	N/A – no missing values
CMV status	positive; negative	1% set to negative
Height	continuous	N/A – no missing values
Weight	continuous	N/A – no missing values
BMI	continuous	N/A – no missing values
BMI group	<25; 25-<30; 30+	N/A – no missing values
Respiratory arrest	no; yes	10% set to no
Cause of death	vascular; trauma; hypoxic; other	2% set to other
<b>TRANSPLANT VARIABLES</b>		
Sex mismatch	DMRM; DMRF; DFRM; DFRF	N/A – no missing values
CMV mismatch	D-R-; D+R+; D-R+; D+R-	1% set to D-R-
Blood group match	Identical; compatible	N/A – no missing values
pHM % difference	continuous	Recipient height and weight imputed first
pHM % difference group	<-10%; -10-10%; >10%	Recipient height and weight imputed first
pHM % difference group2	oversized; undersized	Recipient height and weight imputed first
Ischaemia time	continuous	3% missing imputed using centre and year specific medians
OCS use	no; yes	N/A – no missing values

## RESULTS

7. The variables selected for the overall model (significant at least one time horizon) are shown in **Table 2**, with the effect of each term on the hazard of mortality at 30 day, 90 days, 1 year and 5 years represented by the hazard ratios. For example, donor age, primary disease, mechanical support and ischaemia time were most predictive of 30 day mortality, with those patients on a long-term VAD support having 4.45 times increased risk and those on short-term VAD or ECMO support having 3.31 times increased risk compared to those not on support at time of transplant.

Variable	Category	30 day mortality		90 day mortality		1 year mortality		5 years mortality	
		Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
Donor age	Continuous	1.02 (1.00-1.04)	0.02	1.02 (1.01-1.04)	0.01	1.02 (1.00-1.03)	0.01	1.02 (1.01-1.03)	0.002
Recipient age 60 or over	<60 60+	Reference 1.17 (0.64-2.15)	0.6	Reference 1.45 (0.88-2.39)	0.1	Reference 1.27 (0.82-1.98)	0.3	Reference 1.41 (1.02-1.94)	0.04
Recipient primary disease group	Coronary heart disease Cardiomyopathy Congenital heart disease Other	0.54 (0.25-1.16) Reference 2.44 (1.10-5.39) 2.07 (0.86-4.97)	0.02	0.89 (0.51-1.56) Reference 3.14 (1.60-6.16) 2.36 (1.15-4.88)	0.001	0.70 (0.42-1.18) Reference 2.32 (1.27-4.24) 1.62 (0.80-3.29)	0.009	1.04 (0.75-1.44) Reference 1.48 (0.89-2.46) 1.25 (0.69-2.27)	0.5
Recipient mechanical support at transplant	None Long-term VAD Short-term VAD/ECMO	Reference 4.45 (2.52-7.85) 3.31 (1.70-6.43)	<0.0001	Reference 4.42 (2.68-7.29) 3.50 (1.99-6.14)	<0.0001	Reference 3.36 (2.18-5.18) 3.19 (1.97-5.17)	<0.0001	Reference 1.66 (1.18-2.34) 1.82 (1.21-2.73)	0.0008
Recipient IABP at transplant	No Yes	Reference 2.30 (0.97-5.45)	0.06	Reference 3.07 (1.45-6.49)	0.003	Reference 2.71 (1.35-5.45)	0.005	Reference 1.20 (0.73-1.97)	0.5
Recipient eGFR group at transplant	44 ml/min or below 45-59 ml/min 60-89 ml/min 90 or above	0.80 (0.44-1.46) Reference 1.50 (0.86-2.63) 1.09 (0.55-2.14)	0.3	0.76 (0.45-1.29) Reference 1.76 (1.11-2.81) 0.94 (0.51-1.74)	0.01	0.64 (0.40-1.03) Reference 1.61 (1.07-2.43) 1.06 (0.64-1.76)	0.003	0.73 (0.51-1.05) Reference 1.27 (0.92-1.75) 1.11 (0.79-1.57)	0.05
Recipient hypertension at registration	No Yes	Reference 1.61 (0.95-2.73)	0.08	Reference 1.66 (1.06-2.62)	0.03	Reference 1.69 (1.14-2.51)	0.009	Reference 1.14 (0.82-1.58)	0.4
Recipient bilirubin at registration	Continuous (logged)	0.72 (0.51-1.02)	0.07	0.76 (0.56-1.03)	0.08	0.85 (0.65-1.10)	0.2	0.92 (0.76-1.11)	0.4
Recipient diabetes at registration	No Yes	Reference 1.20 (0.58-2.48)	0.6	Reference 0.98 (0.52-1.87)	0.9	Reference 1.05 (0.61-1.80)	0.9	Reference 1.47 (1.02-2.11)	0.04

Variable	Category	30 day mortality		90 day mortality		1 year mortality		5 years mortality	
		Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
Recipient CMV status	Negative	Reference	0.08	Reference	0.05	Reference	0.02	Reference	0.01
	Positive	1.50 (0.96-2.35)		1.47 (1.00-2.17)		1.51 (1.08-2.12)		1.38 (1.07-1.76)	
Recipient blood group	O	1.42 (0.87-2.30)	0.07	1.55 (1.02-2.35)	0.02	1.52 (1.05-2.21)	0.005	1.09 (0.83-1.44)	0.1
	A	Reference		Reference		Reference		Reference	
	B	0.97 (0.42-2.23)		1.07 (0.53-2.17)		1.63 (0.96-2.75)		1.21 (0.82-1.78)	
	AB	2.89 (1.21-6.91)		2.87 (1.34-6.14)		3.00 (1.56-5.77)		1.85 (1.13-3.01)	
Ischaemia time	Continuous	-	0.03	-	0.05	-	0.05	-	0.2
OCS	No	-	0.004	-	0.006	-	0.007	-	0.1
	Yes								
Ischaemia time * OCS	Ischaemia time for OCS=No	1.44 (1.02-2.04)	-	1.36 (1.01-1.84)	-	1.27 (0.98-1.64)	-	1.07 (0.92-1.25)	-
	Ischaemia time for OCS=Yes	1.19 (0.86-1.64)		1.12 (0.84-1.49)		1.14 (0.88-1.48)		1.12 (0.89-1.41)	

8. The following in-sample concordance statistics were obtained for these models, showing reasonable goodness of fit:

30 days: 0.77

90 days: 0.75

1 year: 0.71

5 year: 0.63

## FUTURE WORK

9. The model will be reviewed every 5 years.

Sally Rushton  
Statistics and Clinical Research

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## APPENDIX – 2015/16 model

Table 1: Heart model results						
Factor	30-day model		1-year model		5-year model	
	p-value	Hazard ratio (95%)	p-value	Hazard ratio (95%)	p-value	Hazard ratio (95%)
<b>Donor factors</b>						
Cause of death	0.01		0.04		0.31	
Vascular		1		1		1
Trauma		0.97 (0.54, 1.74)		1.22 (0.79, 1.89)		1.16 (0.81, 1.66)
Hypoxic		0.74 (0.35, 1.59)		0.91 (0.50, 1.65)		0.89 (0.55, 1.45)
Other		0.16 (0.04, 0.64)		0.47 (0.25, 0.91)		0.72 (0.46, 1.13)
Donor BMI (linear)	0.25	1.03 (0.98, 1.07)	0.03	1.04 (1.00, 1.07)	0.01	1.04 (1.01, 1.07)
Donor age (linear)	0.13	1.01 (1.00, 1.03)	0.01	1.02 (1.01, 1.03)	0.003	1.02 (1.01, 1.03)
Respiratory arrest	0.23		0.37		0.06	
No		1		1		1
Yes		1.40 (0.81, 2.43)		1.22 (0.79, 1.86)		1.39 (0.99, 1.94)
<b>Recipient factors</b>						
Recipient BMI (linear)	0.06	1.05 (1.00, 1.10)	0.71	1.01 (0.97, 1.05)	0.60	1.01 (0.98, 1.04)
Creatinine at transplant (non-linear)	0.91	Non-linear (non-sig)	0.74	Non-linear (non-sig)	0.03	<b>Figure 4</b>
VAD at transplant	0.02		0.06		0.26	
Short-term		No ECMO: 1		1.5 (0.51, 4.42)		0.63 (0.26, 1.54)
Long-term		ECMO: 4.29 (1.49, 12.36)		1		1
ECMO				4.63 (1.66, 12.89)		1.86 (0.76, 4.58)
None				1.55 (0.83, 2.90)		0.84 (0.56, 1.26)
Hospital status at transplant	0.08		0.47		0.68	
Hospital		0.69 (0.46, 1.05)		0.89 (0.65, 1.22)		1.06 (0.82, 1.37)
Not in hospital		1		1		1
Primary disease	0.05		0.42		0.27	
Dilated cardiomyopathy		1		1		1
Coronary heart disease		1.21 (0.71, 2.04)		1.26 (0.87, 1.84)		1.23 (0.90, 1.68)
Congenital heart disease		1.98 (0.93, 4.20)		1.34 (0.71, 2.51)		1.15 (0.65, 2.02)
Other		1.86 (1.16, 2.99)		1.30 (0.89, 1.90)		1.34 (0.98, 1.84)
<b>Transplant factors</b>						
Sex mismatch	0.24		0.03		0.30	
RM : DM		1		1		1
RM : DF		1.15 (0.65, 2.05)		1.08 (0.7, 1.66)		1.07 (0.75, 1.53)
RF : DM		1.89 (1.05, 3.40)		2.06 (1.33, 3.20)		1.48 (1.00, 2.19)
RF : DF		1.01 (0.58, 1.76)		1.11 (0.73, 1.69)		1.02 (0.72, 1.44)