

NHS BLOOD AND TRANSPLANT

CARDIOTHORACIC ADVISORY GROUP – HEART

Outcomes of urgent heart transplantation in patients with LVAD-related complications in the UK

INTRODUCTION

1. LVAD-related complications are a common reason for requesting urgent heart transplant listing via the CTAG Adjudication Panel. An analysis of 66 patients urgently listed due to LVAD-related complications was presented at the Autumn 2021 CTAG-Heart meeting. Forty-eight patients received a heart transplant and the one year survival rate was 56%, significantly lower than for other urgent heart transplant recipients (88%).
2. It was agreed that extra data and analysis was required to understand the factors that lead to poor outcomes in this group of patients. This information will help guide adjudication of cases for urgent listing in the presence of LVAD-related complications and potentially shape discussions on allocation of scarce donor organs.

DATA AND METHODS

3. All adult patients who were referred to the CTAG Adjudication Panel due to LVAD-related complications between 26 October 2016 and 30 September 2021 and received an urgent heart transplant were identified. By extending the cohort to 30 September 2021, 13 patients were added to the previous cohort of 48 patients, resulting in a cohort of 61 patients with varying numbers across centres:

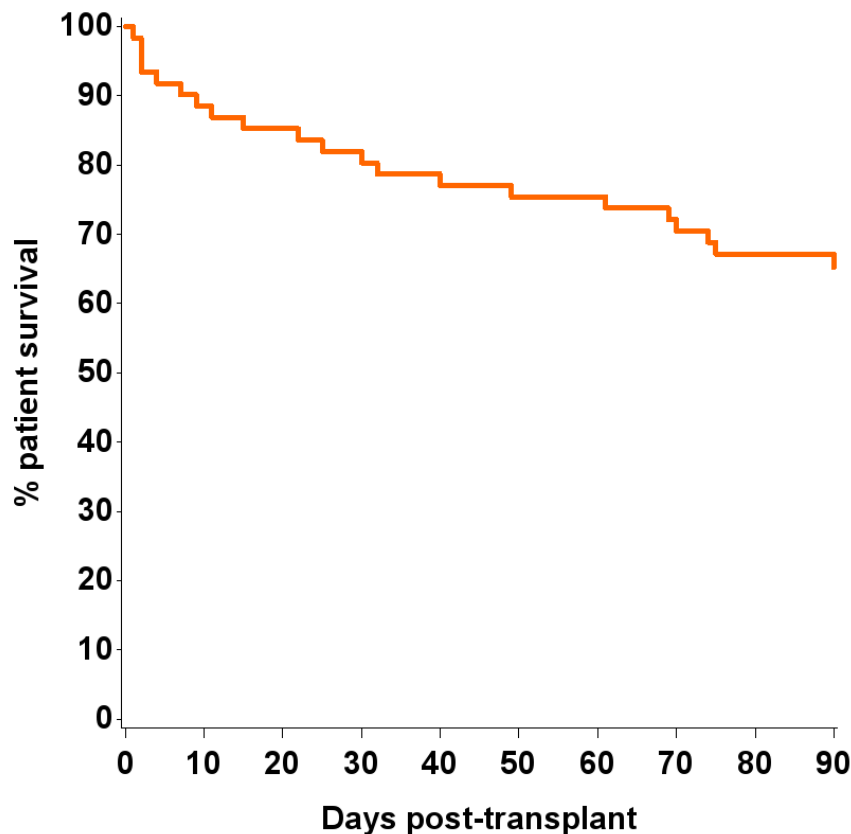
Centre	Number of patients
Birmingham	7
Glasgow	2
Harefield	17
Manchester	12
Newcastle	13
Papworth	10
Total	61

4. Key clinical data were provided by centres from the time of urgent heart transplant and combined with data on the UK Transplant Registry. The aim was to identify factors that explain the poor survival outcome of these patients. Analyses were performed using the Kaplan-Meier estimation method and log-rank test for categorical variables, and univariable Cox model and likelihood ratio test for continuous variables. P-values were considered significant at the 10% level due to the small sample size.
5. The rate of severe PGD was estimated by identifying patients who received short-term Mechanical Circulatory Support (MCS) in the immediate post-transplant period in the VAD Database.
6. A subgroup analysis was performed excluding those who received a Total Artificial Heart (TAH) due to the particularly high mortality in this group of patients.

RESULTS

7. **Figure 1** presents the overall survival of patients in the analysis cohort. The 90 day survival rate was 65.2% (95% CI: 51.7-75.8). Note that the 90 day survival rate post heart transplant as published in the Annual Cardiothoracic Report is 88.3%.

Figure 1 90 day survival of patients who received an urgent heart transplant for LVAD complications



8. **Table 1** examines the effect of different factors on the likelihood of a patient surviving to 90 days post-transplant. These analyses were limited by the small sample size, and only a few factors were associated with increased risk of mortality: type of LVAD, presence of systemic infection, BMI, C-Reactive Protein, centre and ischaemia time. The effect of BMI is unlikely to be associated with BMI itself, as there was 100% survival in the overweight group. Similarly, as ischaemia time is correlated with centre which is also correlated with type of LVAD, the effects observed are likely to be associations rather than true effects. There were also differences identified in the distributions of RAP, PASP and PADP for those that survived vs died within 90 days.
9. The rate of severe PGD in this group was 39%.

Table 1 Examining impact of variables on 90 day survival of urgent patients transplanted due to LVAD-related complications

Variable	Died within 90 days		Alive at 90 days ¹		p-value ²
	N=21		N=40		
	N	%	N	%	
<i>Number of complications</i>					
1	14	35	26	65	0.6735
More than 1	6	32	13	68	
Unknown	1		1		
<i>Presence of complication</i>					
Systemic infection (see Figure 2a)	12	48	13	52	0.0456
Driveline infection	6	26	17	74	0.2195
Thrombosis	2	29	5	71	0.6740
Right heart failure	2	18	9	82	0.2337
<i>Type of LVAD (see Figure 2b)</i>					
Heartware (HVAD)	11	35	20	65	0.0006
Heartmate II	5	38	8	62	
Heartmate III	0	-	11	100	
TAH	5	83	1	17	
<i>More than one VAD/TAH</i>					
No	15	33	31	67	0.5111
Yes (LVAD replaced/Centrimg with LVAD)	6	40	9	60	
<i>VAD duration</i>					
<1 year	4	36	7	64	0.8129
1 year or more	17	34	33	66	
<i>Stroke</i>					
No	16	32	34	68	0.3426
Yes	5	50	5	50	
Missing	0	-	1	100	
<i>AF</i>					
No	15	35	28	65	0.9327
Yes	6	35	11	65	
Missing	1	100	0	-	
<i>GFR group</i>					
90ml/min or more	9	31	20	69	0.6179
60-89 ml/min	8	44	10	56	
59 ml/min or less	4	29	10	71	
<i>BMI (see Figure 2c)</i>					
<25	10	53	9	47	0.0264
25-<30	11	34	21	66	
30 or more	0	-	10	100	
<i>CRP (see Figure 2e)</i>					
<10	6	24	19	76	0.0740
10 or more	13	45	16	55	
Missing	2	29	5	71	
<i>pHM % difference</i>					
Oversized (negative difference)	15	42	21	58	0.1664
Undersized (positive difference)	6	24	19	76	

Table 1 Examining impact of variables on 90 day survival of urgent patients transplanted due to LVAD-related complications

Variable	Died within 90 days N=21		Alive at 90 days ¹ N=40		p-value ²
<i>Ischaemia time (see Figure 2d)</i>					
<4 hours	6	22	21	78	0.0303
4 hours or more	15	52	14	48	
Missing	0	-	5	100	
<i>Centre</i>					
Centre A	12	71	5	29	0.0009
Centre B	3	23	10	77	
Centre C	4	33	8	67	
Centre D	1	10	9	90	
Centre E&F	1	11	8	89	
Recipient age, median (IQR)	51 (17-70)		46.5 (16-65)		
Creatinine (umol/l), median (IQR)	86 (75-108)		94 (73-118)		0.7870
Bilirubin (umol/l), median (IQR)	10 (8-16)		9 (7-17)		0.6846
Missing	0		2		
Platelets (mcL), median (IQR)	234 (186-292)		231 (163-286)		0.5151
Missing	0		1		
RAP, median (IQR)	4.5 (3.5-10)		8 (6-12)		0.0374
Missing	5		6		
PASP, median (IQR)	24 (20-29)		31 (25-35)		0.0323
Missing	6		5		
PADP, median (IQR)	10 (7-11)		12.5 (10-15)		0.0958
Missing	6		8		
MPAP, median (IQR)	16 (13-18.5)		20 (18-24)		0.1471
Missing	5		5		
PAWP, median (IQR)	10 (3.5-13)		12 (9-16)		0.1209
Missing	5		5		
CI, median (IQR)	2.1 (1.9-2.6)		2.4 (2.1-2.7)		0.2037
Missing	5		6		

¹ For 7 patients survival times were less than 90 days (74-89 days)

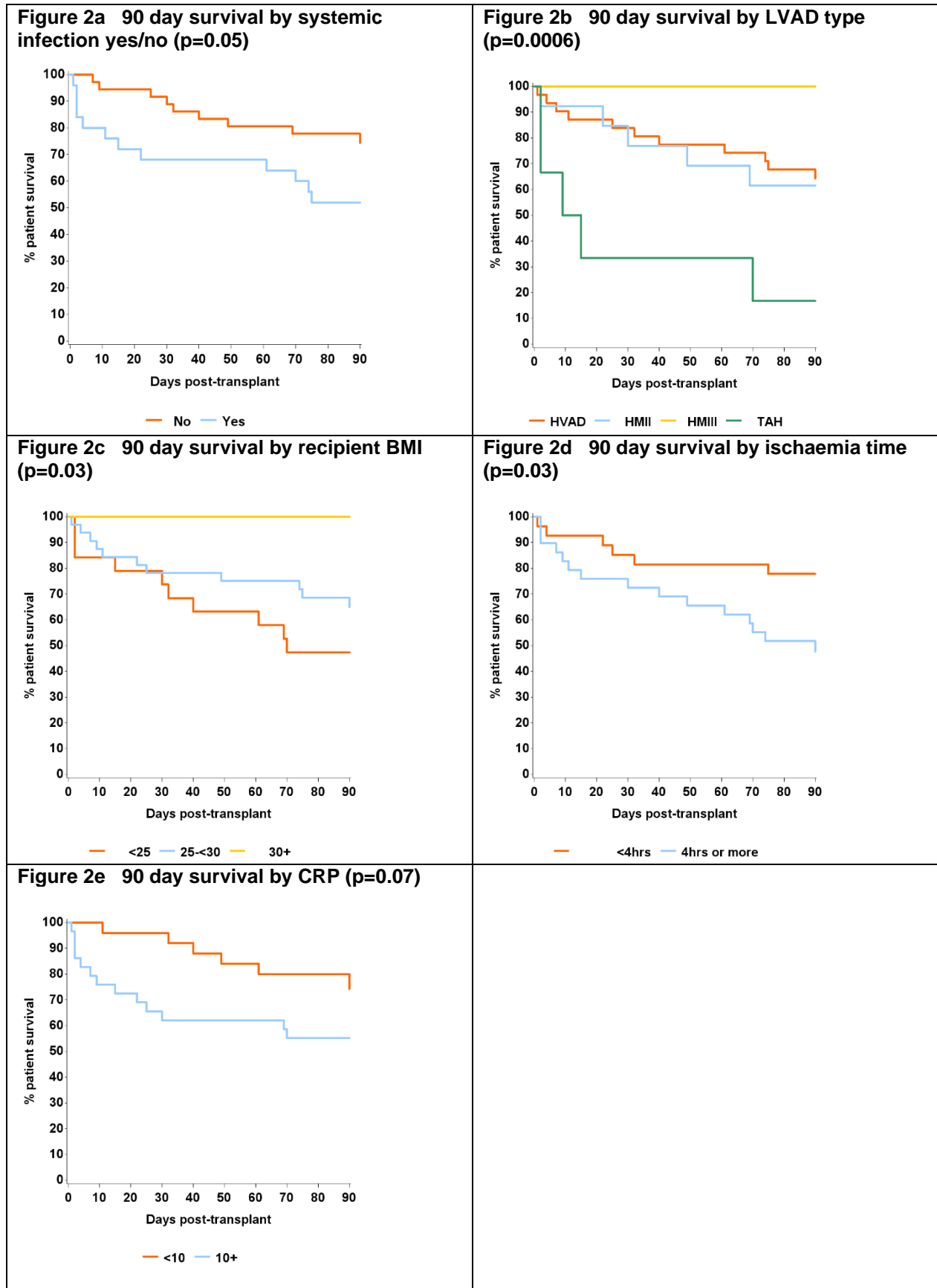
² Log-rank test for categorical variables and likelihood ratio test for continuous variables

10. Variables not analysed as inconsistently or under reported, or too few indicated:

Diabetes
 Ventilated
 Pre-transplant dialysis
 GCS
 Inotrope score
 MAP
 PaO₂
 FiO₂

11. **Figure 2** displays the unadjusted Kaplan-Meier survival curves for some of the variables that were found to be significantly associated with 90 day survival.

Figure 2 90 day survival of patients who received an urgent heart transplant for LVAD complications, stratified by significant variables



Results excluding TAH recipients

12. **Figure 9** presents the overall survival excluding those who received a TAH. The 90 day survival rate was 70.5% (95% CI: 56.3-80.8). The variables displayed in Table 1 were tested in this reduced cohort and six showed a significant association with 90 day survival; these are displayed in **Table 2**. The survival curves stratified by two of the variables are shown in **Figure 4**.

Figure 4 90 day survival of patients who received an urgent heart transplant for LVAD complications excluding TAH

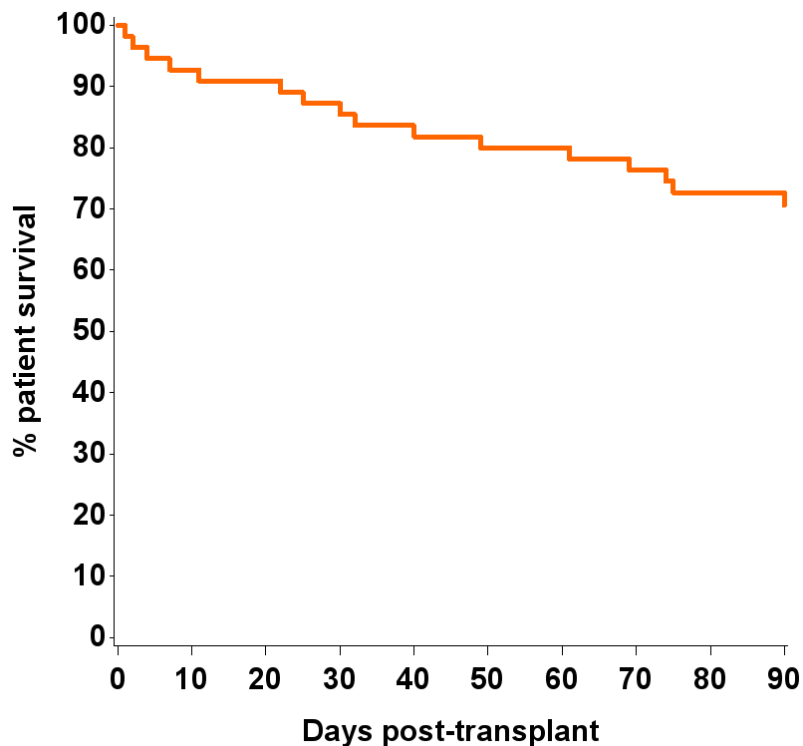


Table 2 Impact of significant variables on 90 day survival of urgent patients transplanted due to LVAD-related complications, excluding TAH

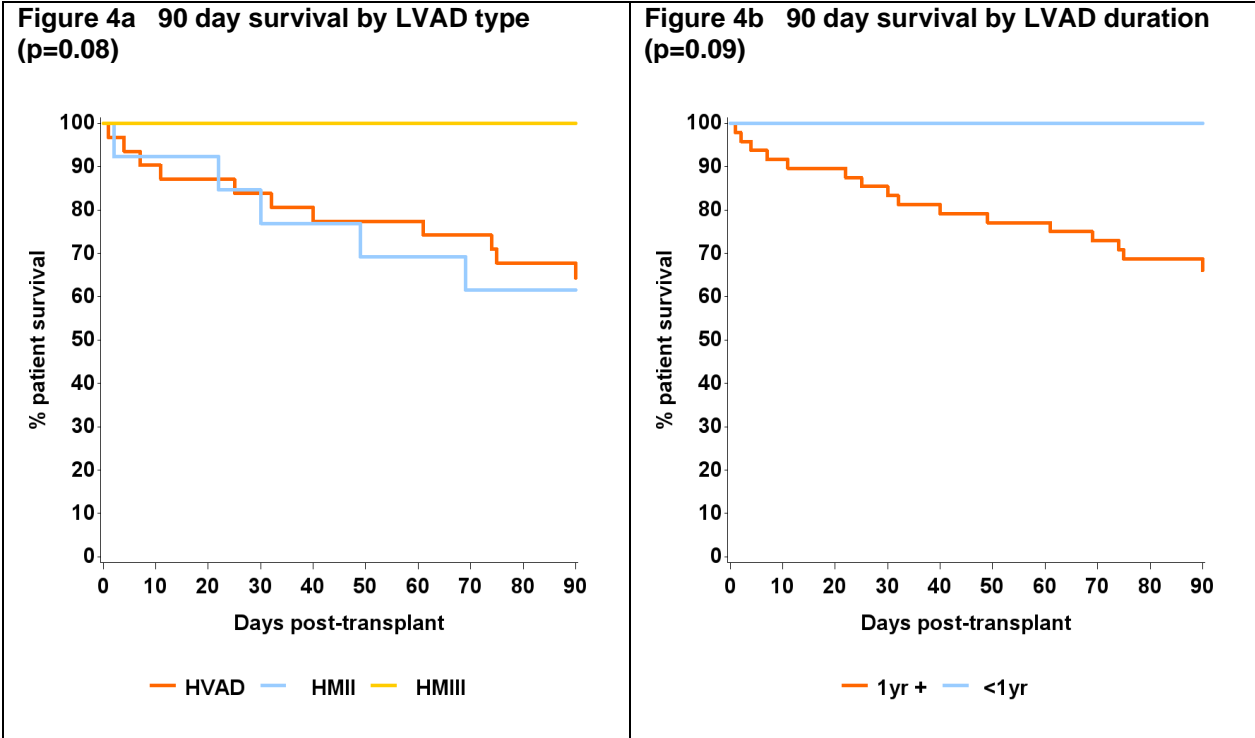
Variable	Died within 90 days N=21		Alive at 90 days ¹ N=40		p-value ²
	N	%	N	%	
<i>Type of LVAD (see Figure 4a)</i>					
Heartware (HVAD)	11	35	20	65	0.0838
Heartmate II	5	38	8	62	
Heartmate III	0	-	11	100	
<i>LVAD duration (see Figure 4b)</i>					
<1 year	0	-	7	100	0.0906
1 year or more	16	33	32	67	
<i>Centre</i>					
Centre A	7	64	4	36	0.0259
Centre B	3	23	10	77	
Centre C	4	33	8	67	
Centre D	1	10	9	90	
Centre E&F	1	11	8	89	
RAP, median (IQR)	4.5 (3.5-10)		8 (6-12)		0.0374
Missing	0		5		

Table 2 Impact of significant variables on 90 day survival of urgent patients transplanted due to LVAD-related complications, excluding TAH

Variable	Died within 90 days N=21	Alive at 90 days ¹ N=40	p-value ²
PASP, median (IQR)	24 (20-29)	31 (25-35)	0.0323
Missing	1	4	
PADP, median (IQR)	10 (7-11)	12.5 (10-15)	0.0958
Missing	1	7	

¹ For 7 patients survival times were less than 90 days (74-89 days)
² Log-rank test for categorical variables and likelihood ratio test for continuous variables

Figure 4 90 day survival of patients who received an urgent heart transplant for LVAD complications, excluding TAH, stratified by significant variables



CONCLUSIONS

13. In a cohort of 61 patients who received an urgent heart transplant due to LVAD-related complications, the survival at 90 days was 65.2% (lower than the 88.3% presented in the Annual Cardiothoracic Report). Poorer survival was associated with presence of systemic infection, the type of LVAD, recipient BMI, increased CRP, centre, ischaemia time and lower RAP, PASP and PADP, however some of these factors were highly correlated with each other and may represent unmeasured effects.
14. Patients who received a TAH had particularly poor outcomes. After removing these recipients from the cohort, the survival rate at 90 days was 70.5%. Six variables were associated with poorer survival: LVAD type, LVAD duration, centre, RAP, PASP and PADP.
15. This analysis should be interpreted with caution due to the small sample size and unadjusted nature of the tests.

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