ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

Concomitant Cardiac Procedures during Implantation of Long-Term Continuous-Flow LVADs: A European Registry for Patients with Mechanical Circulatory Support (EUROMACS) Analysis

APRIL 22-25, 2020
MONTRÉAL, CANADA
PALAIS DE CONGRÈS DE MONTRÉAL
ISHLT 2020

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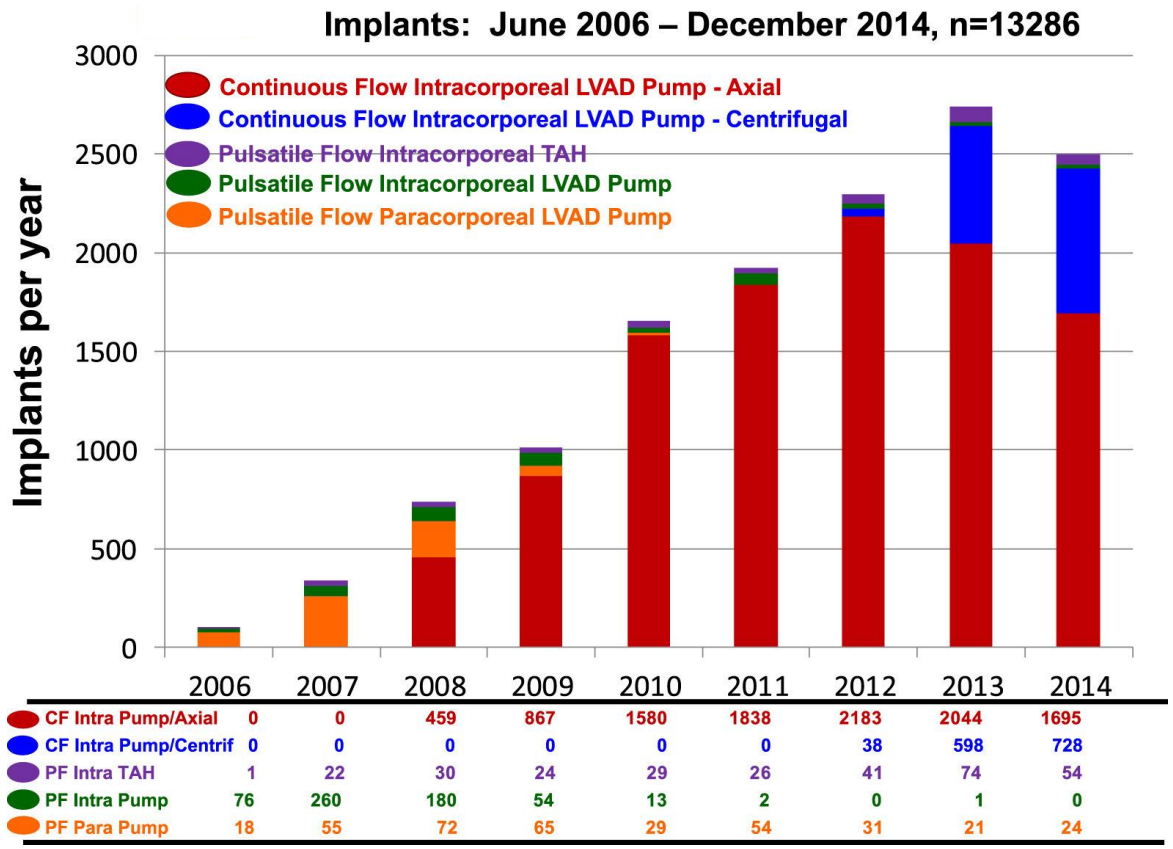
CCP in EUROMACS ....why??



Kirklin JK, JISHLT, December 2015

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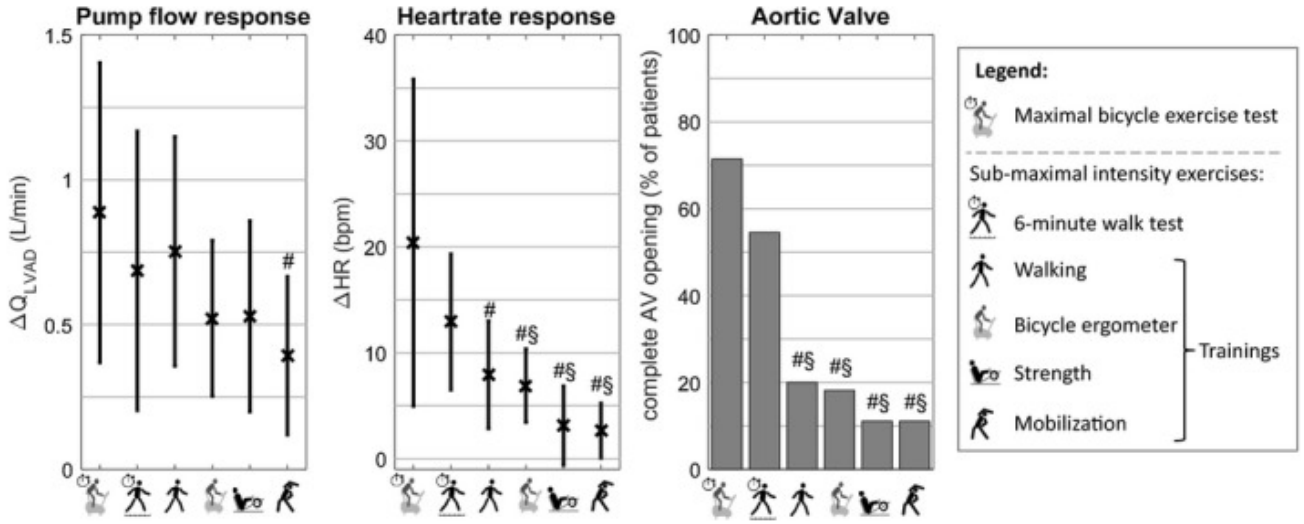
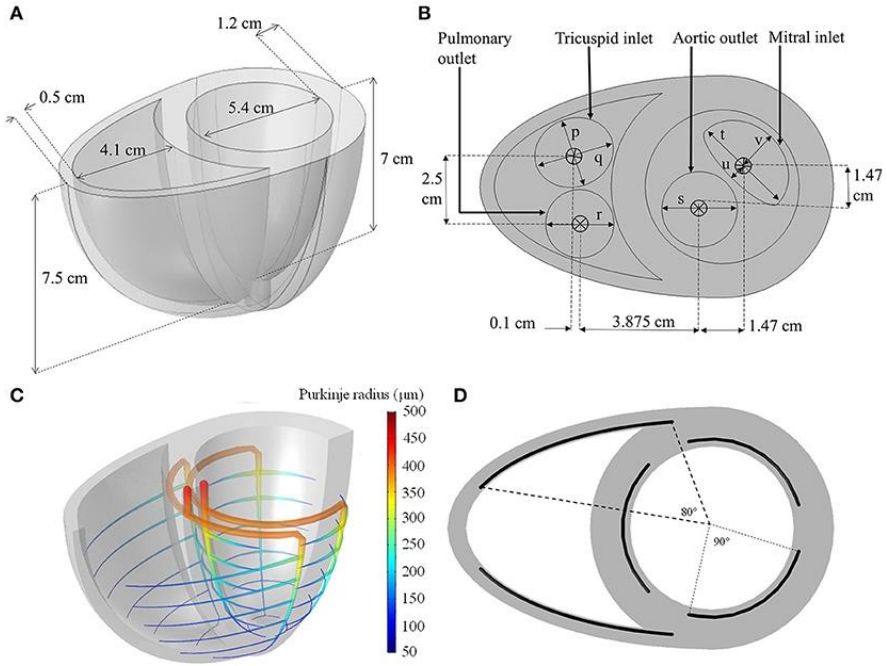
LVAD Pump Flow Does Not Adequately Increase With Exercise



Gross C et al, Artificial Organs 2018

”Ideal biventricular geometry”



Bakir AA et al, Front Physiol, September 2018

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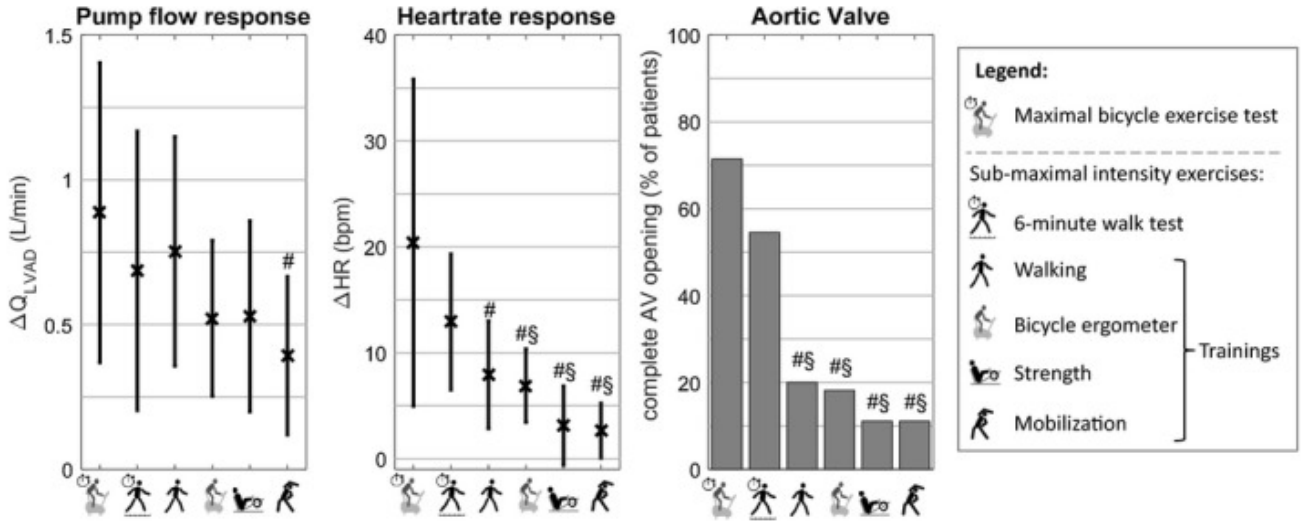

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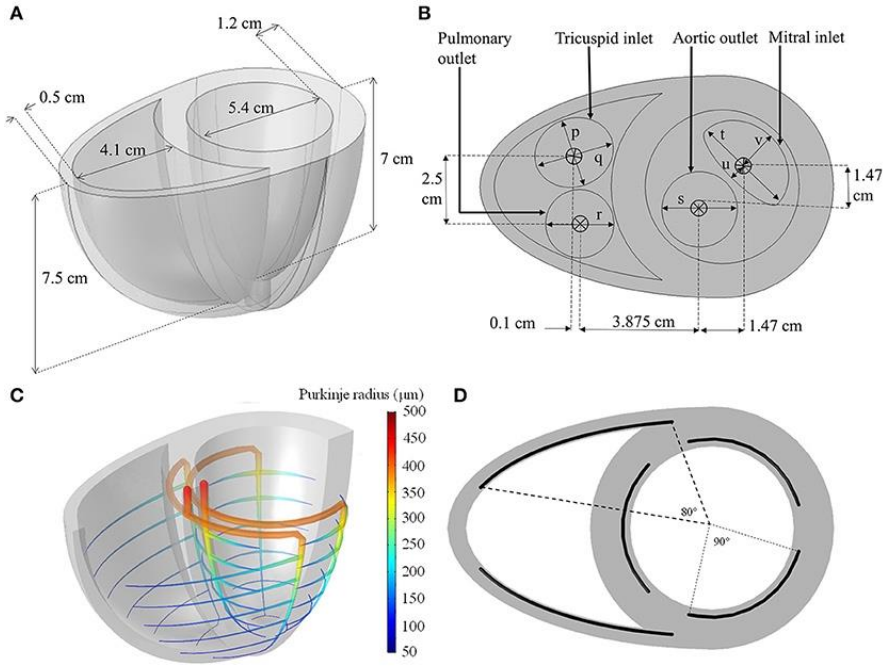

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CCP in EUROMACS ....why??

2019 EACTS Expert Consensus on long-term mechanical circulatory support

Evgenij V. Potapov[a,*†] (EACTS Chairperson), Christiaan Antonides[b,†], Maria G. Crespo-Leiro[c], Alain Combes[d,e], Gloria Färber[f], Margaret M. Hannan[g], Marian Kukucka[h], Nicolaas de Jonge[i], Antonio Loforte[j], Lars H. Lund[k], Paul Mohacsi[l], Michiel Morshuis[m], Ivan Netuka[n], Mustafa Özbaran[o], Federico Pappalardo[p], Anna Mara Scandroglio[q], Martin Schweiger[r], Steven Tsui[s], Daniel Zimpfer[t] and Finn Gustafsson[u,*] (EACTS Chairperson), The Task Force on Long-Term Mechanical Circulatory Support of the EACTS

6. CONCOMITANT CARDIAC CONDITIONS INCLUDING ARRHYTHMIAS

To increase survival and to reduce the complication rates after the operation, preoperative evaluation and identification of other cardiac conditions are of utmost importance. Presence of concomitant cardiac diseases requires appropriate intraoperative planning [33, 67]. Although it is clear that mechanical valves in the aortic position must be replaced by a bioprosthetic valve prior to implantation of an LVAD or BiVAD, there is accumulating experience with leaving mechanical mitral valves *in situ*. Clearly, more data in this area are needed before firm recommendations regarding the requirement to replace the mechanical mitral valve can be made.

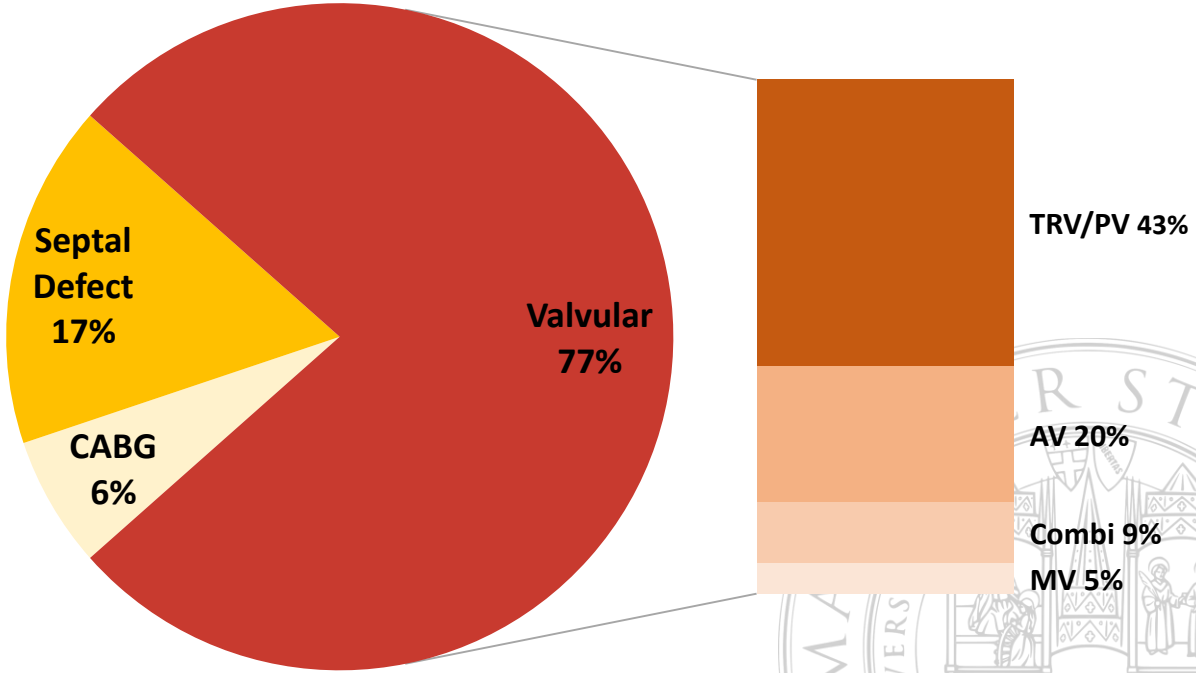
Recommendation	Class	Level
Aortic valve and root diseases		
Biological valve replacement in patients with more than mild aortic insufficiency should be considered.	IIa	B
Application of a central leaflet coaptation stitch may be considered in patients with more than mild aortic insufficiency.	IIb	B
Closure of aortic valve in patients with more than mild aortic insufficiency is not recommended.	III	C
It is recommended that a functional bioprosthesis be left in place.	I	C
Replacement of a mechanical aortic valve with a biological valve is recommended.	I	C
Closure of mechanical aortic valves is not recommended.	III	C
Surgical correction of an ascending aorta aneurysm at the time of implantation of a ventricular assist device should be considered.	IIa	C
Mitral valve disease		
Correction of moderate or severe mitral stenosis of any cause (including transcatheter interventions) is recommended.	I	C
In selected patients, the repair of severe mitral insufficiency may be considered.	IIb	C
Exchange of a functional mitral mechanical or biological prosthesis at the time of long-term mechanical circulatory support device implantation is not recommended.	III	C
In patients previously treated with a MitraClip, a thorough evaluation to rule out the existence of mitral valve stenosis is recommended.	I	C
Tricuspid valve disease and right ventricular dysfunction		
Correction of severe tricuspid stenosis at the time of long-term mechanical circulatory support implantation is recommended.	I	C
Re-evaluation of patients with moderate to severe tricuspid regurgitation after treatment with diuretic therapy, if condition permits, is recommended.	I	C
In carefully selected patients, tricuspid valve repair for moderate to severe tricuspid regurgitation at the time of long-term mechanical circulatory support implantation may be considered.	IIb	C
Implantation of a biventricular assist device or a total artificial heart in patients with severe tricuspid regurgitation and right ventricular dysfunction may be considered.	IIb	C

LVAD+CCP (n=533 pts) vs. isolated LVAD (n=2227 pts) cohorts

Propensity Score Matching 481 vs. 481

EUROMACS

PREOPERATIVE FEATURES	UNMATCHED groups (n=2760) LVAD (n=2227)		LVAD+CCP (n=533)			MATCHED groups (n=962) LVAD (n=481)		LVAD+CCP (n=481)		
	n	*%*	*n*	*%*	*p-value*	*n*	*%*	*n*	*%*	*p-value*
Age	52.5 ± 12.6		54.7 ± 11.7		**0.001**					
Male	1869	83.9	433	81.2	**0.070**	385	80.0	394	81.9	0.460
BSA	1.96 ± 0.23		1.96 ± 0.24		0.803	1.95 + 0.23		1.97 + 0.24		0.086
Etiology					**0.000**					0.422
Idiopathic dilatative	850	38.1	244	45.8		250	51.9	242	50.3	
Hypertrophic	24	1.1	3	0.6		3	0.6	2	0.4	
Restrictive	12	0.5	3	0.6		3	0.6	2	0.4	
Valvular	33	1.5	21	3.9		12	2.4	21	4.3	
Ischemic	961	43.0	212	39.8		209	43.5	205	42.6	
Congenital	18	0.8	10	1.9		4	0.8	9	1.8	
missing data	329	14.7	40	7.5						
NYHA class					**0.001**					0.554
III	160	7.2	28	5.3		22	4.5	26	5.4	
IV	1998	89.7	502	94.2		459	95.4	455	94.6	
Unknown	69	3.1	3	0.6						
INTERMACS profile					**0.009**					0.230
Level 1	309	13.9	72	13.5		88	18.3	67	13.9	
Level 2	695	31.2	200	37.5		175	36.4	177	36.8	
Level 3	566	25.4	153	28.7		121	25.2	141	29.3	
Level 4	406	18.2	75	14.1		75	15.6	70	14.6	
Level 5	86	3.9	12	2.3		14	2.9	12	2.5	
Level 6	38	1.7	12	2.3		4	0.8	11	2.2	
Level 7	32	1.4	3	0.6		4	0.8	3	0.6	
Unknown	95	4.3	6	1.1						



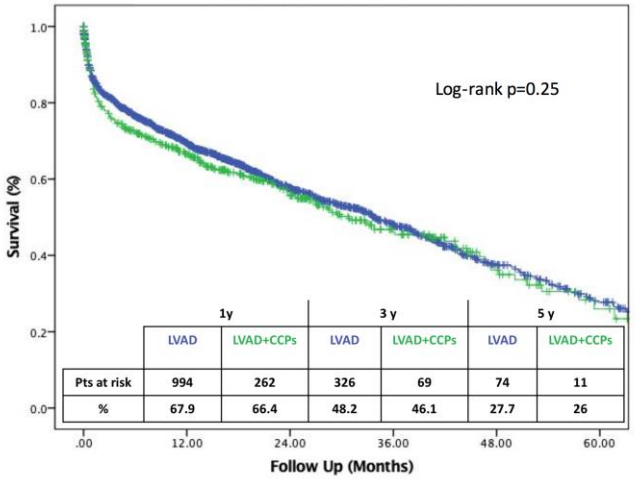
	UNMATCHED groups (n=2760)					MATCHED groups (n=962)				
	LVAD (n=2227)		LVAD+CCP (n=533)			LVAD (n=481)		LVAD+CCP (n=481)		
	n	*%*	*n*	*%*	*p-value*	*n*	*%*	*n*	*%*	*p-value*
Ejection fraction					**0.010**					**0.042**
<20%	956	42.9	230	43.2		245	50.9	224	46.6	
20-29%	570	25.6	168	31.5		124	25.8	167	34.7	
30-39%	70	3.1	17	3.2		24	4.9	17	3.5	
40-50%	9	0.4	3	0.6		3	0.6	1	0.2	
>50%	12	0.5	5	0.9		3	0.6	5	1.0	
Aortic regurgitation grade					**0.000**					**0.000**
Moderate	34	1.5	32	6.0		10	2.1	31	6.4	
Severe	12	0.5	5	0.9		3	0.6	5	1.0	
Mitral regurgitation grade					0.143					0.444
Moderate	534	23.9	137	25.7		134	27.8	135	28.0	
Severe	313	14.0	105	19.7		77	16.0	103	21.4	
Tricuspid regurgitation grade					**0.000**					**0.000**
Moderate	446	20.0	146	27.4		115	23.9	140	29.1	
Severe	201	9.0	124	23.3		42	8.7	94	19.5	
Inotropic/mechanical support										
Norepinephrine	293	13.1	126	23.6	**0.000**	81	16.8	122	25.4	**0.002**
Levosimendan	142	6.4	75	14.1	**0.000**	32	6.7	74	15.4	**0.000**
Milrinone	364	16.3	138	25.9	**0.000**	91	18.9	138	28.7	**0.001**
Nitric Oxyde	455	20.4	9	1.7	**0.035**	3	0.6	9	1.9	0.092
IABP	229	10.3	47	8.8	0.124	63	13.1	44	9.1	**0.044**
ECMO	230	10.3	54	10.1	0.857	64	13.3	50	10.4	0.144
CBP time	84.5 ± 46.8		121.4 ± 49.5		**0.000**	82.3 ± 52.3		125.6 ± 63.7		**0.000**
Time for implant	244.6 ± 95.3		287.6 ± 154.3		**0.000**	246.7 ± 114.4		299.8 ± 165.6		**0.000**
LVAD brand										**0.000**
Heartware HVAD	1147	51.5	263	49.3		279	58.0	247	51.4	
HeartMate II	665	29.9	169	31.7		124	25.8	144	29.9	
Heartmate III	206	9.3	78	14.6		47	9.8	73	15.2	
Others	209	9.3	23	4.3		31	6.4	17	3.5	

RISK FACTOR ANALYSIS FOR OVERALL SURVIVAL (matched population)	Multivariate		
	p-value	*HR*	*CI*
Age	0.302	1.01	0.99-1.03
BMI	**0.000**	1.08	1.04-1.13
Dilatative idiopathic etiology	0.716	1.08	0.72-1.62
NYHA class	0.365	0.54	0.14-2.06
INTERMACS level	0.232	0,86	0.68-1.10
Major miocardial infarction	0.587	1.21	0.61-2.40
Intubation	0.491	1.36	0.57-3.23
Dialysis	0.697	1.28	0.37-4.47
REDO	0.143	3.14	0.68-14.55
Paced	0.139	1.38	0.90-2.10
Mitral regurgitation grade	**0.035**	0.84	0.71-0.99
Hemodynamics			
PAPs	0.634	1.01	0.99-1.03
PAPd	0.957	1.00	0.97-1.04
PWCP	**0.032**	0.97	0.94-1.00
Cardiac Output	**0.055**	0.86	0.74-1.00
Inotropic/mechanical support			
Epinephrine	0.070	0.68	0.45-1.03
Norepinephrine	**0.008**	1.95	1.19-3.20
IABP	0.059	0.49	0.24-1.00
ECMO	**0.028**	1.38	0.48-3.93

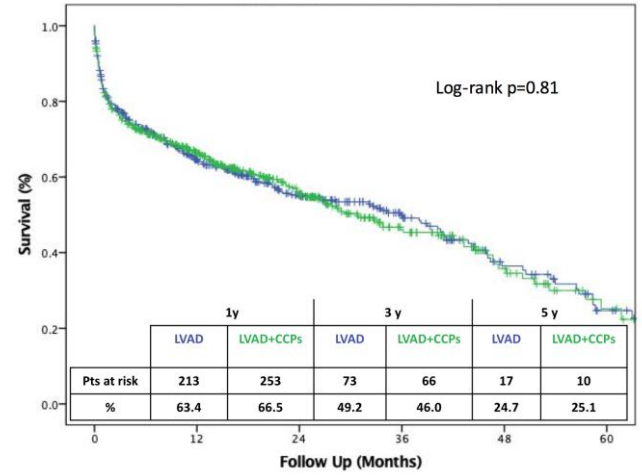
EARLY OUTCOMES	UNMATCHED groups (n=2760)					MATCHED groups (n=962)				
	LVAD (n=2227)		LVAD+CCP (n=533)			LVAD (n=481)		LVAD+CCP (n=481)		
	n	*%*	*n*	*%*	*p-value*	*n*	*%*	*n*	*%*	*p-value*
ICU stay (days)	19.6 ± 27.0		27.2 ± 34.5		**0.000**	20.9 ± 26.8		25.5 ± 32.3		**0.019**
Reoperation for bleeding (within 48h)	145	6.5	43	8.1	0.195	48	10.0	48	10.0	1.000
Reoperation for bleeding (after 48h)	115	5.2	50	9.4	**0.000**	39	8.1	47	9.7	0.366
Dialysis	89	4.0	35	6.6	**0.014**	25	5.2	35	7.2	0.182
Ventilation time (hours)	202.2 ± 365.2		268.3 ± 382.7		**0.001**	230.6 ± 352.1		261.5 ± 373.2		0.219
Respiratory failure	55	2.5	22	4.1	**0.038**	18	3.7	21	4.3	0.624
Right heart failure (inotropic + mechanical)	319	14.3	88	16.5	0.193	59	12.3	53	11.0	0.546
RVAD support	109	4.9	39	7.3	**0.033**	34	7.0	36	7.5	0.804
Inotropic support	200	9.3	49	9.2	0.188	25	5.3	17	3.5	**0.046**
In hospital morbidity (30-days)										
Infection	28	1.3	6	1.1	0.531	21	4.3	32	6.6	0.143
Bleeding	27	1.2	16	3.0	**0.010**	20	4.1	35	7.2	**0.027**
Stroke	20	0.9	9	1.7	0.218	11	2.3	12	2.4	0.679
Pump thrombosis	14	0.6	4	0.8	0.973	7	1.4	9	1.9	0.527
In hospital mortality (30-days)	314	14.1	114	21.4	**0.000**	84	17.4	107	22.2	**0.063**

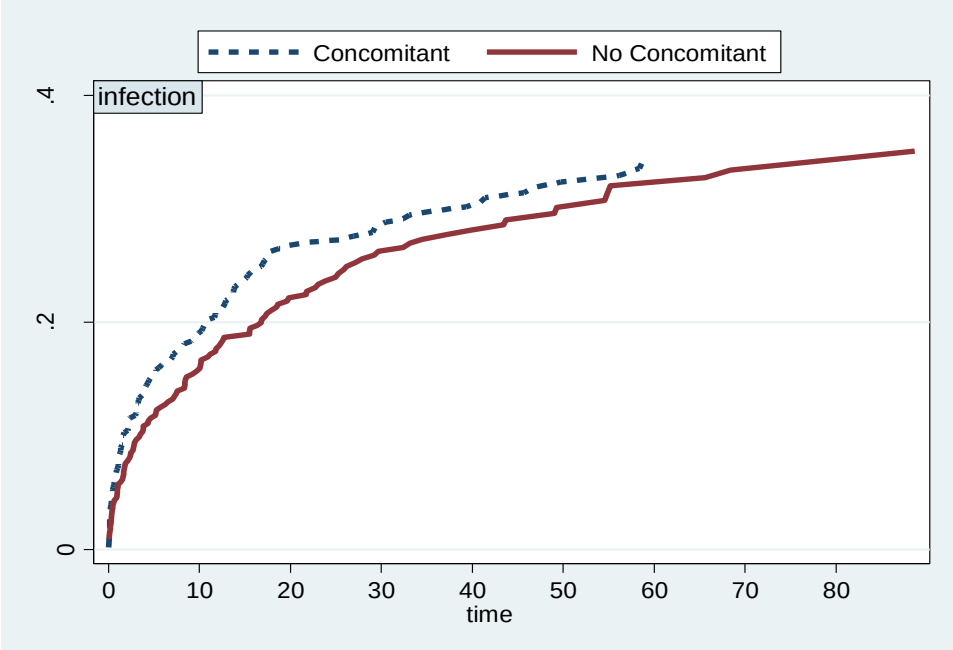
LONG-TERM (FU) OUTCOMES	Unmatched groups (n=2760)					Matched groups (n=962)				
	LVAD (n=2227)		LVAD+CCP (n=533)			LVAD (n=481)		LVAD+CCP (n=481)		
		%	*n*	*%*	*p-value*	*n*	*%*	*n*	*%*	*p-value*
Long-term (FU) mortality	486	21.8	104	19.5	0.151	108	22.5	98	20.3	0.432
Heart Transplantation	554	24.9	148	27.8	0.231	122	25.4	146	30.4	0.084
Early morbidity (< 6 months)										
Infection	91	4.1	20	3.8	**0.041**	46	9.6	74	15.4	**0.022**
Bleeding	65	2.9	29	5.4	**0.011**	33	6.9	52	10.8	**0.031**
Stroke	75	3.4	18	3.4	0.719	29	6.0	23	4.7	0.446
Pump thrombosis	49	2.2	7	1.3	0.114	19	4.0	10	2.0	0.100
Late morbidity (> 6 months)										
Infection	415	18.6	208	39.0	**0.036**	68	14.1	62	12.9	0.613
Bleeding	188	8.4	55	10.3	0.199	25	5.2	22	4.6	0.548
Stroke	188	8.4	43	8.1	0.683	35	7.3	34	7.0	0.760
Pump thrombosis	219	9.8	54	10.1	0.937	42	8.7	51	10.6	0.578

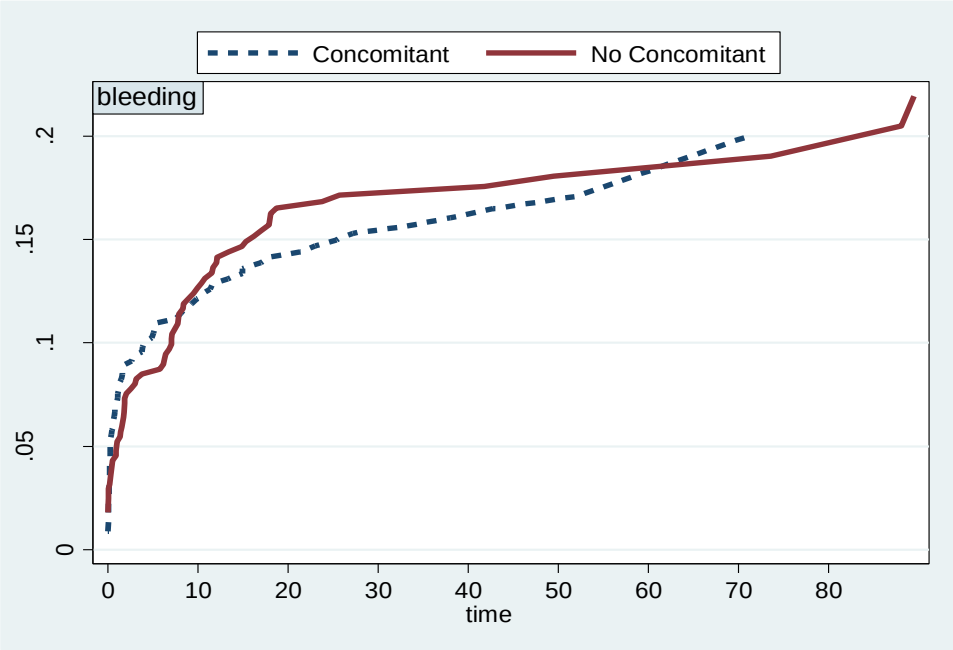
A. UNMATCHED



B. MATCHED

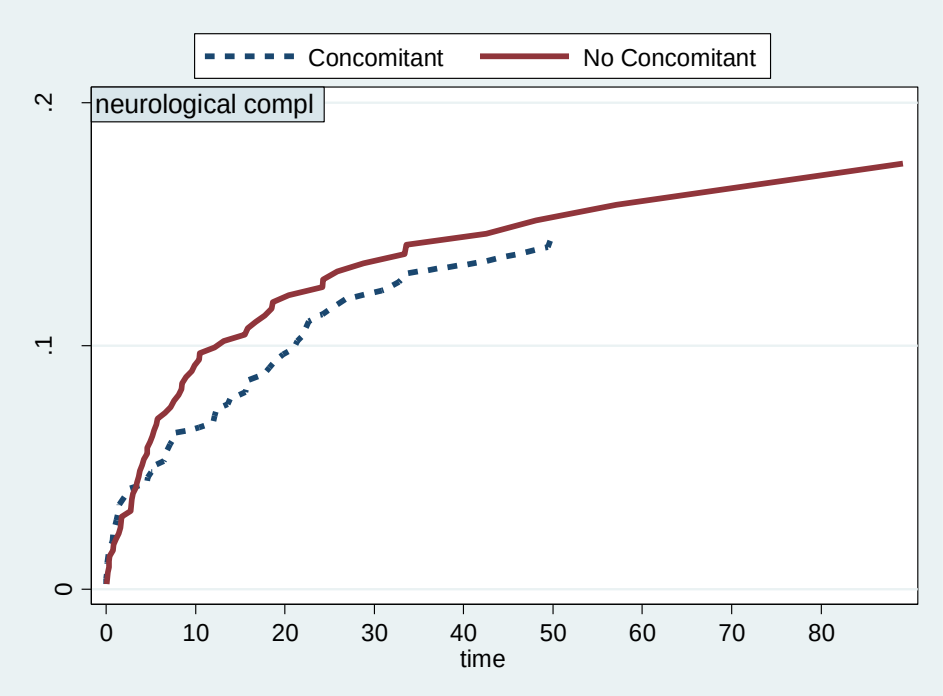


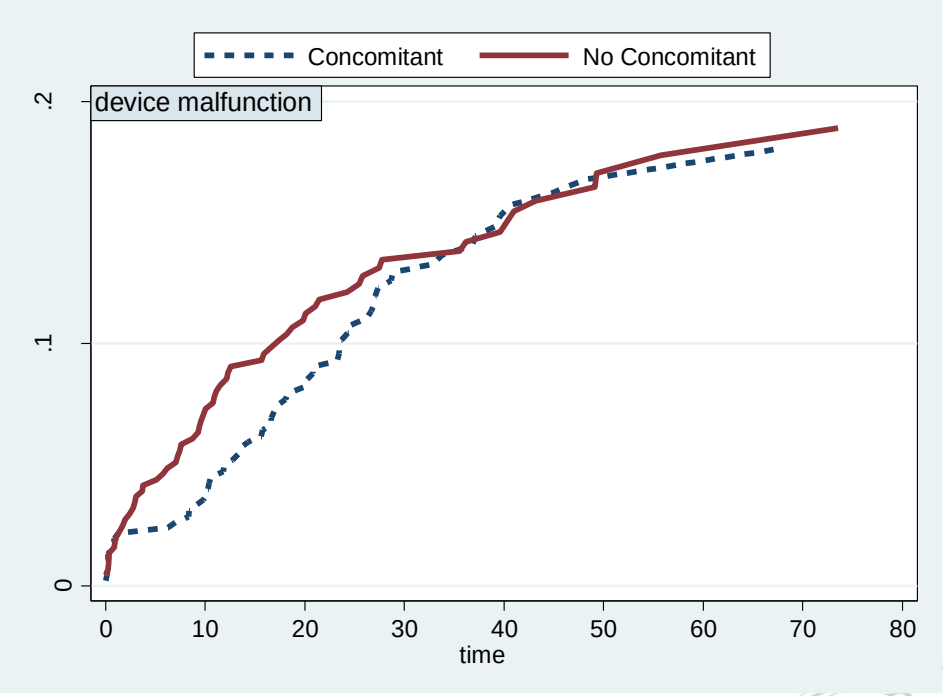




	Risk factor analysis for INFECTION						
	UNIVARIATE				MULTIVARIATE		
	p-value	*HR*	*CI*		*p-value*	*HR*	*CI*
Inotropes	**0.001**	0.42	0.25	0,71	**0.003**	0.45	0.26-0.76
Norepinephrine	**0.045**	1.37	1.01	1,86	0.411	1.16	0.82-1.65
ECMO	**0.001**	1.92	1.33	2,78	**0.003**	1.58	1.05-2.38
LVAD brand							
Heartware HVAD	**0.000**	2.47	1.77	3,44	0.181	0.83	0.64-1.09

	Risk factor analysis BLEEDING					
	UNIVARIATE			MULTIVARIATE		
	p-value	*HR*	*CI*	*p-value*	*HR*	*CI*
Age	**0.000**	1.03	1.01-1.05	**0.033**	1.03	1.00-1.07
Coronary disease	**0.039**	1.44	1.02-2.03	0.133	1.64	0.86-3.11
INTERMACS level	**0.011**	1.19	1.04-1.36	**0.028**	1.30	1.03-1.63
Dialysis	**0.004**	2.58	1.35-4.91	**0.000**	12.69	3.57-45.14
Mitral regurgitation grade	0.064	1.17	0.99-1.38	0.130	1.25	0.94-1.66
PVR (dynes)	0.083	1.01	1.00-1.01	0.171	1.01	1.01-1.01
Time for implant	**0.000**	1.01	1.00-1.01	**0.000**	1.01	1.01-1.01





Risk factor analysis for Neurological dysfunction

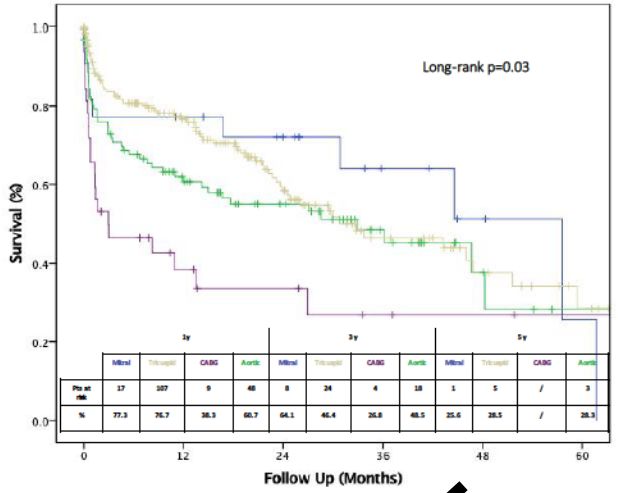
	UNIVARIATE			MULTIVARIATE		
	p-value	*HR*	*CI*	*p-value*	*HR*	*CI*
Dilatative etiology	**0.020**	0.64	0.44-0.93	0.086	0.71	0.48-1.05
Intubation	**0.040**	1.72	1.03-2.89	0.552	1.22	0.64-2.33
Inotropes	0.077	0.66	0.41-1.05	0.071	0.65	0.40-1.04
ECMO	**0.008**	2.01	1.20-3.38	0.182	1.56	0.81-3.01
LVAD brand						
Heartware HVAD	**0.001**	1.90	1.28-2,82	**0,004**	1.80	1.20-2.69

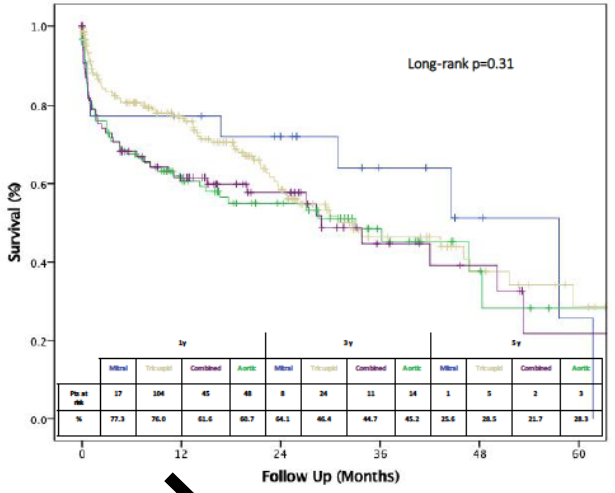
Risk factor analysis for Device malfunction

	UNIVARIATE			MULTIVARIATE		
	p-value	*HR*	*CI*	*p-value*	*HR*	*CI*
Male	**0.043**	0.65	0.43-0.99	0.475	0.84	0.53-1.35
BSA	**0.032**	0.43	0.20-0.93	0.126	0.51	0.21-1.21
Major miocardial infarction	**0.026**	1.67	1.06-2.64	**0.041**	1.64	1.02-2.64
Inotropes	**0.030**	0.61	0.39-0.95	**0.014**	0.56	0.36-0.89
Strategy						
Bridge to candidacy	**0.022**	1.52	1.06-2.16	**0.008**	1.63	1.14-2.35
LVAD brand						
HeartMate II	0.079	0.71	0.48-1.04	0.115	0.73	0.49-1.08

Concomitant Subgroups

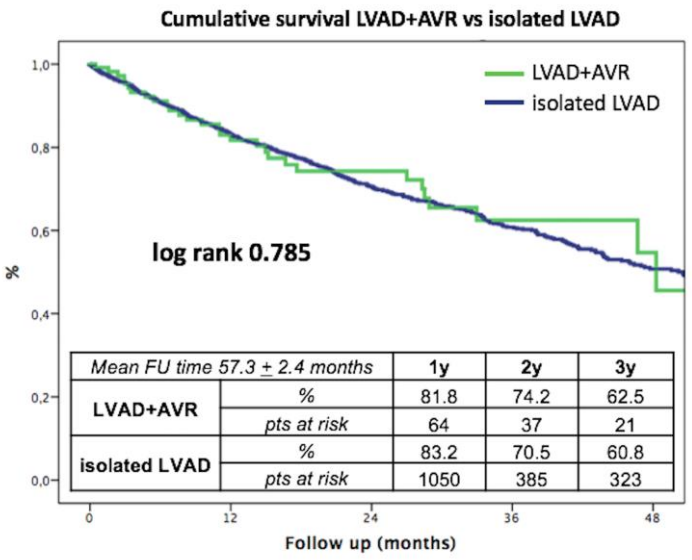
	logistic regression for inhospital mortality					
	Unmatched population			Matched population		
	p-value	*OR*	*IC*	*p-value*	*OR*	*IC*
LVAD + CCP	**0.000**	1.65	1.30-2.10	0.064	1.35	0.98-1.86
CABG	**0.041**	2.03	1.03-4.02	**0.043**	2.08	1.02-4.25
VALVULAR	0.500	0.85	0.53-1.37	0.086	1.35	0.96-1.90
Aortic valve	**0.007**	1.83	1.18-2.86	**0.001**	2.08	1.34-3.22
Mitral valve	**0.013**	2.36	1.20-4.64	0.079	1.89	0.93-3.84
Tricuspid valve	**0.032**	1.42	1.03-1.97	0.300	1.22	0.82-1.81
SEPTAL DEFECTS	0.408	0.78	0.42-1.42	0.775	0.91	0.49-1.68





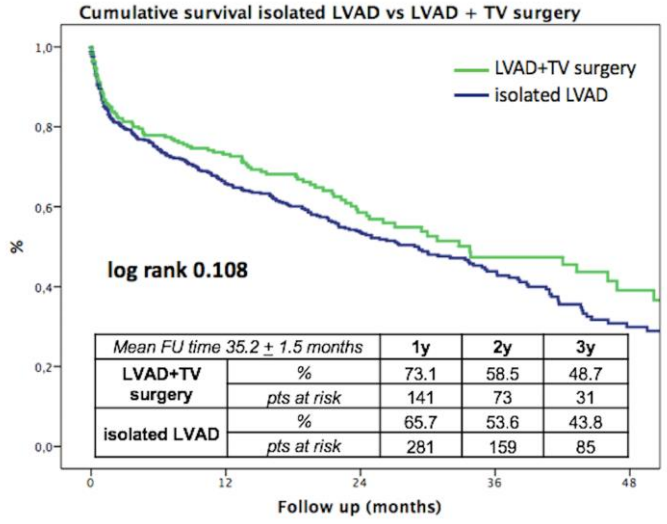
CCPs matched cohorts Kaplan-Meier survival analysis.

AVs vs Overall



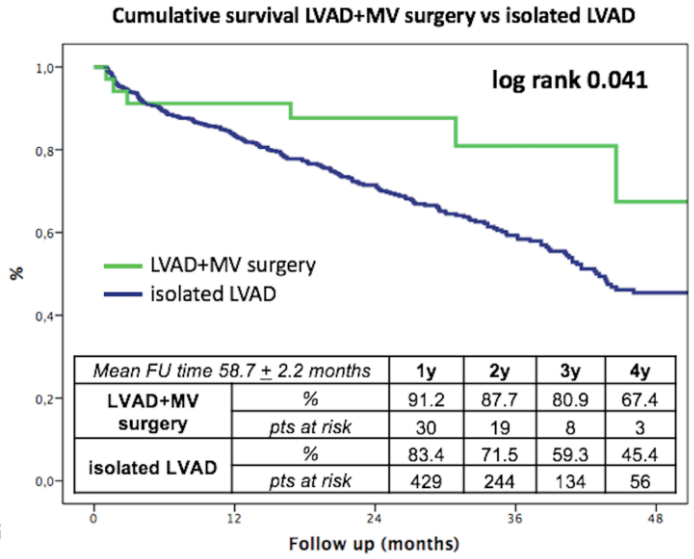
Mean FU time 57.3 ± 2.4 months		1y	2y	3y
LVAD+AVR	%	81.8	74.2	62.5
	pts at risk	64	37	21
isolated LVAD	%	83.2	70.5	60.8
	pts at risk	1050	385	323

TVs vs Overall



Mean FU time 35.2 ± 1.5 months		1y	2y	3y
LVAD+TV surgery	%	73.1	58.5	48.7
	pts at risk	141	73	31
isolated LVAD	%	65.7	53.6	43.8
	pts at risk	281	159	85

MVs vs Overall



Mean FU time 58.7 ± 2.2 months		1y	2y	3y	4y
LVAD+MV surgery	%	91.2	87.7	80.9	67.4
	pts at risk	30	19	8	3
isolated LVAD	%	83.4	71.5	59.3	45.4
	pts at risk	429	244	134	56

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Impact of concurrent surgical valve procedures in patients receiving continuous-flow devices

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Results: Patients undergoing HMII + VP were significantly older, had higher blood urea nitrogen levels and central venous pressure, and decreased right ventricular stroke work index; intraoperatively, the median cardiopulmonary bypass times were also longer. The unadjusted 30-day mortality was significantly higher in patients undergoing HMII + VP (10.3% vs 4.8% for LVAD alone, $P = .005$). Subgroup analysis of individual VPs showed that higher mortality occurred in patients with HMII plus 2 or more VPs (13.5%, $P = .04$) followed by trends for increased mortality with HMII plus mitral alone (11.5%, $P =$ NS), HMII plus aortic alone (10.9%, $P =$ NS), and HMII plus tricuspid (8.9%, $P =$ NS) procedures. Of these various groups, only patients undergoing HMII + isolated aortic VP ($P = .001$) and HMII + multiple VPs ($P = .046$) had significantly worse long-term survival compared with patients undergoing HMII alone. Right heart failure and right ventricular assist device use was increased in patients undergoing VPs, but there was no difference in the incidence of bleeding or stroke.

Conclusions: Patients frequently require concurrent VPs at the time of LVAD placement; these patients are sicker and have higher early mortality. Furthermore, right ventricular dysfunction is increased in these patients. Further studies to develop selection criteria for concurrent valve interventions are important to further improve clinical outcomes. (J Thorac Cardiovasc Surg 2014;147:581-9)

Outcomes after tricuspid valve surgery concomitant with left ventricular assist device implantation in the EUROMACS registry: a propensity score matched analysis

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RESULTS

In total, 3323 patients underwent LVAD implantation of which 299 (9%) had TVS. After matching, 258 patients without TVS were matched to 258 patients with TVS. In the matched population, hospital deaths, days on inotropic support, temporary right ventricular assist device implants and hospital stay were comparable, whereas stay in the intensive care unit was higher in the TVS cohort (11 vs 15 days; $P = 0.026$). Late deaths ($P = 0.17$), cumulative incidence of unexpected hospital readmission ($P = 0.15$) and right heart failure ($P = 0.55$) were comparable between patients with and without concomitant TVS. In the matched population, probability of moderate-to-severe TR immediately after surgery was lower in patients with concomitant TVS compared to patients without TVS (33% vs 70%; $P = 0.001$). Nevertheless, the probability of moderate-to-severe TR decreased more quickly in patients without TVS ($P = 0.030$), resulting in comparable probabilities of moderate-to-severe TR within 1.5 years of follow-up.

CONCLUSIONS

In matched patients, TVS concomitant with LVAD implant does not seem to be associated with better clinical outcomes. Concomitant TVS reduced TR significantly early after LVAD implant; however, differences in probability of TR disappeared during the follow-up period.

Conclusions

- CCPs performed during implantation of a long-term CF LVAD may not increase the peri-operative ICU outcomes and in-hospital mortality. Type of CCP surgery addressed should be properly weighted (particularly focusing on CABG and AVR).
- Mitral valve repair may be protective in the long-term period, while tricuspid valve repair may not have any influence.
- Mid- to long-term conditional survival (and PS matched) is not influenced by CCPs at the time of LVAD primary implantation.
- This, however, remains a delicate population to be strictly monitored and homogeneously managed to preserve satisfactory outcomes.

Thank You!