Surgical treatment of end-stage heart failure in hemopathic patients

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Heart failure: etiologies

DISEASED MYOCARDIUM		
Ischaemic heart disease	Myocardial scar	
	Myocardial stunning/hibernation	
	Epicardial coronary artery disease	
	Abnormal coronary microcirculation	
	Endothelial dysfunction	
Toxic damage	Recreational substance abuse	Alcohol, cocaine, amphetamine, anabolic steroids.
	Heavy metals	Copper, iron, lead, cobalt.
	Medications	Cytostatic drugs (e.g. anthracyclines), immunomodulating drugs (e.g. interferons monoclonal antibodies such as trastuzumab, cetuximab), antidepressant drugs, antiarrhythmics, non-steroidal anti-inflammatory drugs, anaesthetics.
	Radiation	
Immune-mediated and inflammatory damage	Related to infection	Bacteria, spirochaetes, fungi, protozoa, parasites (Chagas disease), rickettsiae, viruses (HIV/AIDS).
	Not related to infection	Lymphocytic/giant cell myocarditis, autoimmune diseases (e.g. Graves' disease, rheumatoid arthritis, connective tissue disorders, mainly systemic lupus erythematosus), hypersensitivity and eosinophilic myocarditis (Churg–Strauss).
Infiltration	Related to malignancy	Direct infiltrations and metastases.
	Not related to malignancy	Amyloidosis, sarcoidosis, haemochromatosis (iron), glycogen storage diseases (e.g. Pompe disease), lysosomal storage diseases (e.g. Fabry disease).
Metabolic derangements	Hormonal	Thyroid diseases, parathyroid diseases, acromegaly, GH deficiency, hypercortisolaemia, Conn's disease, Addison disease, diabetes, metabolic syndrome, phaeochromocytoma, pathologies related to pregnancy and peripartum.
	Nutritional	Deficiencies in thiamine, L-carnitine, selenium, iron, phosphates, calcium, complex malnutrition (e.g. malignancy, AIDS, anorexia nervosa), obesity.
Genetic abnormalities	Diverse forms	HCM, DCM, LV non-compaction, ARVC, restrictive cardiomyopathy (for details see respective expert documents), muscular dystrophies and laminopathies.
ABNORMAL LOADING CONDITIONS		
Hypertension		
Valve and myocardium structural defects	Acquired	Mitral, aortic, tricuspid and pulmonary valve diseases.
	Congenital	Atrial and ventricular septum defects and others (for details see a respective expert document).
Pericardial and endomyocardial pathologies	Pericardial	Constrictive pericarditis Pericardial effusion
	Endomyocardial	HES, EMF, endocardial fibroelastosis.
High output states		Severe anaemia, sepsis, thyrotoxicosis, Paget's disease, arteriovenous fistula, pregnancy.
Volume overload		Renal failure, iatrogenic fluid overload.
ARRHYTHMIAS		
Tachyarrhythmias		Atrial, ventricular arrhythmias.
Bradyarrhythmias		Sinus node dysfunctions, conduction disorders.

Eur J Heart Fail. 2016 Aug;18(8):891-975

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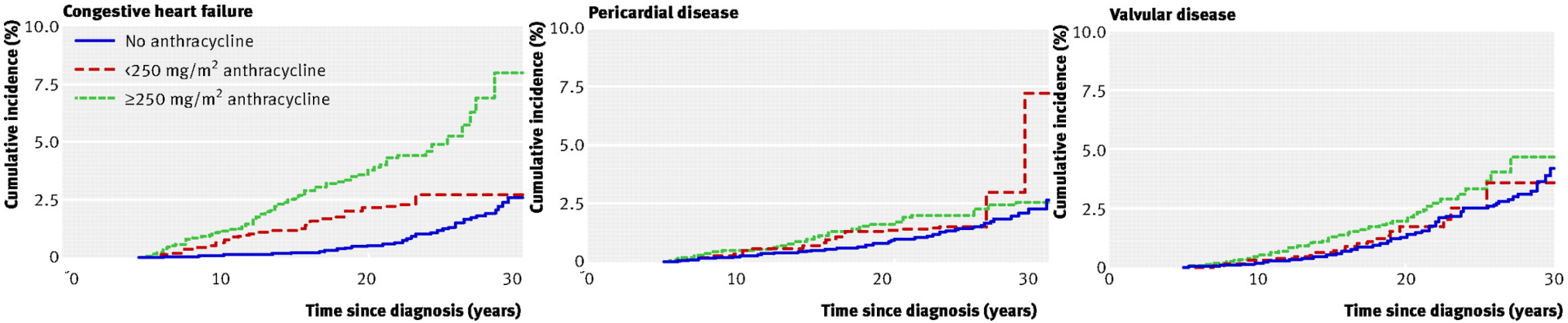
Heart failure: cardiac disorders in cancer survivors

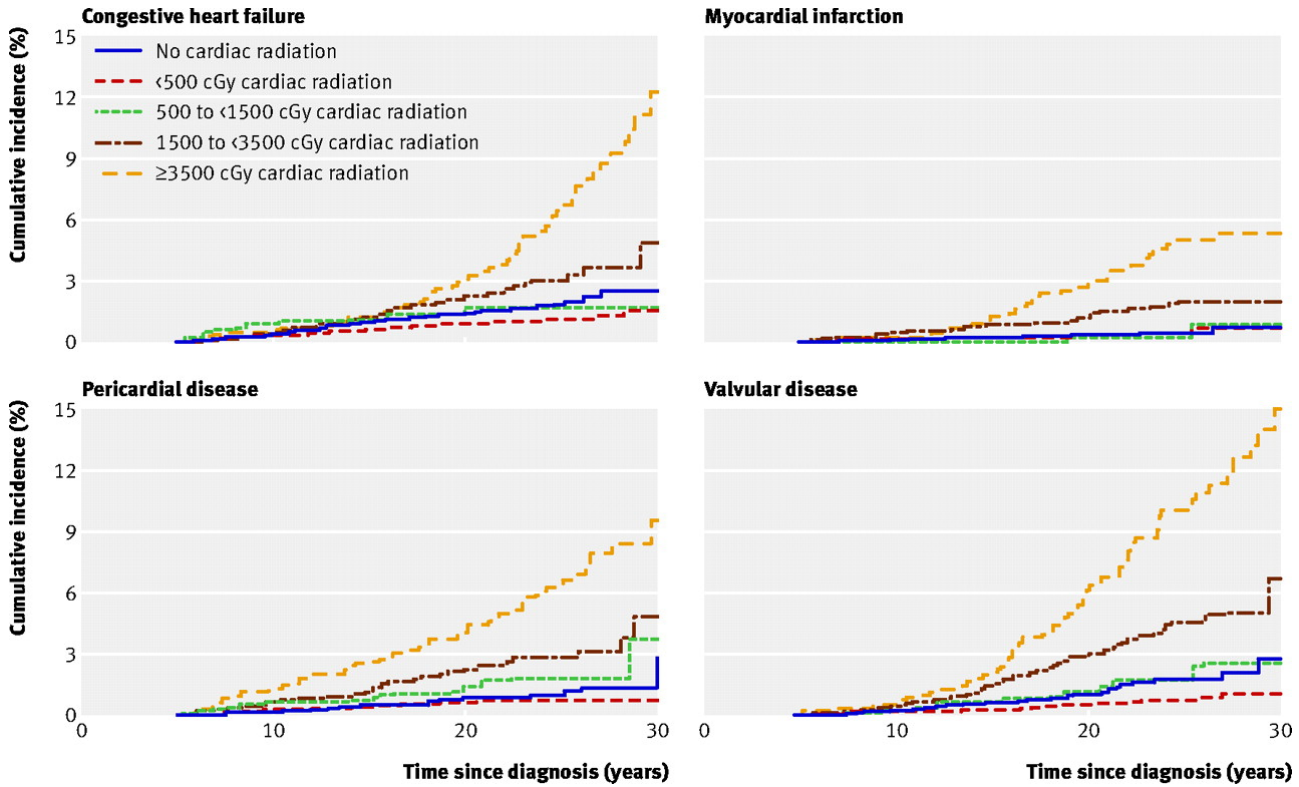
Cumulative incidence of cardiac disorders among childhood cancer survivors by anthracycline dose



Mulrooney D.A. et al. BMJ 2009;339:bmj.b4606

Heart failure: cardiac disorders in cancer survivors

Cumulative incidence of cardiac disorders among childhood cancer survivors by average cardiac radiation dose



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Eligibility to heart transplant

History of malignancy

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ISHLT GUIDELINE

The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update

Pre-existing neoplasms are diverse, and many are treatable with excision, radiotherapy, or chemotherapy to induce cure or remission. In these patients needing cardiac transplantation, collaboration with oncology specialists should occur to stratify each patient as to their risk of tumor recurrence. Cardiac transplantation should be considered when tumor recurrence is low based on tumor type, response to therapy, and negative metastatic work-up. The specific amount of time to wait to transplant after neoplasm remission will depend on the aforementioned factors and no arbitrary time period for observation should be used (**Class I, Level of Evidence: C**).

Eligibility to heart transplant

Cardiac amyloidosis

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ISHLT GUIDELINE

The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update

CrossMark

Table 3 Criteria for Prognostic Stratification of Cardiac Involvement in Amyloid Light-Chain Amyloidosis[a]

Stages	Criteria
Stage I	NT-pro BNP < 332 ng/L **and** troponin T < 0.035 μg/L
Stage II	NT-pro BNP > 332 ng/L **or** troponin T > 0.035 μg/L
Stage III	NT-pro BNP > 332 ng/L **and** troponin T > 0.035 μg/L
Low risk stage III	NT-pro BNP 332 to 8,500 ng/L **and** SBP > 100 mm Hg
Intermediate risk stage III	NT-pro BNP > 8,500 ng/L **or** SBP < 100 mm Hg
High risk stage III	NT-pro BNP > 8500 ng/L **and** SBP < 100 mm Hg

NT-pro BNP, N-terminal prohormone brain natriuretic peptide; SBP, systolic blood pressure.

[a]Adapted from Dispenzieri et al[61] and Wechalekar et al.[62]

Eligibility to heart transplant

Cardiac amyloidosis

ELSEVIER

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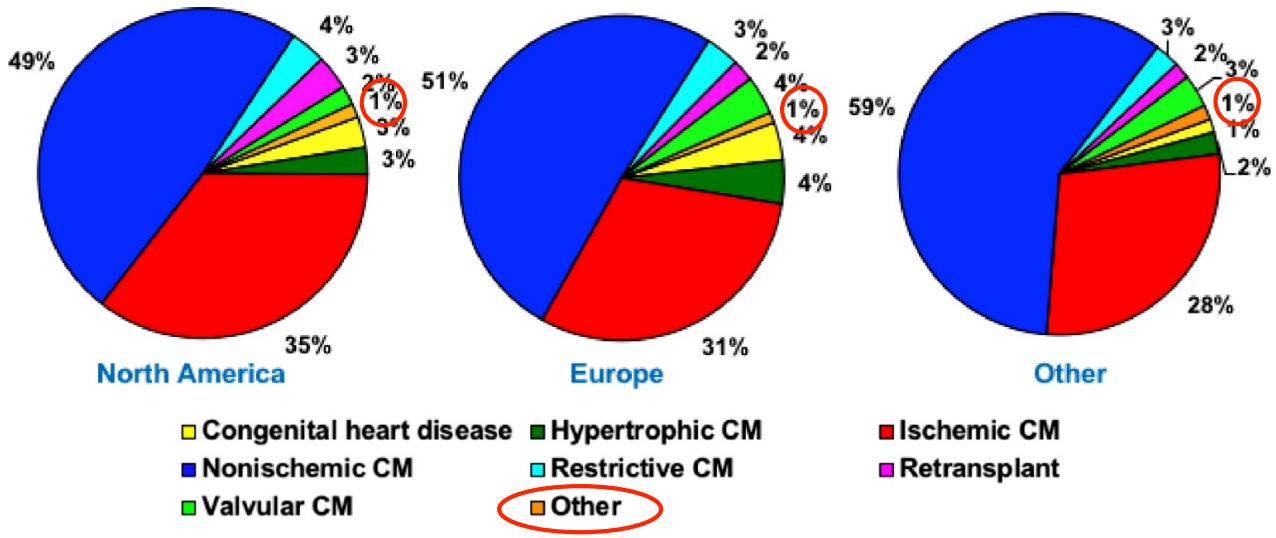
Recommandations	
AL amyloidosis pts not candidates for disease-specific therapies due to cardiovascular compromise. Autologous stem-cell transplantation should be planned.	**IIa B**
TTR cardiac amyloidosis may be considered for HTx	**IIa B**
Familial TTR cardiac amyloidosis pts should be considered for combined heart and liver transplant	**IIa B**
Amyloid extra-cardiac involvement must be carefully evaluated. Severe extra-cardiac amyloid organ dysfunction should be considered a contraindication to HTx	**IIa B**

Heart transplant: the current picture

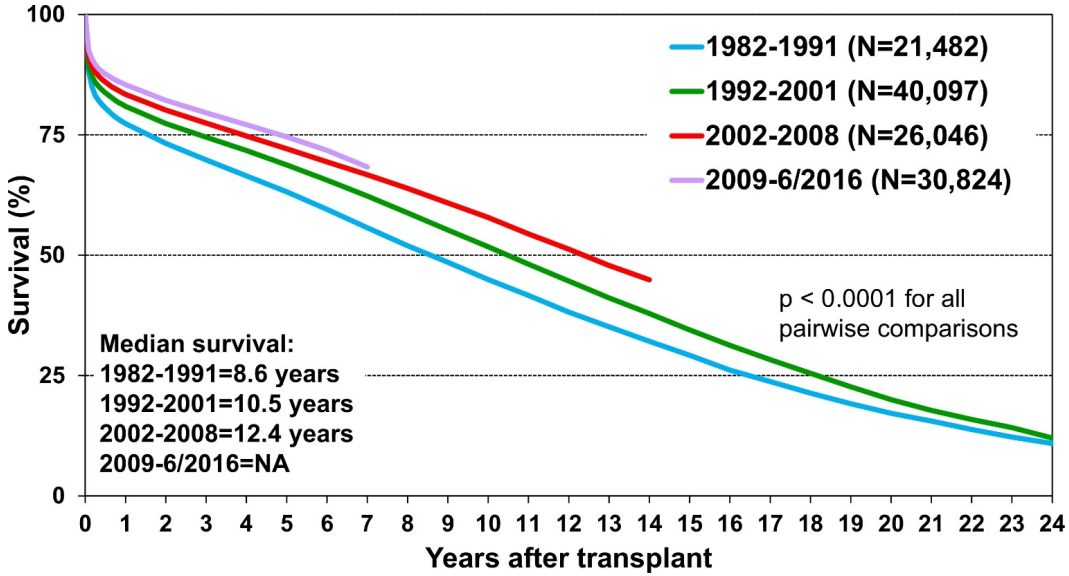
Primary diagnosis by geographic location (adult heart transplants: January 2009 to June 2017)



The 35th ISHLT report on adult heart transplantation
(J Heart and Lung Transplant, 2018, 37:1155-1168)

Heart transplant: the current picture

Kaplan–Meier survival by era (adult heart transplants: January 1982 to June 2016).



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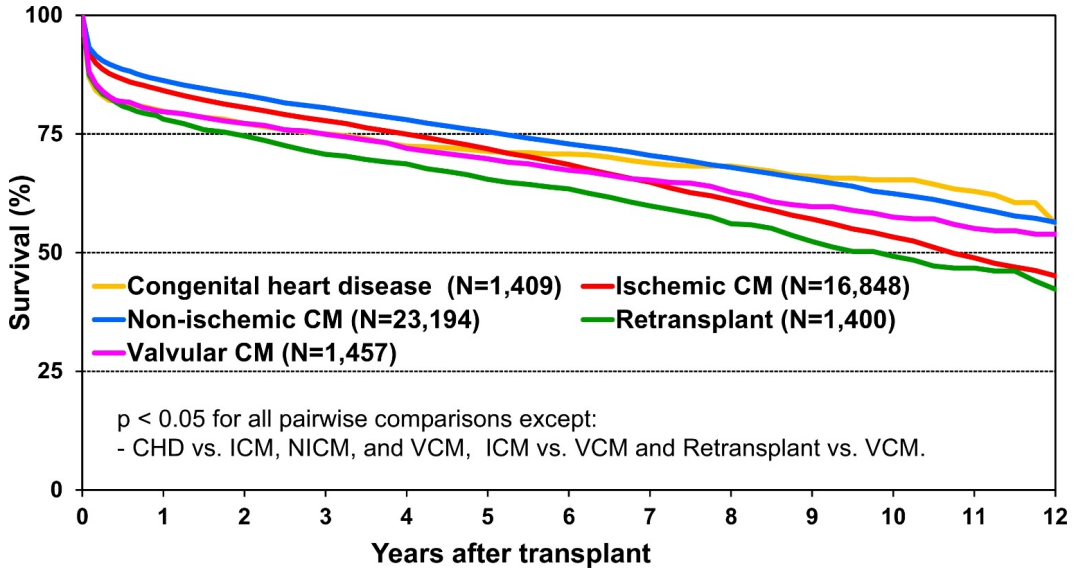
Heart transplant: the current picture

Kaplan–Meier survival by diagnosis (adult heart transplants: January 1982 to June 2016).



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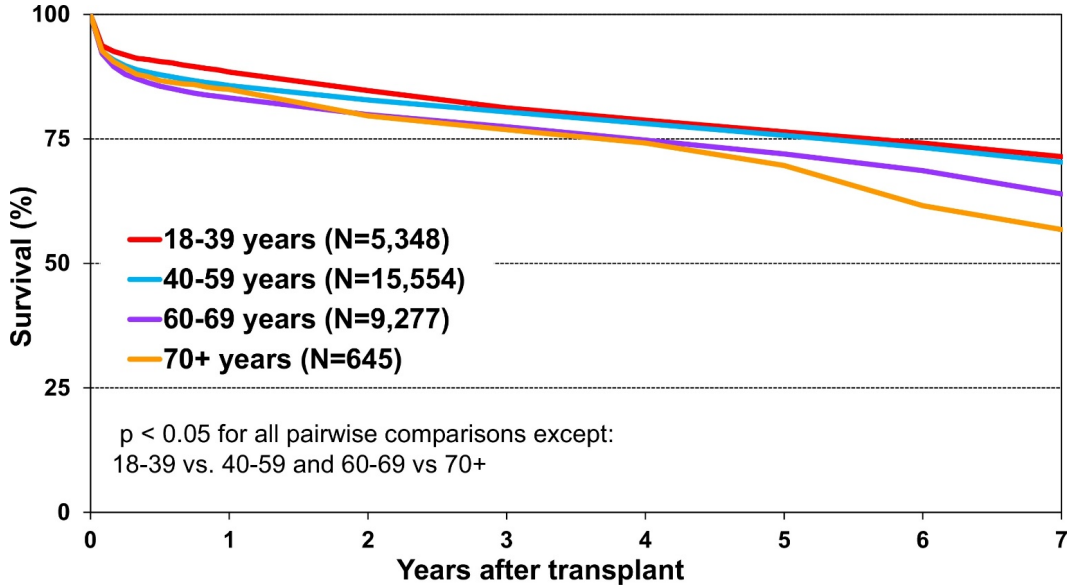
Heart transplant: the current picture

Kaplan–Meier survival by recipient age group (years) (adult heart transplants: January 1982 to June 2016).



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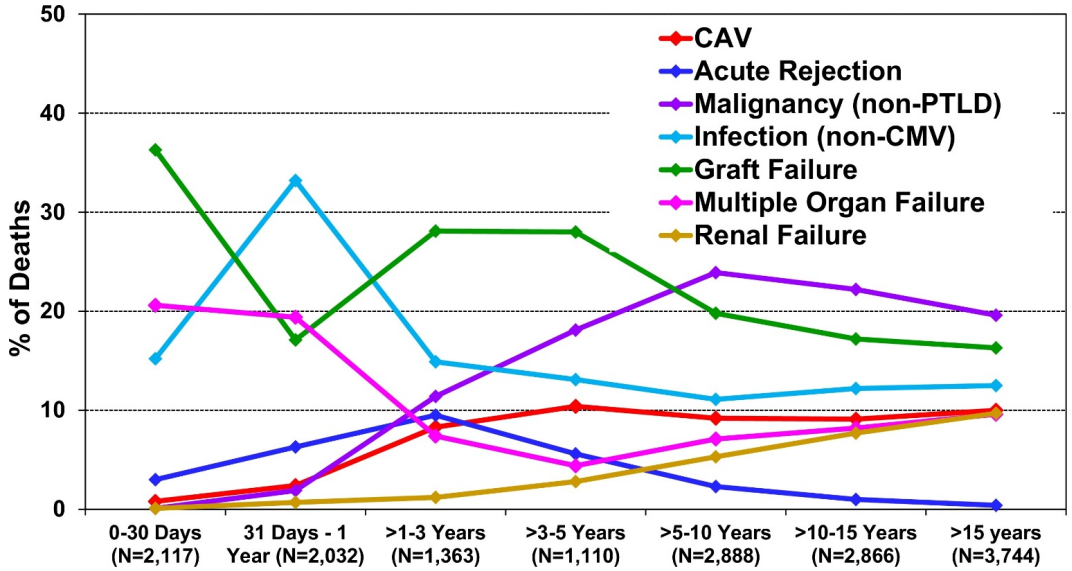
Heart transplant: the current picture

Relative incidence of leading causes of death (adult heart transplants, deaths: January 2009 to June 2017)



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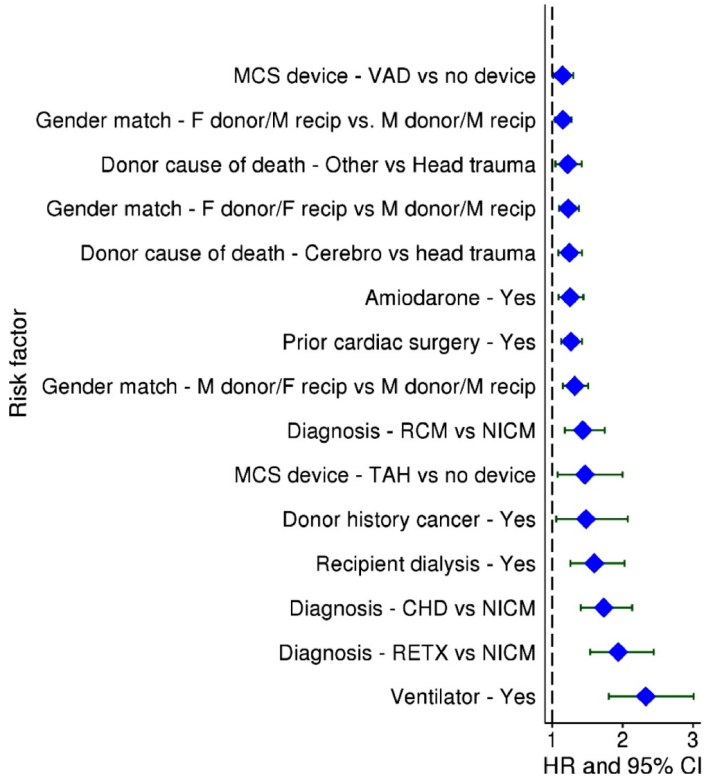
Heart transplant: the current picture

Relative incidence of leading causes of death (adult heart transplants, deaths: January 2009 to June 2017)

Cause of Death	0-30 Days (N=7,048)	31 Days - 1 Year (N=6,076)	>1-3 Years (N=4,298)	>3-5 Years (N=3,693)	>5-10 Years (N=9,428)	>10-15 Years (N=6,759)	>15 Years (N=5,176)
Cardiac Allograft Vasculopathy	90 (1.3%)	212 (3.5%)	494 (11.5%)	483 (13.1%)	1,201 (12.7%)	834 (12.3%)	560 (10.8%)
Acute Rejection	294 (4.2%)	516 (8.5%)	413 (9.6%)	172 (4.7%)	177 (1.9%)	62 (0.9%)	28 (0.5%)
Lymphoma	2 (0.0%)	64 (1.1%)	104 (2.4%)	115 (3.1%)	312 (3.3%)	183 (2.7%)	109 (2.1%)
Malignancy, Other	4 (0.1%)	151 (2.5%)	529 (12.3%)	720 (19.5%)	2,036 (21.6%)	1,438 (21.3%)	985 (19.0%)
CMV	3 (0.0%)	58 (1.0%)	21 (0.5%)	6 (0.2%)	8 (0.1%)	4 (0.1%)	2 (0.0%)
Infection, Non-CMV	981 (13.9%)	1,928 (31.7%)	574 (13.4%)	389 (10.5%)	1,006 (10.7%)	736 (10.9%)	638 (12.3%)
Graft Failure	2,858 (40.6%)	1,074 (17.7%)	1,137 (26.5%)	888 (24.0%)	1,835 (19.5%)	1,176 (17.4%)	862 (16.7%)
Technical	500 (7.1%)	93 (1.5%)	31 (0.7%)	28 (0.8%)	94 (1.0%)	81 (1.2%)	68 (1.3%)
Other	312 (4.4%)	401 (6.6%)	338 (7.9%)	281 (7.6%)	719 (7.6%)	449 (6.6%)	381 (7.4%)
Multiple Organ Failure	1,243 (17.6%)	964 (15.9%)	261 (6.1%)	209 (5.7%)	650 (6.9%)	571 (8.4%)	486 (9.4%)
Renal Failure	30 (0.4%)	53 (0.9%)	57 (1.3%)	114 (3.1%)	516 (5.5%)	538 (8.0%)	509 (9.8%)
Pulmonary	189 (2.7%)	230 (3.8%)	175 (4.1%)	164 (4.4%)	429 (4.6%)	318 (4.7%)	252 (4.9%)
Cerebrovascular	542 (7.7%)	332 (5.5%)	164 (3.8%)	124 (3.4%)	445 (4.7%)	369 (5.5%)	296 (5.7%)
Total Deaths (N)	8,121	6,979	5,276	4,647	12,489	9,763	7,735

Heart transplant: determinants of outcomes



	HR	LCL	UCL	pvalue	N
MCS device - VAD vs no device	1.15	1.01	1.30	0.03	5227
Gender match - F donor/M recip vs. M donor/M recip	1.15	1.04	1.27	<0.01	3645
Donor cause of death - Other vs Head trauma	1.22	1.04	1.42	0.01	1377
Gender match - F donor/F recip vs M donor/M recip	1.23	1.10	1.38	<0.01	3532
Donor cause of death - Cerebro vs head trauma	1.24	1.09	1.42	<0.01	3322
Amiodarone - Yes	1.25	1.09	1.44	<0.01	2850
Prior cardiac surgery - Yes	1.27	1.13	1.42	<0.01	6640
Gender match - M donor/F recip vs M donor/M recip	1.32	1.15	1.51	<0.01	2159
Diagnosis - RCM vs NICM	1.43	1.18	1.74	<0.01	719
MCS device - TAH vs no device	1.47	1.07	2.00	0.02	167
Donor history cancer - Yes	1.48	1.06	2.07	0.02	178
Recipient dialysis - Yes	1.60	1.26	2.03	<0.01	348
Diagnosis - CHD vs NICM	1.73	1.41	2.13	<0.01	667
Diagnosis - RETX vs NICM	1.94	1.54	2.44	<0.01	532
Ventilator - Yes	2.33	1.80	3.01	<0.01	198

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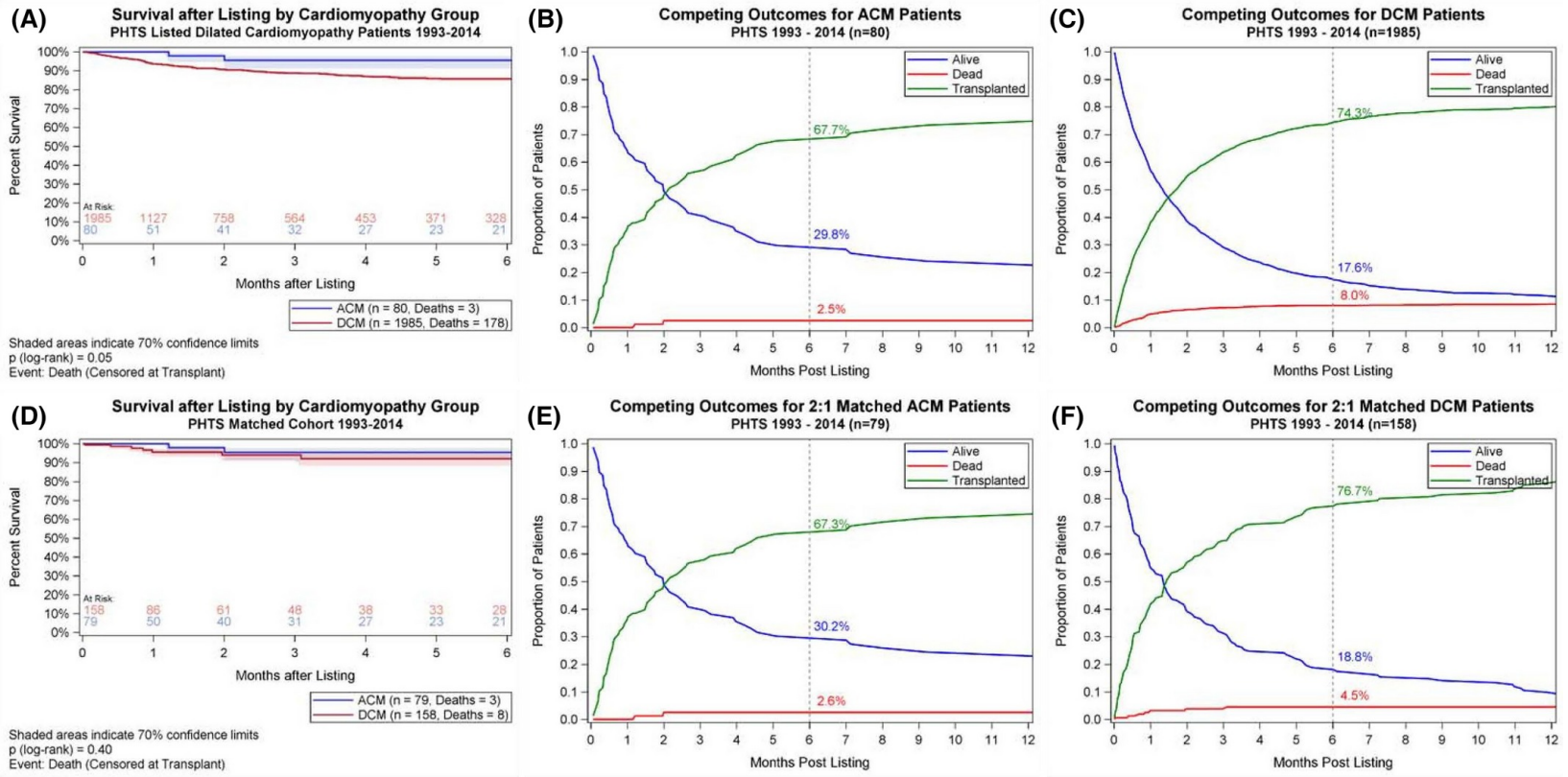
Heart transplant in anthracycline cardiomyopathy (ACM)



Bock M.J. et al. Pediatr Transplant. 2017 Aug;21(5). doi: 10.1111/petr.12923

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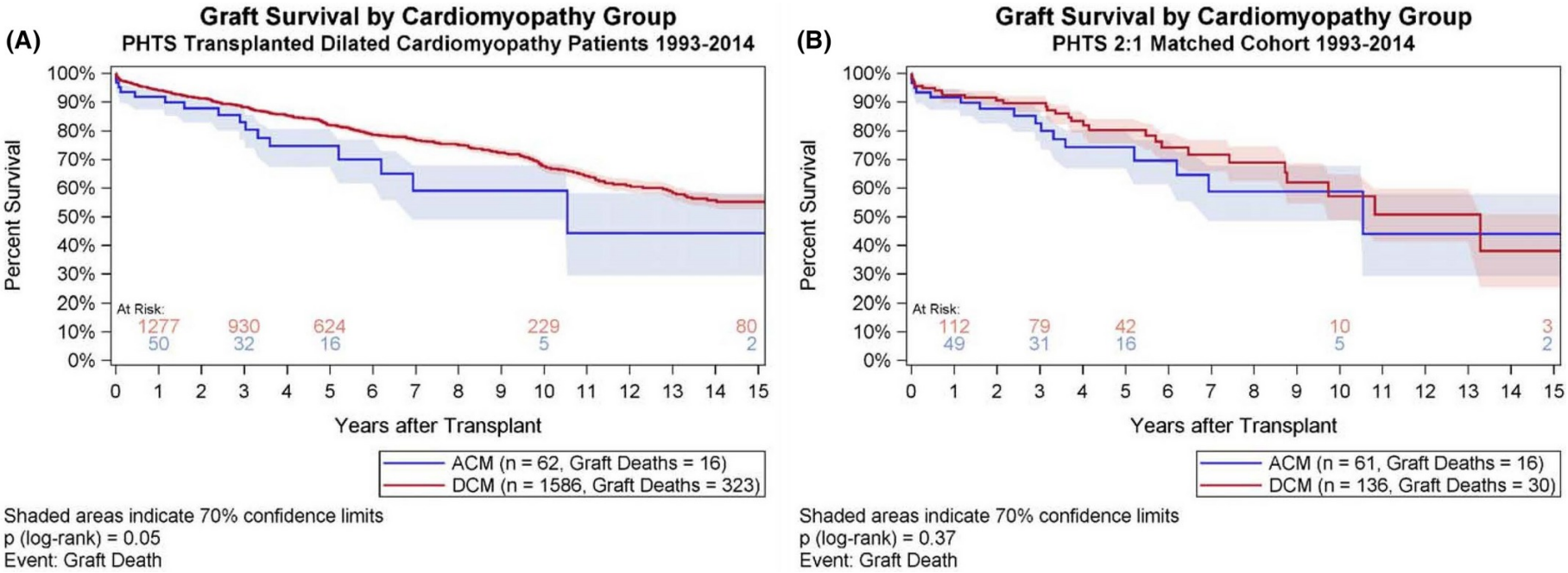

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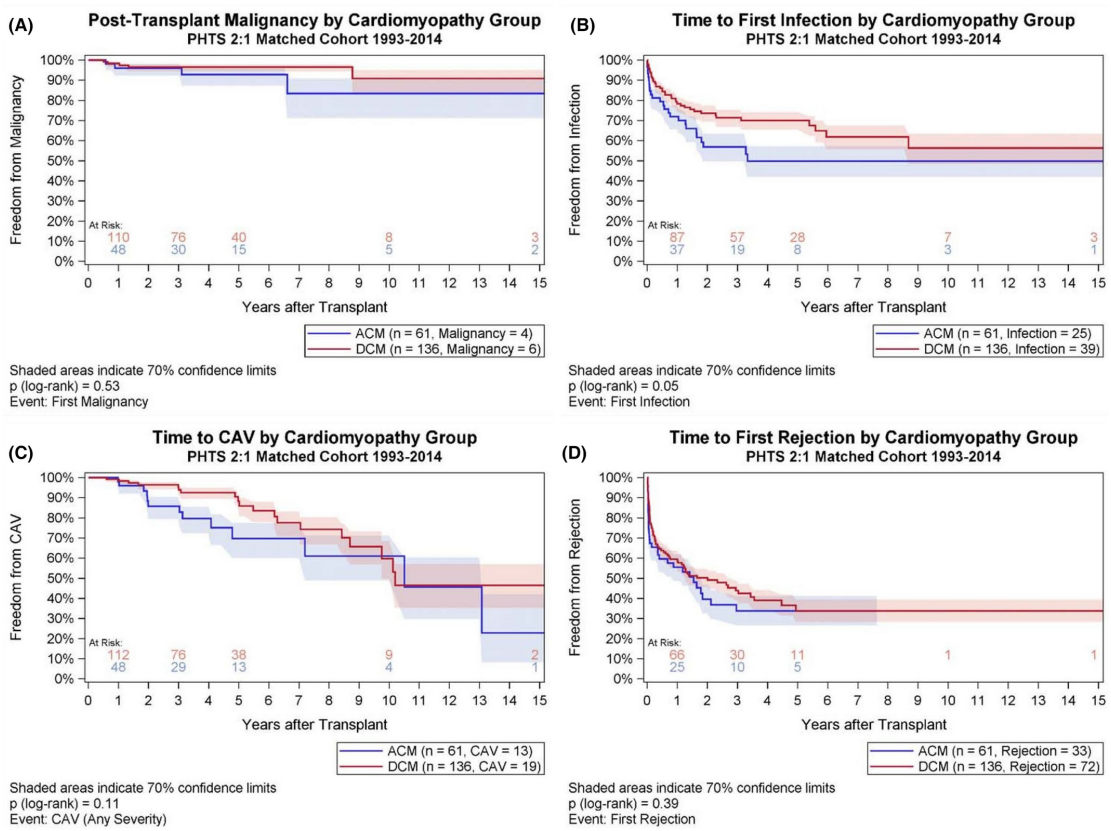

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Heart transplant in anthracycline cardiomyopathy (ACM)

TABLE 3 Multivariate analysis of matched cohort (ACM[b]+matched DCM[c])

Variable	Hazard Ratio	95% CL[d]	*P*-value[a]
Diagnosis of ACM	1.51	0.80, 2.88	.21
Older age at listing	1.08	0.99, 1.18	.09
Female gender	1.88	1.01, 3.53	.05
VAD[e] at listing	3.59	1.14, 11.26	.03
Status 1 at listing	0.61	0.32, 1.16	.13
Earlier era of listing	1.83	1.29, 2.59	<.0001

[a]*P*-values are based on the Cox proportional hazards model with a step-wise selection approach.
[b]anthracycline cardiomyopathy; [c]dilated cardiomyopathy; [d]95% hazard ratio confidence limits; eventricular assist device.
n=197+; Events=52; +—conditional on survival to transplant.

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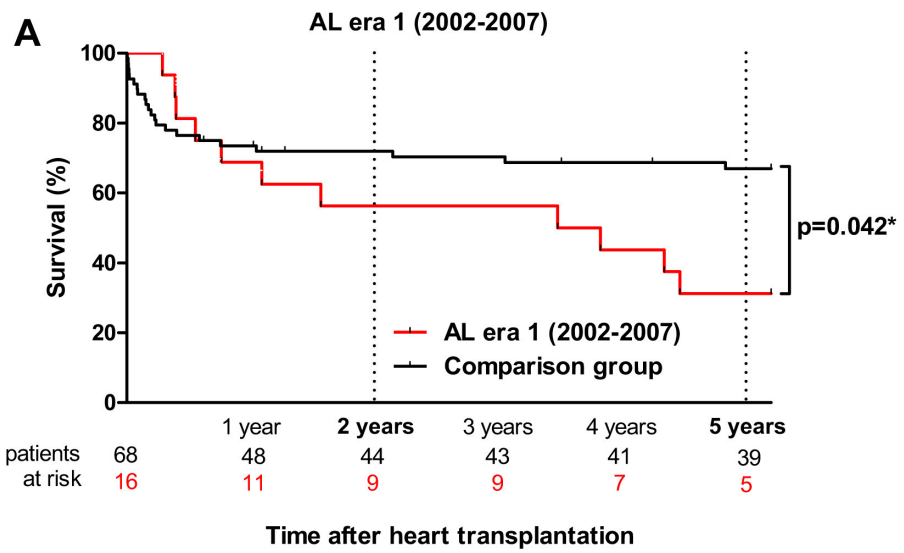
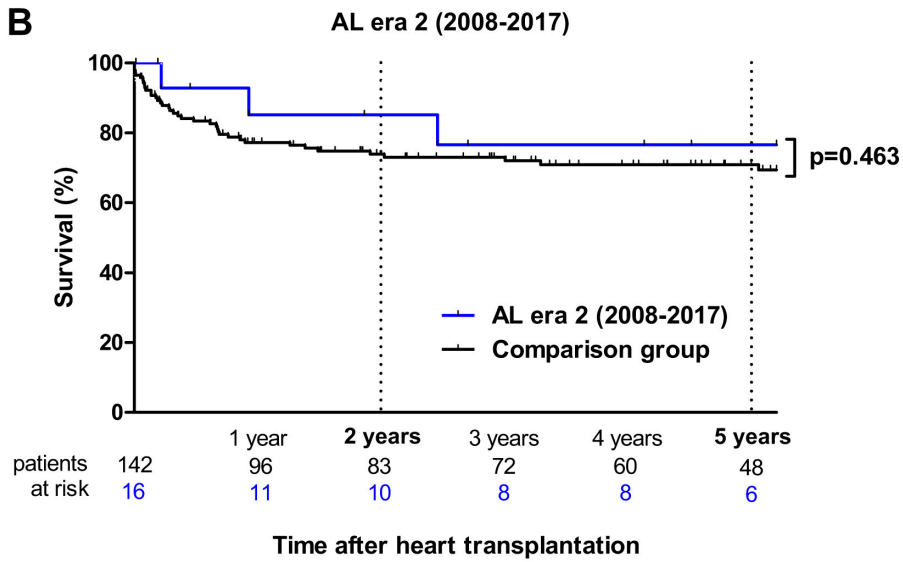
Heart transplant in cardiac amyloidosis

AL amyloidosis





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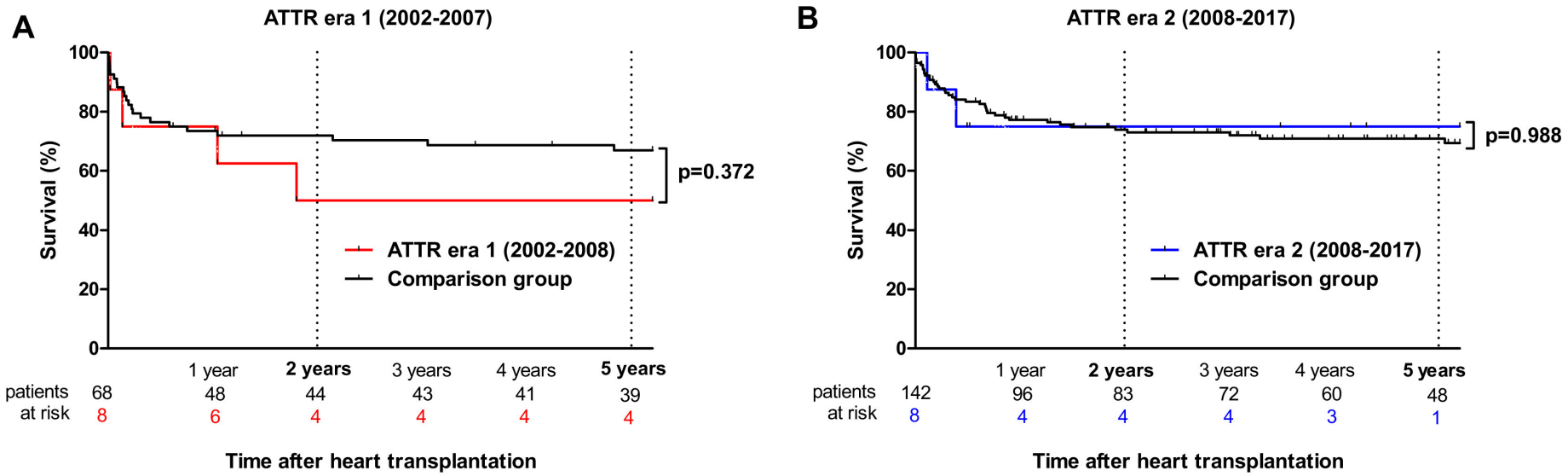
Heart transplant in cardiac amyloidosis

TTR amyloidosis



Kristen A.V. et al. J Heart Lung Transplant. 2018 May;37(5):611-618

Heart transplant ineligible or high risk pts

What to do?

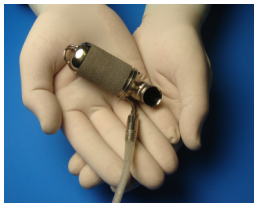
Left ventricular assist device (LVAD)

- ✓ Bridge to transplant
- ✓ Bridge to candidacy
- ✓ Destination therapy

1st generation **2nd generation** **3rd generation**

HeartMate XVE

HeartMate II

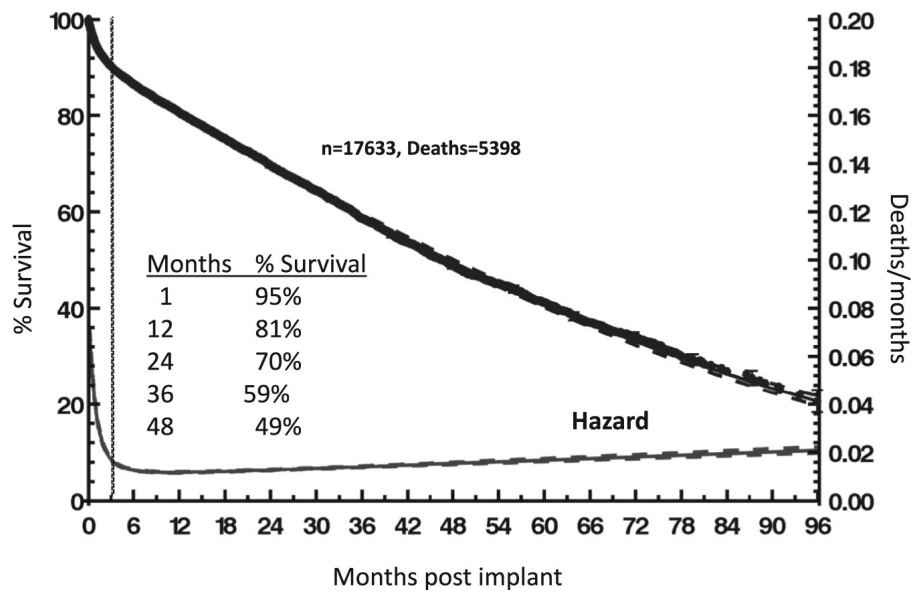


Jarvik 2000

HVAD

HeartMate 3

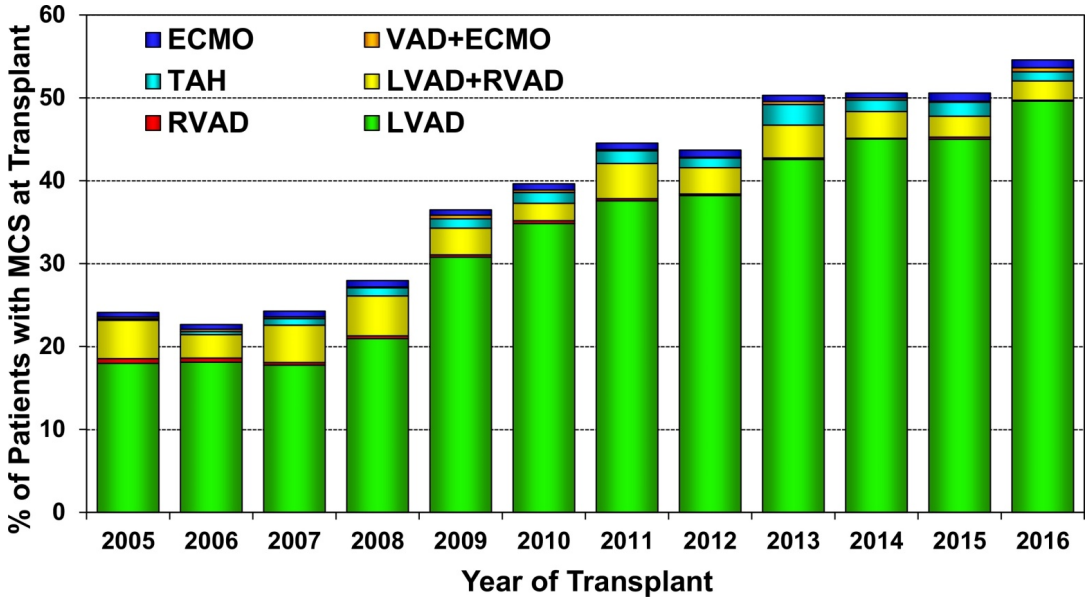
Overall survival of LVAD pts



Eight annual INTERMACS report. J HeartLungTransplant2017;36:1080–1086

LVAD as bridge to transplant

Percent of patients bridged with mechanical circulatory support (MCS) by year and device type (adult heart transplants: 2005 to 2016)



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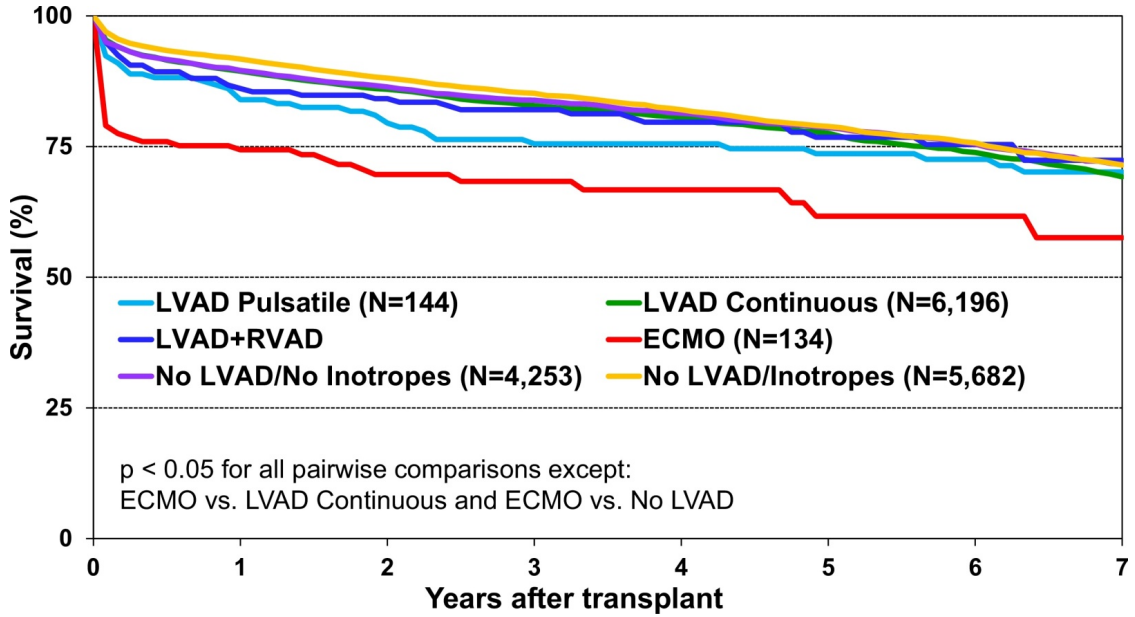
LVAD as bridge to transplant

Kaplan–Meier survival by pre-transplant mechanical circulatory support use (adult heart transplants: January 2009 to June 2016)



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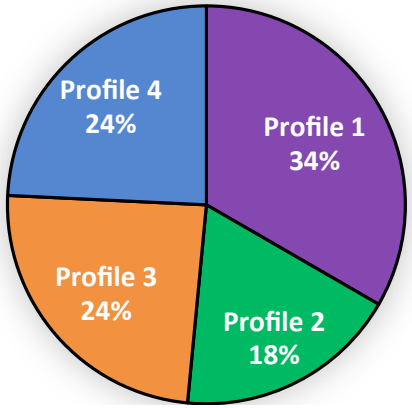
LVAD: the Padova experience (2008-2017)

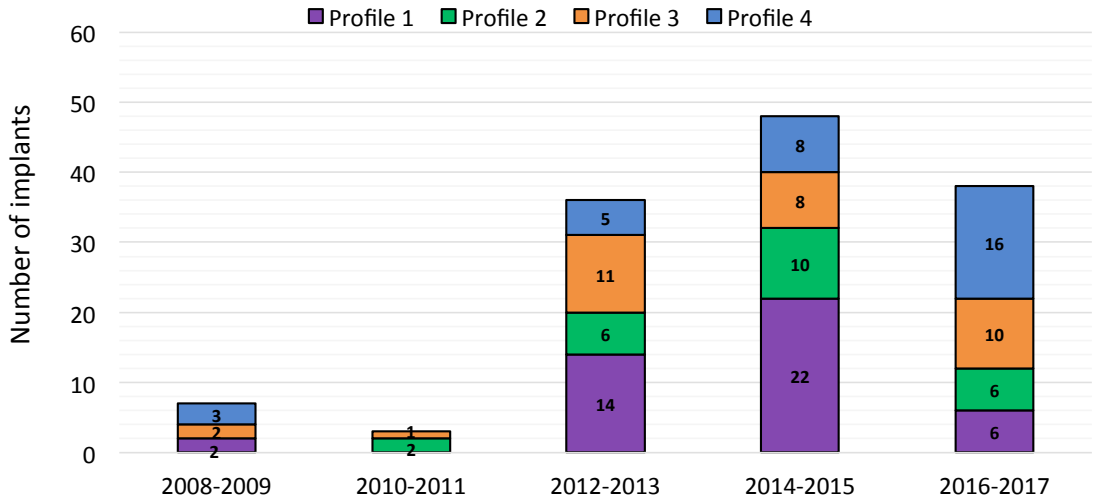
10-year period (Jan 2008 – Dec 2017)

132 LVAD implants

INTERMACS Profiles



Distribution of INTERMACS profiles by era

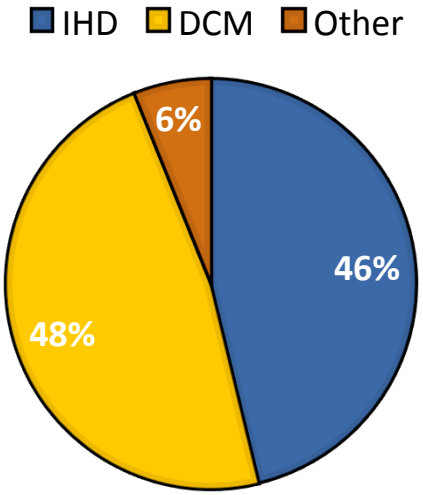


LVAD: the Padova experience (2008-2017)

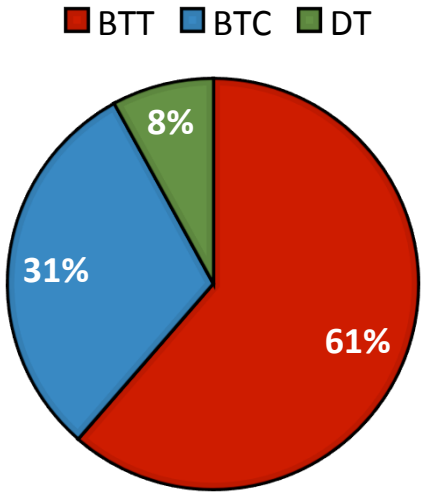
10-year period (Jan 2008 – Dec 2017)

132 LVAD implants

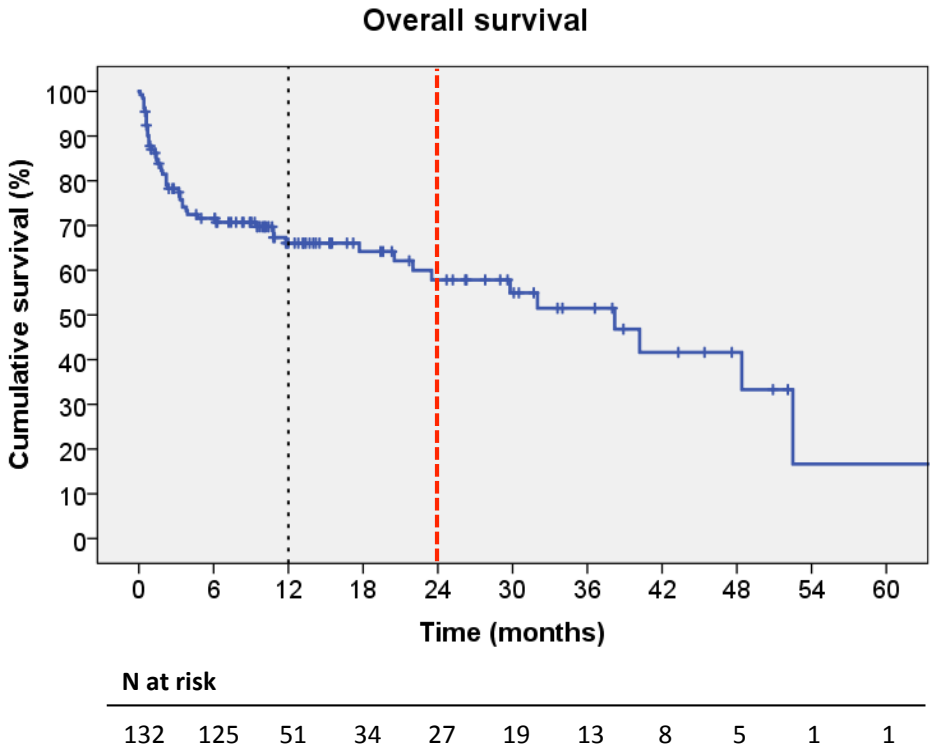
Diagnosis



Device strategy



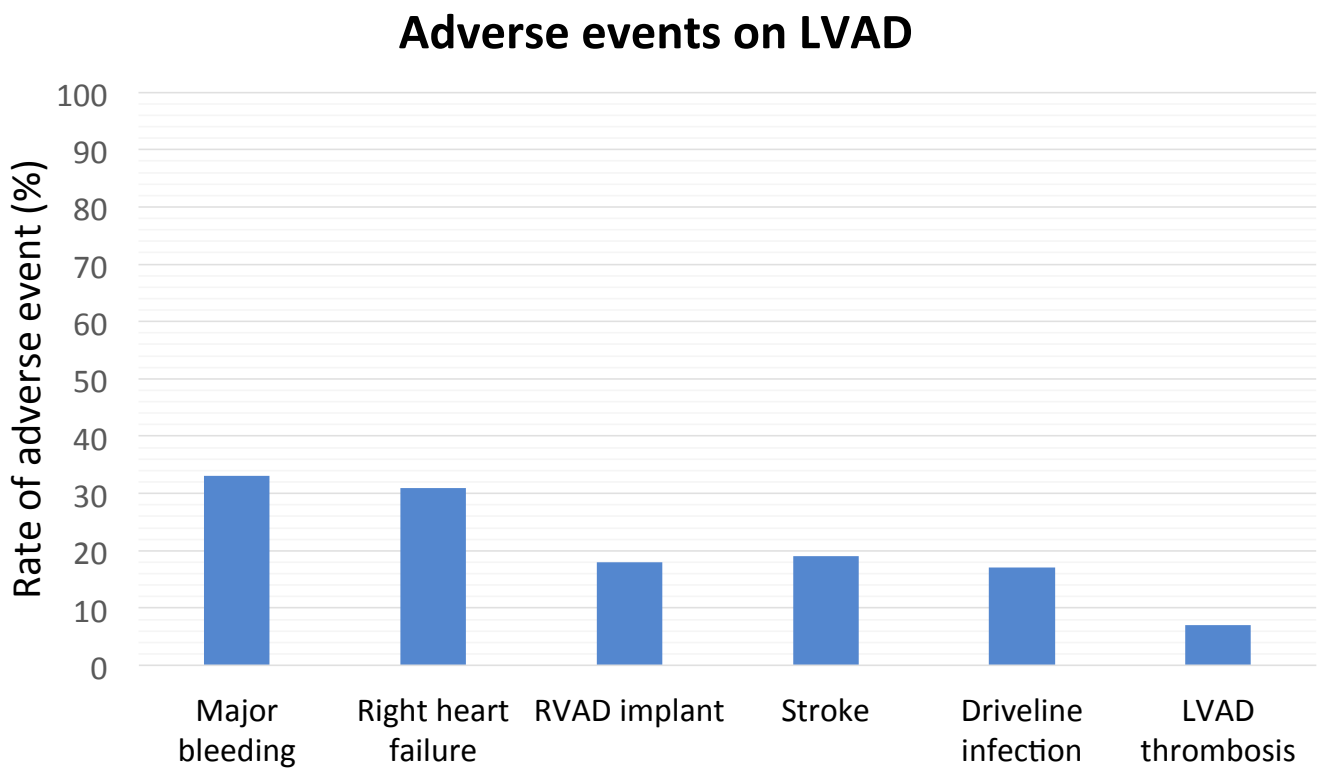
LVAD: the Padova experience (2008-2017)



12-month survival
66% (CI: 57-74%)

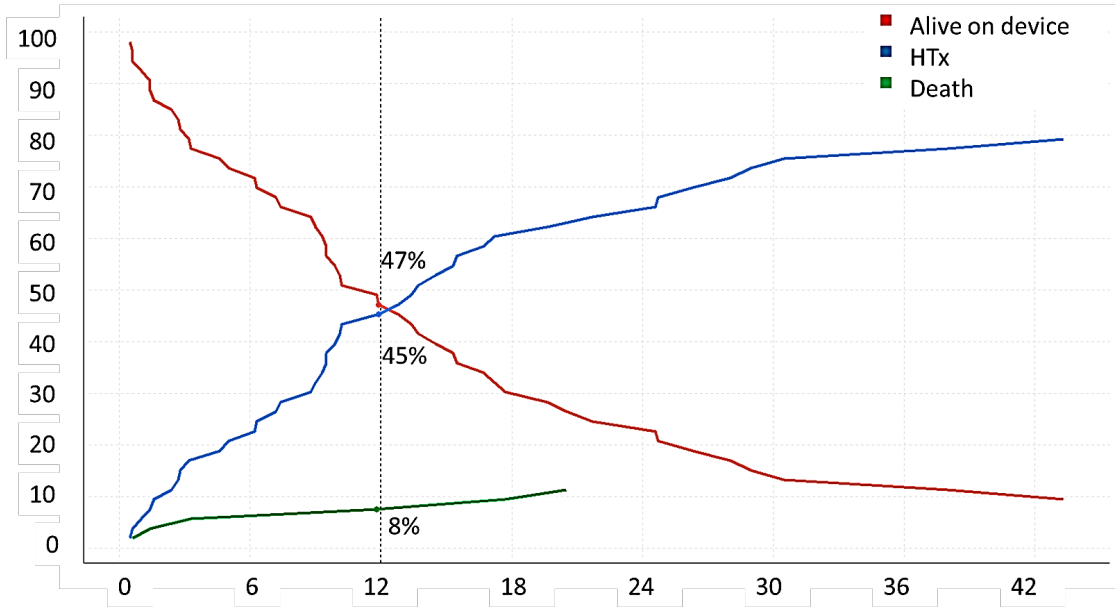
24-month survival
58% (CI: 47-69%)

LVAD: the Padova experience (2008-2017)

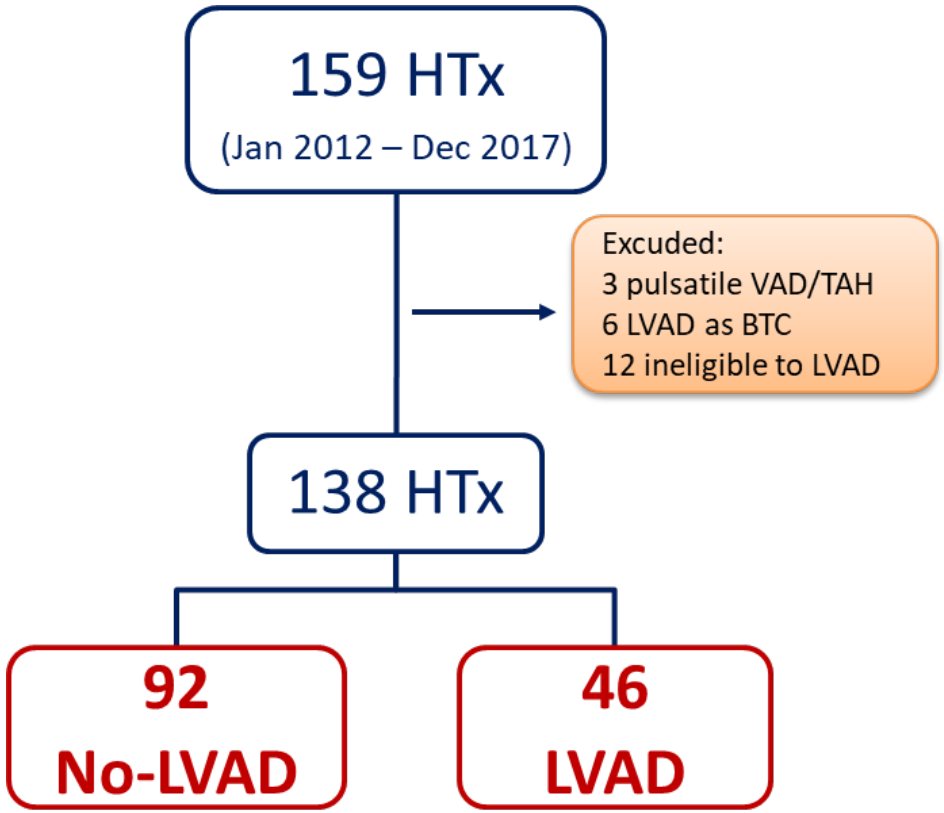


LVAD: the Padova experience (2008-2017)

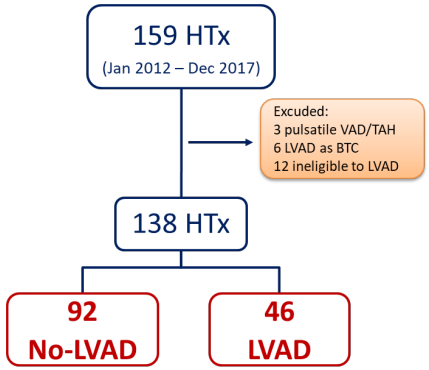
Competing outcomes in BTT patients

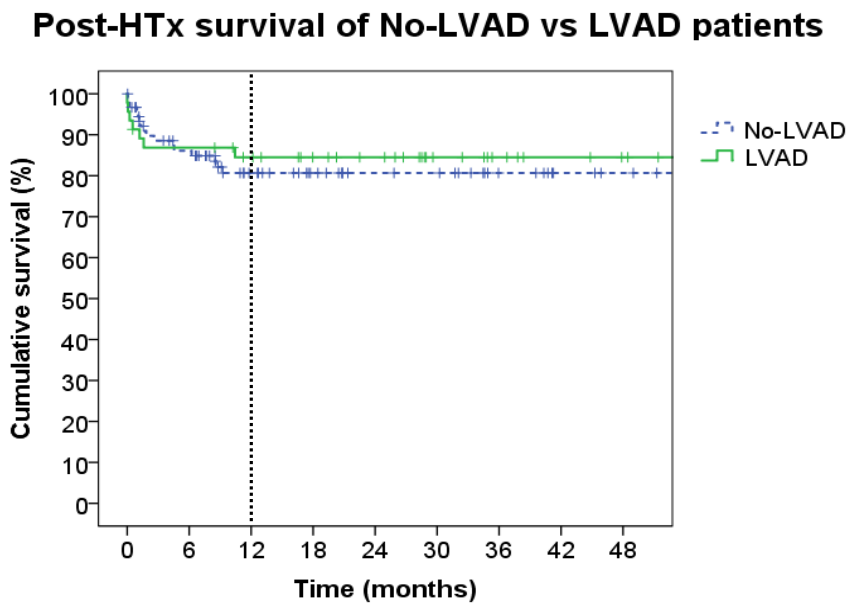


Heart transplant: the Padova experience



LVAD: the Padova experience (2008-2017)

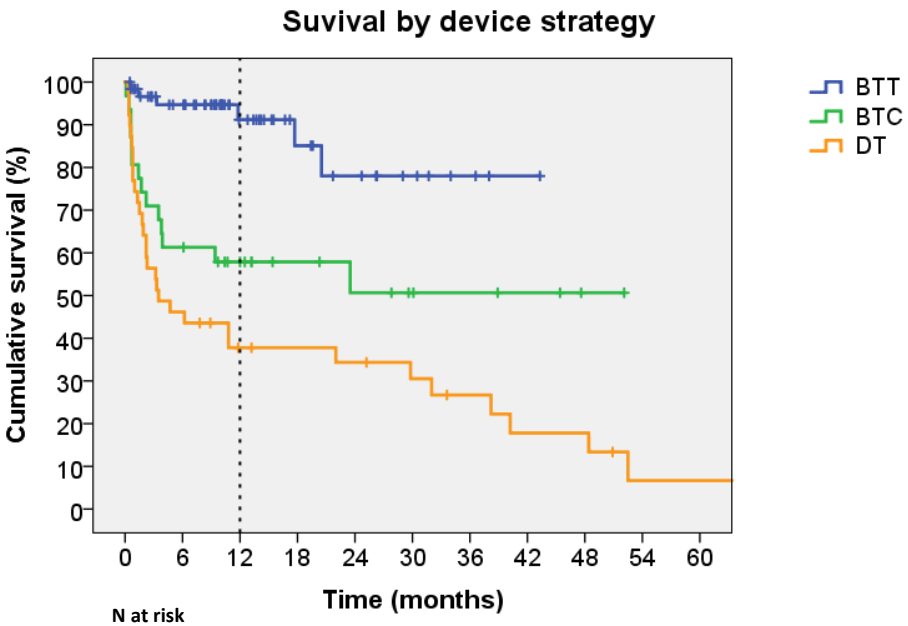




N at risk									
No-LVAD	92	70	51	41	35	33	26	21	19
LVAD	46	39	35	30	26	19	15	12	9

K-M survival of No-LVAD vs LVAD patients. Log-rank p=0.67

LVAD: the Padova experience (2008-2017)



N at risk											
BTT	62	47	25	14	10	5	3	1	0	0	0
BTC	31	19	14	9	7	5	4	3	2	0	0
DT	39	18	12	11	10	8	6	4	4	1	1

12-month survival

- **BTT**
  91% (CI: 82-100%)
- **BTC**
  58% (CI: 41-75%)
- **DT**
  38% (CI: 23-53%)

Log Rank p<0.01

Take-home messages

Take-home messages

- Limited literature on post HTx and post LVAD results of hemopathic patients
- HTx results in ACM comparable to other cardiomyopathies
- HTx results in selected cardiac amyloidosis (no extracardiac involvement) are favourable
- LVAD in HTx ineligible or high risk pts

Thank you