

Medium Term Survival and Functional Status in Patients with Severe Aortic Stenosis Treated by Transcatheter Aortic Valvular Implantation in the PARTNER EU Trial

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Data Extract 7 Aug 09



Disclosure Statement

Nothing to disclose

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Steering Committee:

Wimmer-Greinecker, Schächinger,
Lefevre, De Bruyne, Nataf, DeJaegere

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Trial Overview & Methods

Purpose

- Establish interventional cardiology/ cardiac surgery partnerships to identify, jointly screen and treat adult severe aortic stenosis patients by transfemoral or transapical TAVI

Design

- Prospective, multicenter, non- randomized, observational trial of the Edwards SAPIEN™ THV

Primary Safety Endpoint

- Freedom from death from the index procedure to 30 days and 6 months

Primary Efficacy Endpoint

- Hemodynamic, QOL and NYHA improvement at 12 months

Trial Conduct

- Enrollment period
 - April 2007 – January 2008 – initiated in pre-commercialization period
- Investigator and Site Training
 - 2 day didactic, simulator training, case observations
 - 2 proctored cases each approach (TF/TA)
- Follow-up and Monitoring
 - 30 day, 6, 12 and 18 month intervals
 - 100% monitoring in progress

Trial Oversight

- Echo Corelab – Columbia University Medical Center, NYC (Dr. L. Gillam)
- CEC and DSMB - independent committees to review safety & adjudicate events
 - Administration- European Center for Cardiovascular Research (CERC), Paris
 - 100% event adjudication in progress

Key Inclusion/Exclusion Criteria

- **Inclusion Criteria**

- Logistic EuroSCORE $\geq 20\%$ and/or STS score ≥ 10
- Comorbidities – if EuroSCORE < 20
 - Porcelain aorta, surgically unmanageable ascending aortic calcification
 - Chest deformities that preclude open chest procedures
- Senile degenerative symptomatic aortic valve stenosis with a documented AVA < 0.8 cm², mean gradient > 40 mmHg and/or jet velocity > 4.0 m/s

- **Exclusion Criteria**

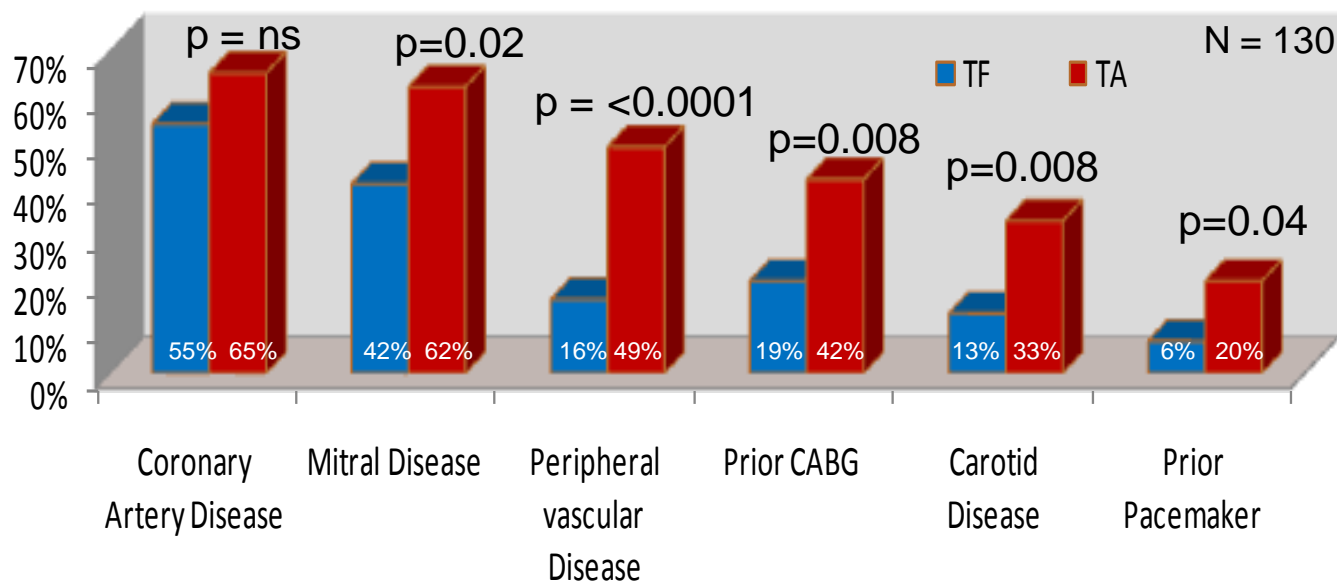
- Evidence of an acute myocardial infarction within 14 days of the intended treatment
- Any therapeutic invasive cardiac procedure, other than BAV, performed within 30 days of the index procedure
- Native aortic annulus < 16 mm or > 25 mm (per baseline ECHO)
- Life expectancy < 12 months due to non-cardiac co-morbid conditions
- Unprotected left main disease ($> 70\%$)
- Active infection or endocarditis
- Acute coronary insufficiency

Baseline Demographics – ITT

	Transfemoral n = 61	Transapical n = 69
Mean Age (yrs)	82.3 ± 5.2 (Range: 69.1-92.5)	81.9 ± 5.7 (Range: 67.7-93.3)
Gender	Female: 61% Male: 39%	Female: 51% Male: 49%
NYHA	I: 2% III: 68% II: 15% IV: 16%	I: 1% III: 68% II: 13% IV: 17%
Mean Aortic Valve Area	0.7 ± 0.2 (Range: 0.3-1.2)	0.7 ± 0.4 (Range: 0.3-2.7)
Mean Gradient	47.3 ± 19.9 (Range: 10-120)	46.7 ± 18.6 (Range: 18-87)
Mean Ejection Fraction	52.7 ± 17.7 (Range: 15.0-86.1)	53.0 ± 14.6 (Range: 17.3-77.0)
Logistic EuroSCORE	25.7 ± 11.5 (Range: 6.4-65.5) Median = 24.4	33.8 ± 14.4 (Range: 5.1-72.1) Median = 29.8
STS Score	11.3 ± 6.1 (Range: 3.7-32.7)	11.8 ± 6.8 (Range: 2-41)

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Comorbidities



• **TA Cohort had greater comorbidities with higher:**

CAD, Mitral disease, PVD, Prior CABG, Carotid Disease, Prior Pacemaker

• **At least one-third of patients enrolled had underlying:**

- Systemic hypertension (71% TF, 77% TA)
- Pulmonary disease (48% TF, 35% TA)
- Chronic kidney disease (37% TF, 46% TA)

Study Flow Chart

▶ Signed Informed Consent

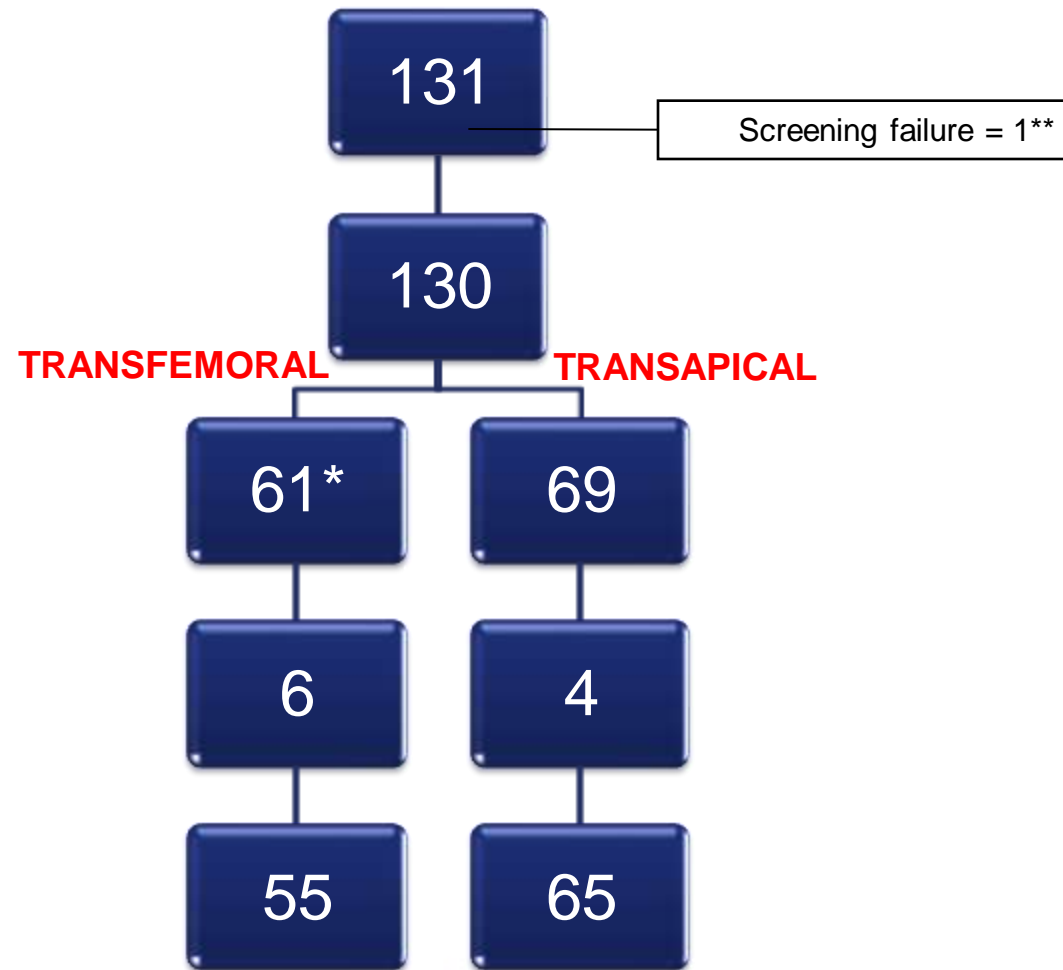
INTENTION-TO-TREAT (ITT)

▶ Attempted Procedure

▶ Aborted Procedure
(No valve implant attempted)

DEVICE IMPLANT PERFORMED

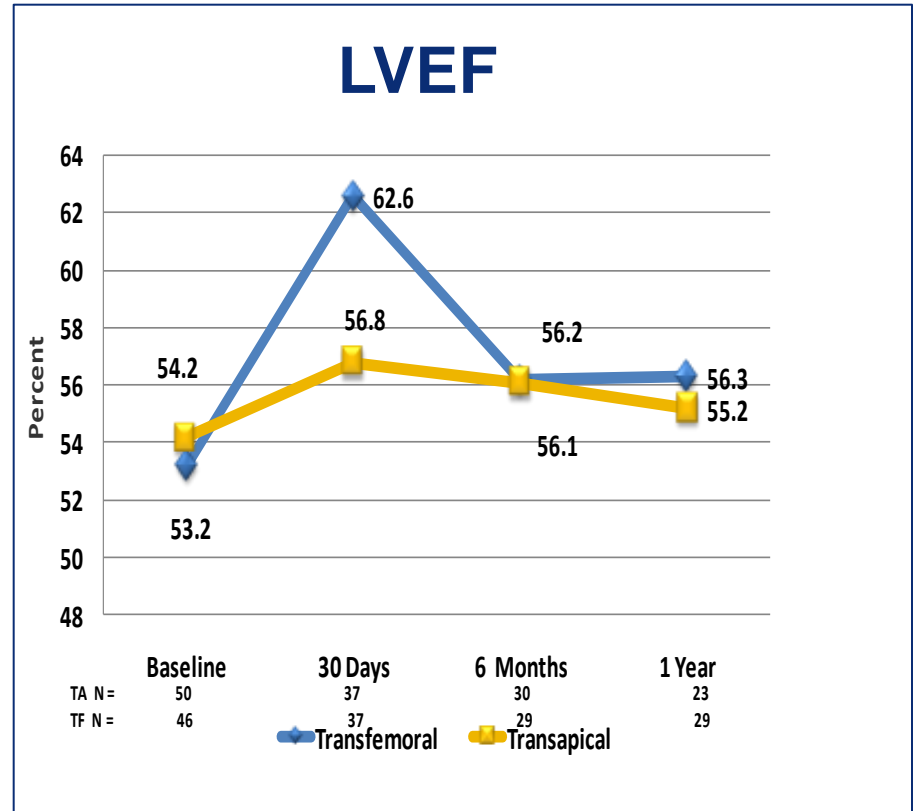
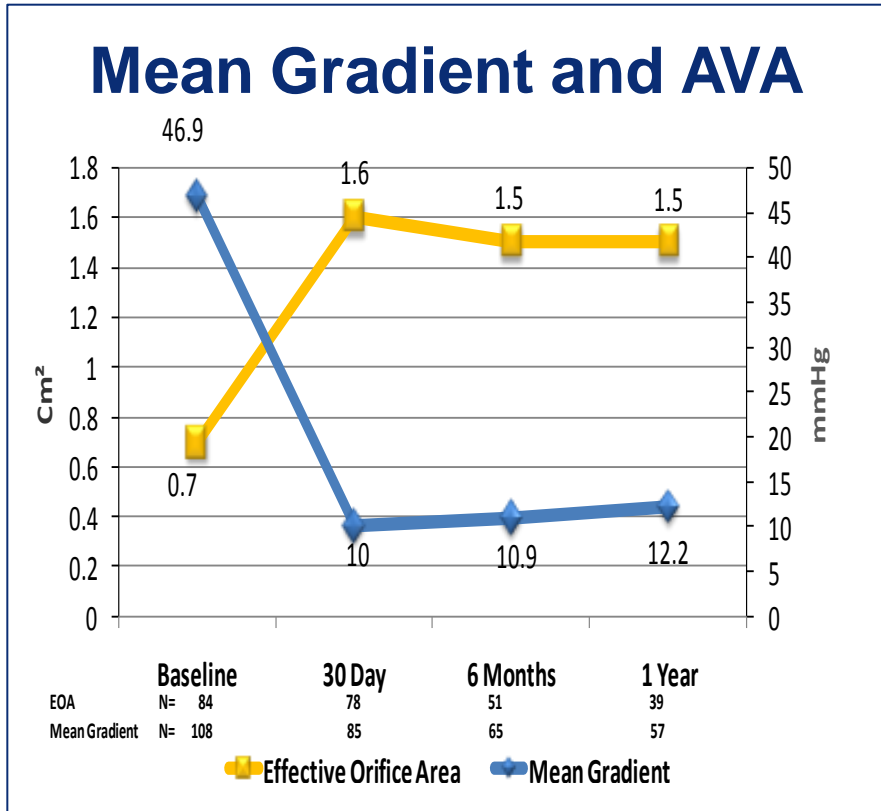
▶ Patient followed per protocol “as intended” (AI)



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* One TF cross-over to TA analyzed is in TF cohort per PARTNER EU Trial Executive Committee ruling
** One screening failure – active endocarditis - 131 patients signed informed consents

Hemodynamics and Valve Performance



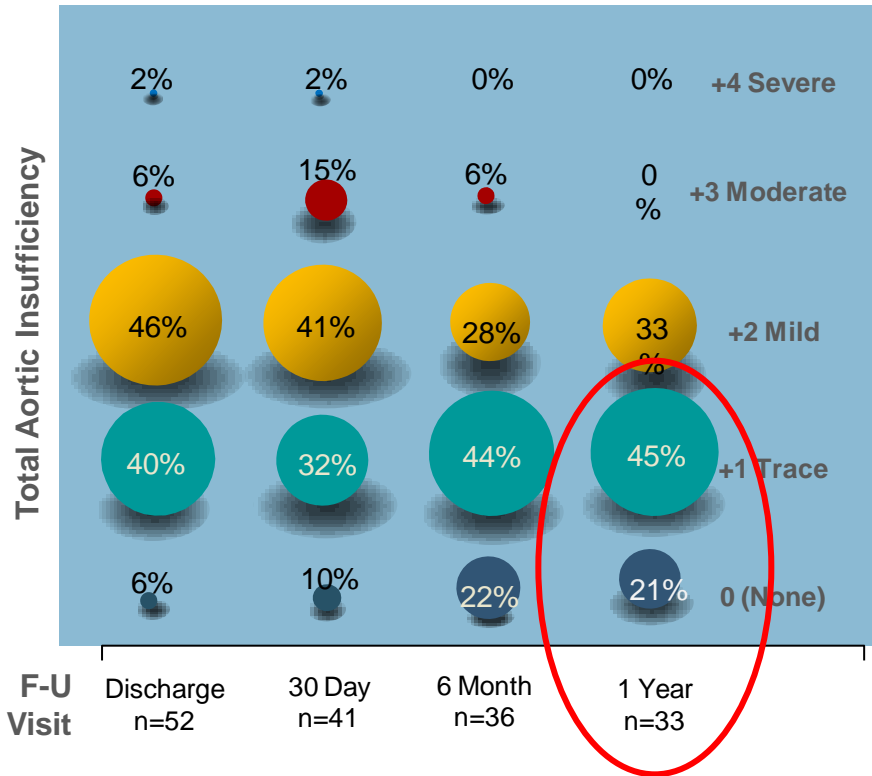
Valve performs as intended with relief of severe stenosis and return to low gradients

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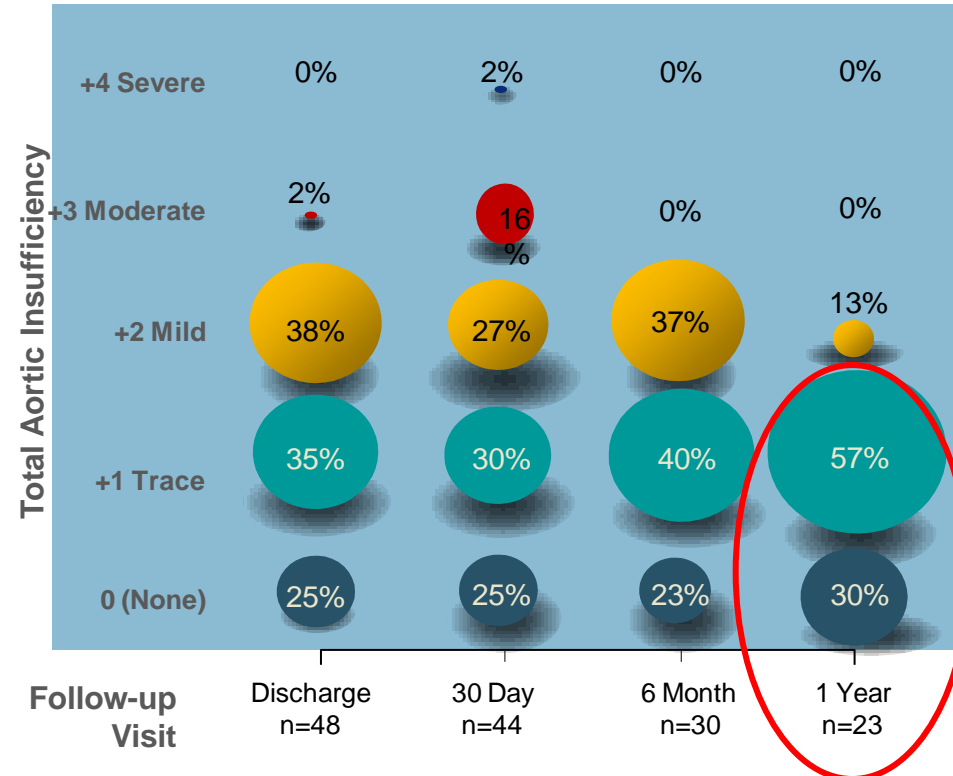


Aortic Insufficiency

Transfemoral



Transapical



**At one year post implant:
66%: 0 or 1+**

**At one year post implant:
87%: 0 or 1+**

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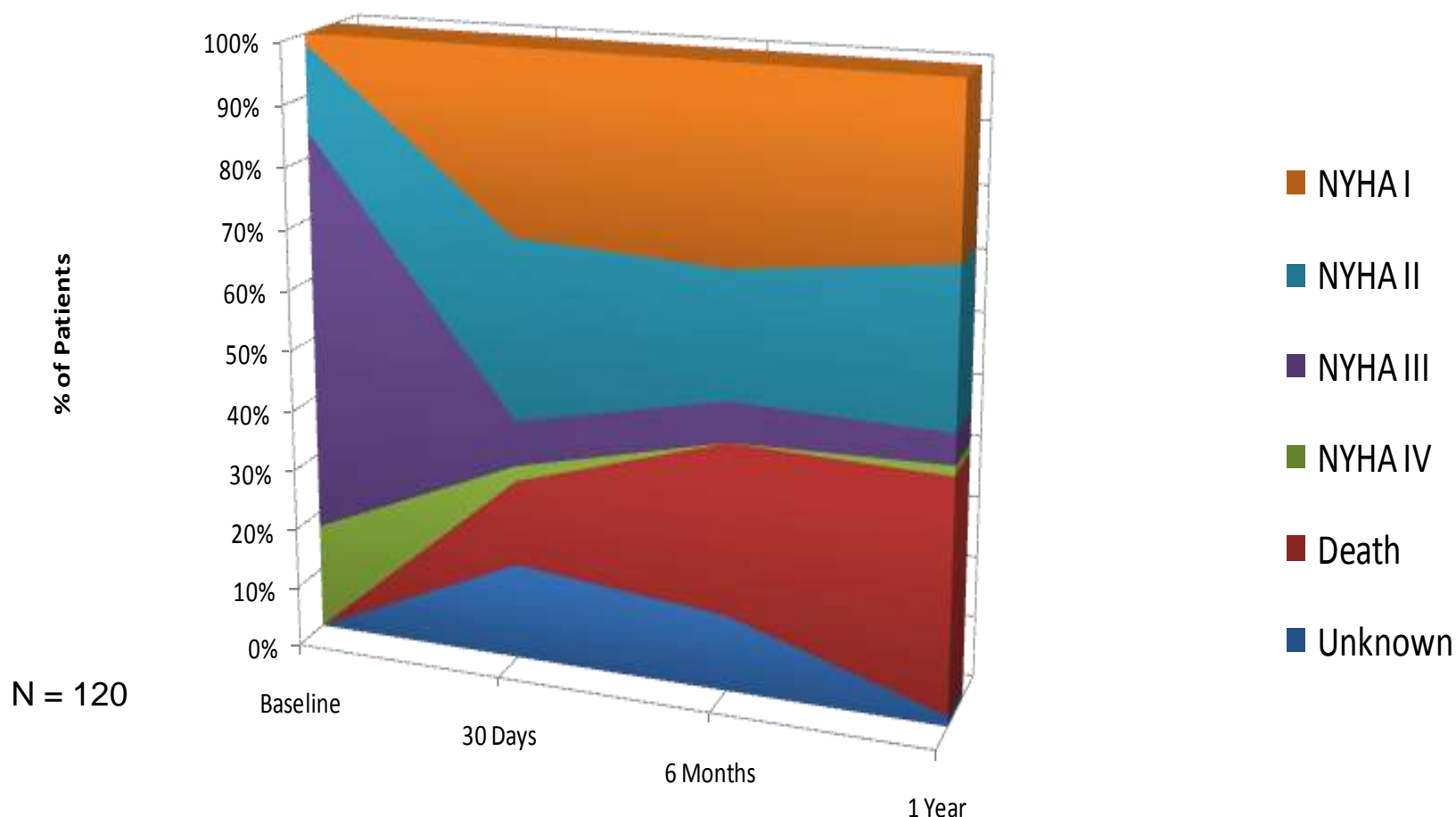


Functional Status

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1-Year NYHA Classification



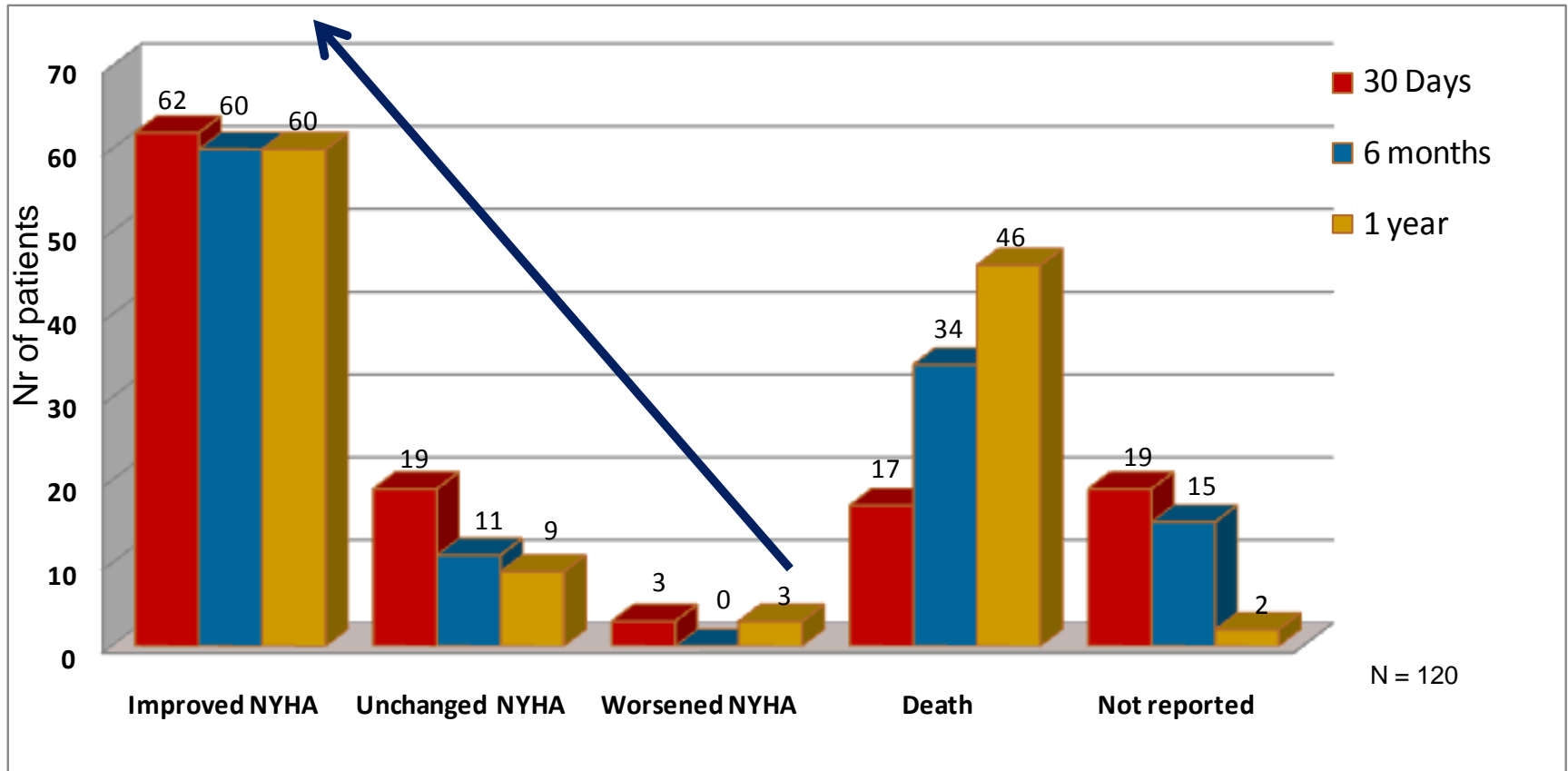
89% of surviving patients in NYHA Class 1 or 2

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N=120

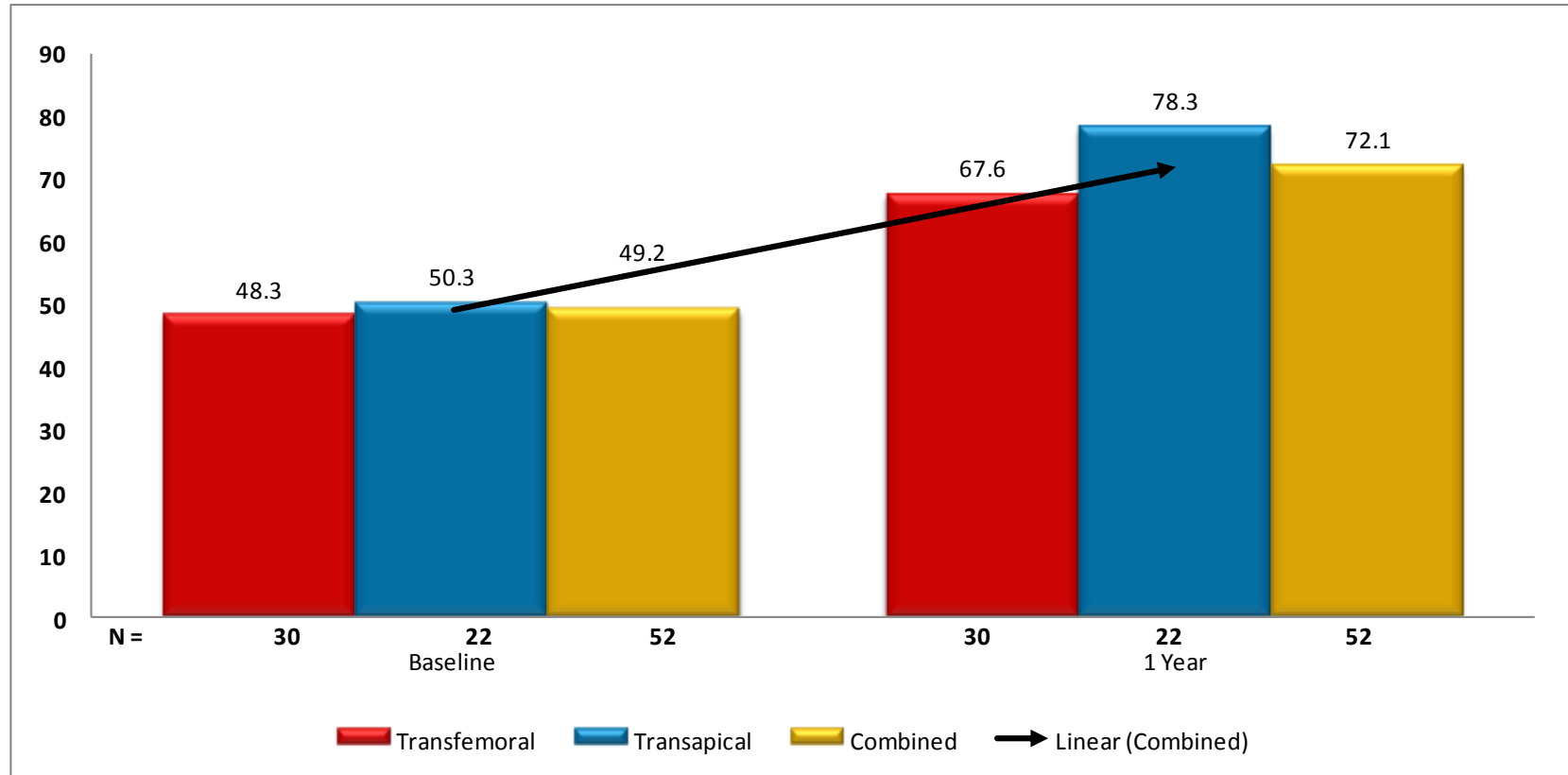
1-Year NYHA Classification



81% had improved NYHA class at 12 months

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Quality of Life – Overall Summary Score

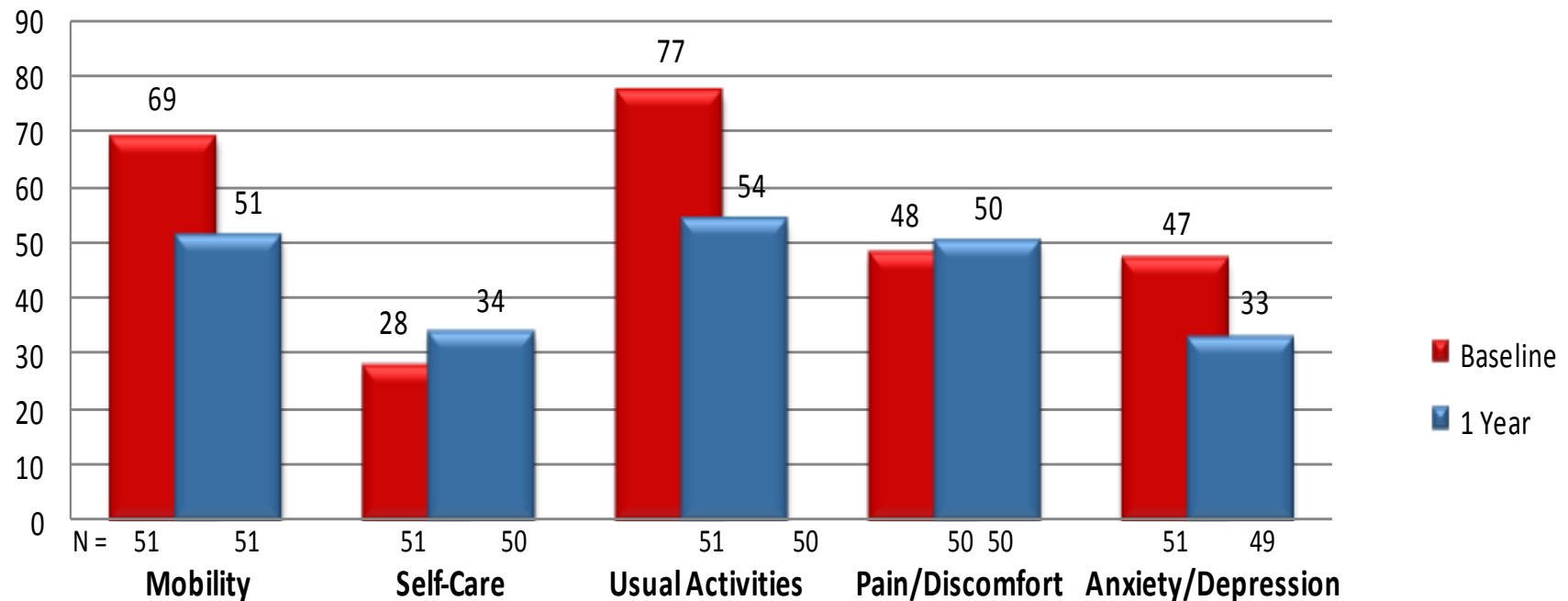


At 1 year post implantation, a large treatment effect is noted by a 22.9 point improvement

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Quality of Life – EQ-5D

% Patients Reporting Problems

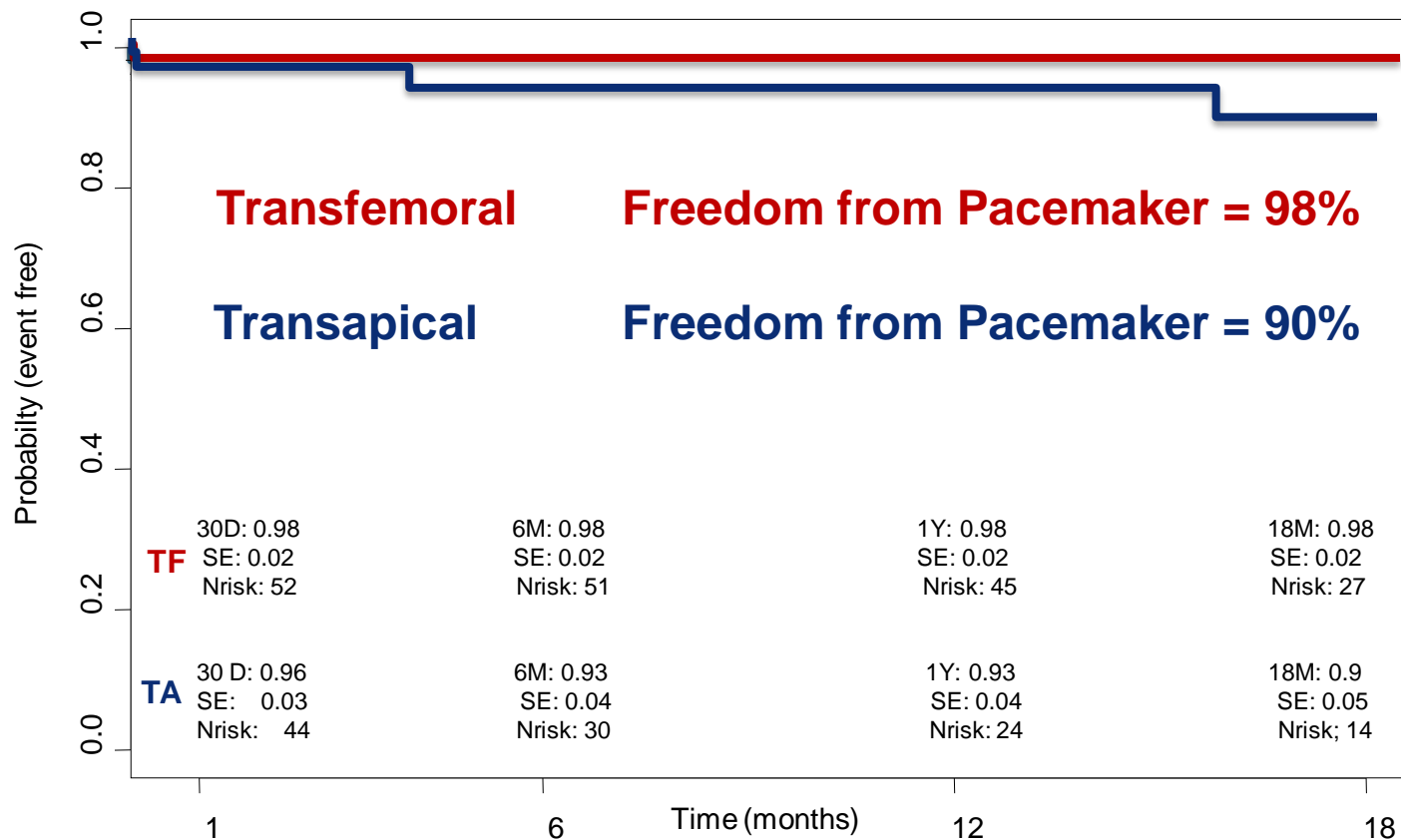


At 1 year post implantation, a meaningful improvement in most activities of daily living is noted

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18 Months - Arrhythmias Requiring Pacemaker

N = 130



30 day pacemaker in conventional AVR = 3.2% – 8.5%¹

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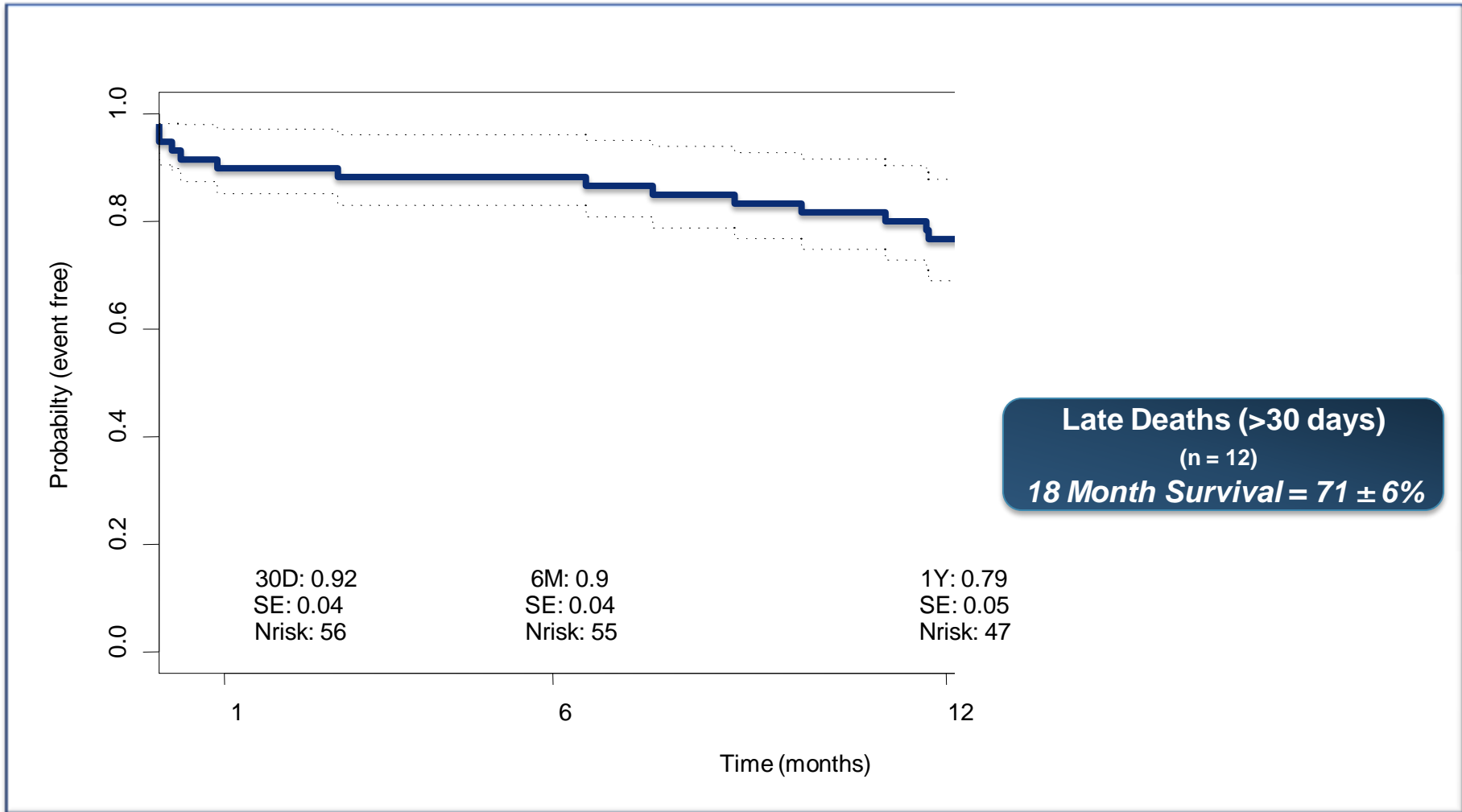
1. Dawkins et al. Permanent Pacemaker Implantation After Isolated AVR, Ann Thorac Surg, 2008, 85:108-12

Survival at 18 months

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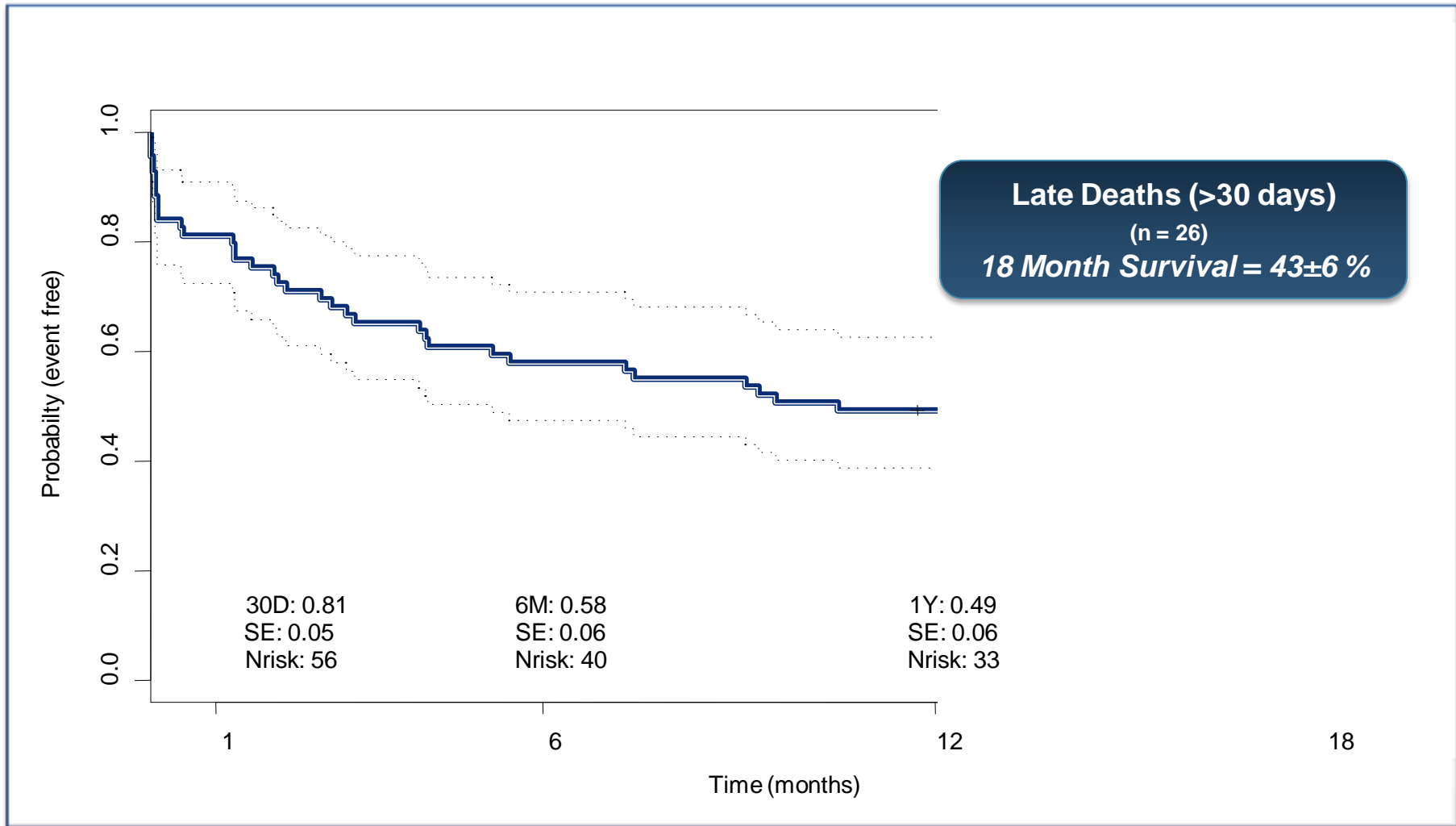
Transfemoral Survival to 18 Months



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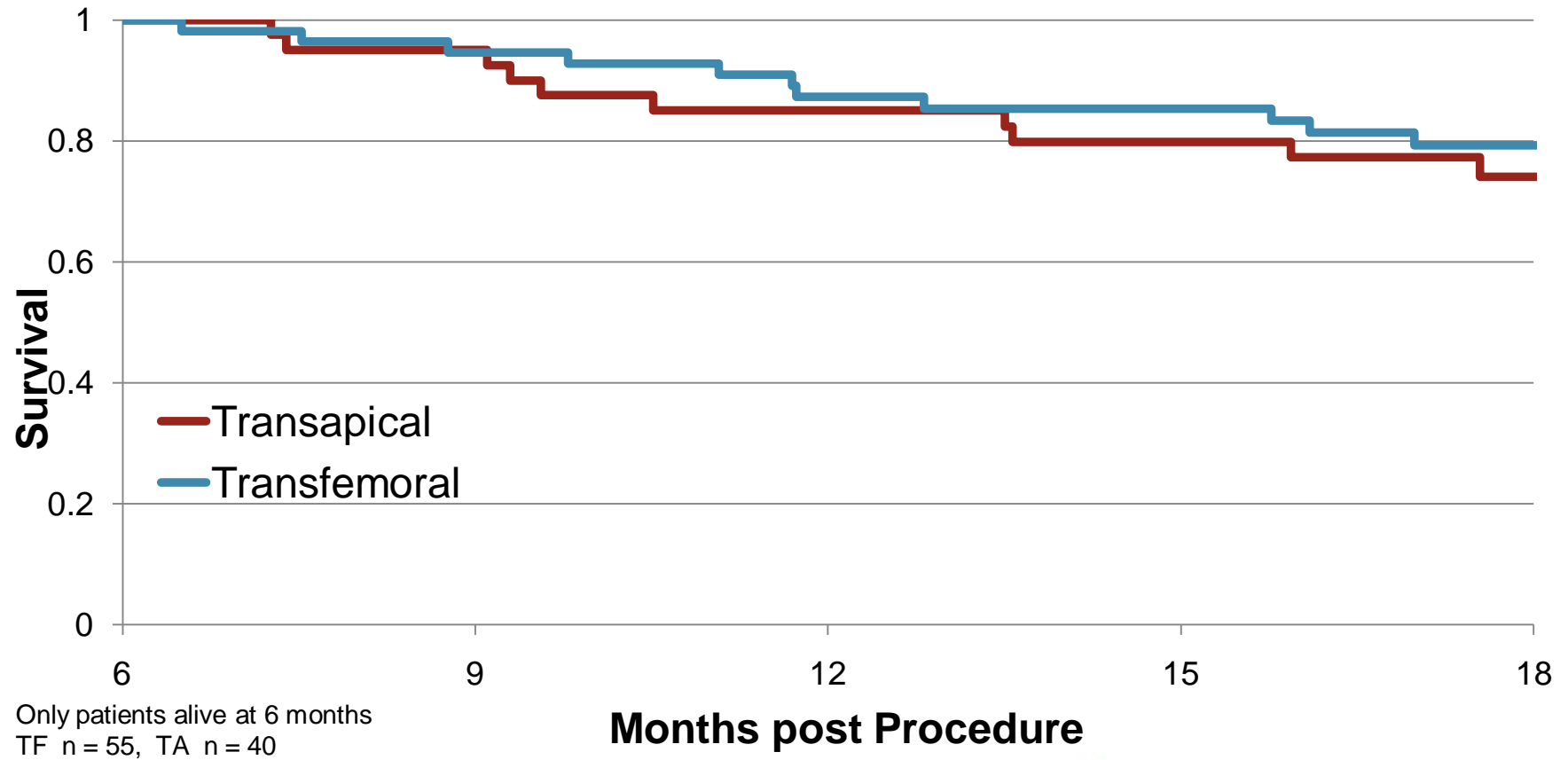
Transapical Survival to 18 Months



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KM Survival Estimate Between 6 and 18 months



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Conclusions

- The PARTNER EU Trial is the first TAVI trial where implant approach (TF or TA) was determined jointly by interventional cardiologists and cardiac surgeons.
- Comparison of survival between TF and TA is problematic due to variability in baseline co morbidity.
- The Edwards SAPIEN™ THV valve shows excellent hemodynamic performance (AR 0 or 1 in the majority of patients), which translates into a marked improvement in functional status and physical and mental wellbeing.
- The Kaplan-Meier survival estimates between 6 to 18 months after implantation are very favorable with no signs of valve deterioration.