



Final five-year clinical and echocardiographic results of treatment for severe aortic stenosis with a self-expanding bioprosthesis from the ADVANCE Study

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for the ADVANCE study investigators



I do not have any potential conflict of interest

I have the following potential conflicts of interest to report:

- Honorarium:
- Institutional grant/research support:
- Consultant: Medtronic, Boston Scientific
- Employment in industry:
- Owner of a healthcare company:
- Stockholder of a healthcare company:
- Other(s): Paid proctor for Medtronic and Boston Scientific

CoreValve ADVANCE Study Background

- Short-term safety and efficacy of transcatheter aortic valve implantation (TAVI) is established for patients with aortic stenosis at high or extreme risk of surgical mortality.^{1,2}
- TAVI with the CoreValve bioprosthesis has also been shown to be non-inferior to surgical valve replacement in patients considered intermediate-risk for surgical mortality.³
- As adoption of TAVI expands into younger, lower-risk patients, longer-term clinical outcomes and bioprosthetic valve durability are of increasing importance.

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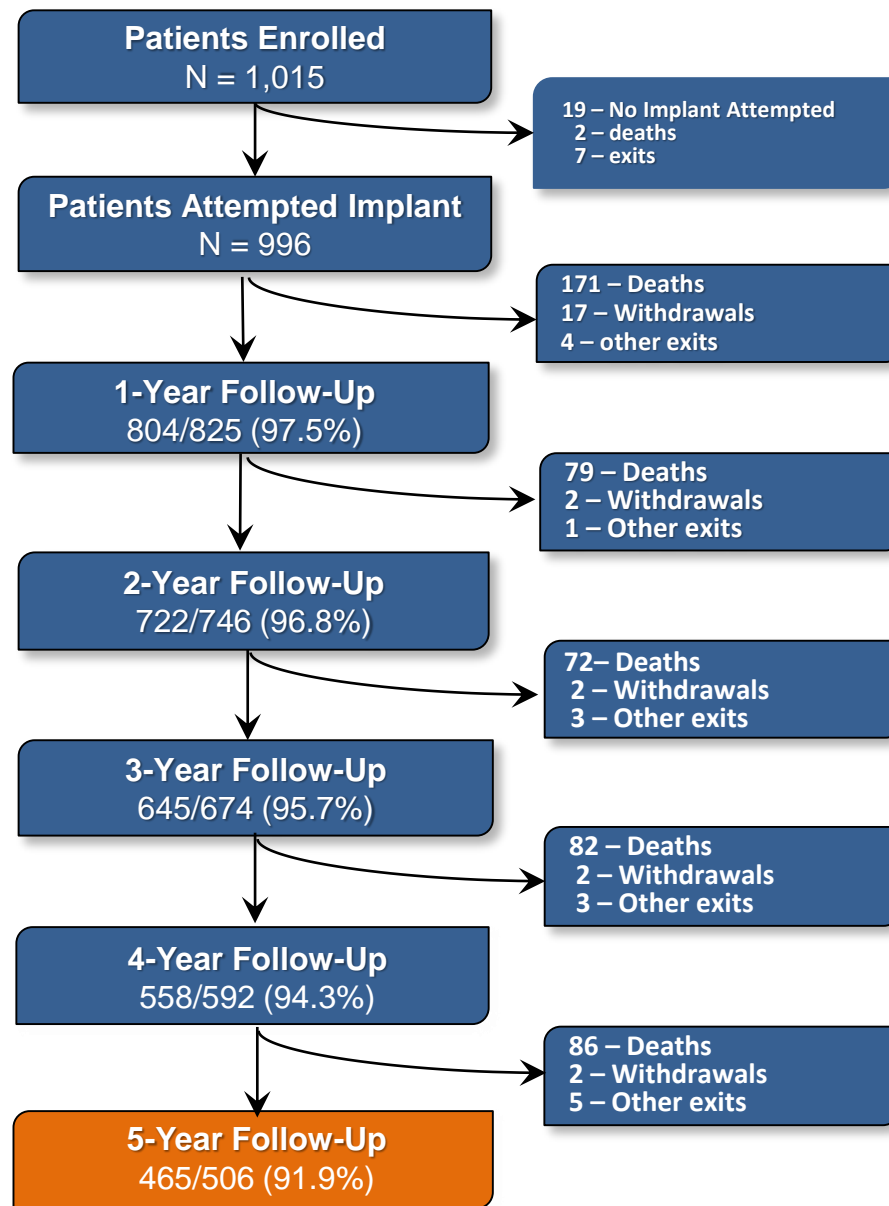
Design and Methods

- ADVANCE is a multicenter, prospective, single-arm, observational study to evaluate safety and performance of the CoreValve bioprosthesis in a routine hospital setting.
- The current analysis includes:
 - 5-year clinical and echocardiographic follow-up of 996 “real world” patients
 - 5-year mortality stratified by pacemaker use, logistic EuroSCORE and discharge aortic regurgitation
 - Multivariable predictors of mortality through 5 years
 - Analysis of valve durability using VARC-2 criteria for valve dysfunction, re-interventions after 30 days and proportion of patients with >50% increase in mean gradient from 1 month to 5 years

- 1,015 patients enrolled from March 2010 to July 2011
- 44 centres in 12 countries in Western Europe, Asia, and South America
- Clinical endpoints reported according to VARC 1
- 100% of patients were monitored
- All endpoints adjudicated by an independent CEC
- Site reported echo data

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Patient Flow



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Baseline Characteristics

mean \pm standard deviation or %	CoreValve N=996
Age (years)	81.1 \pm 6.4
Male	49.3
STS PROM score (%)	6.4 \pm 4.4
Logistic EuroSCORE (%)	19.3 \pm 12.3
New York Heart Association class III/IV	80.0
Diabetes mellitus	31.3
Renal failure	14.4
Chronic obstructive pulmonary disease	22.8
Cerebrovascular disease	13.4
Prior PCI	31.4
Prior CABG	21.3
Atrial fibrillation	33.5
Peripheral vascular disease	19.9
Coronary artery disease	57.9

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Clinical Outcomes

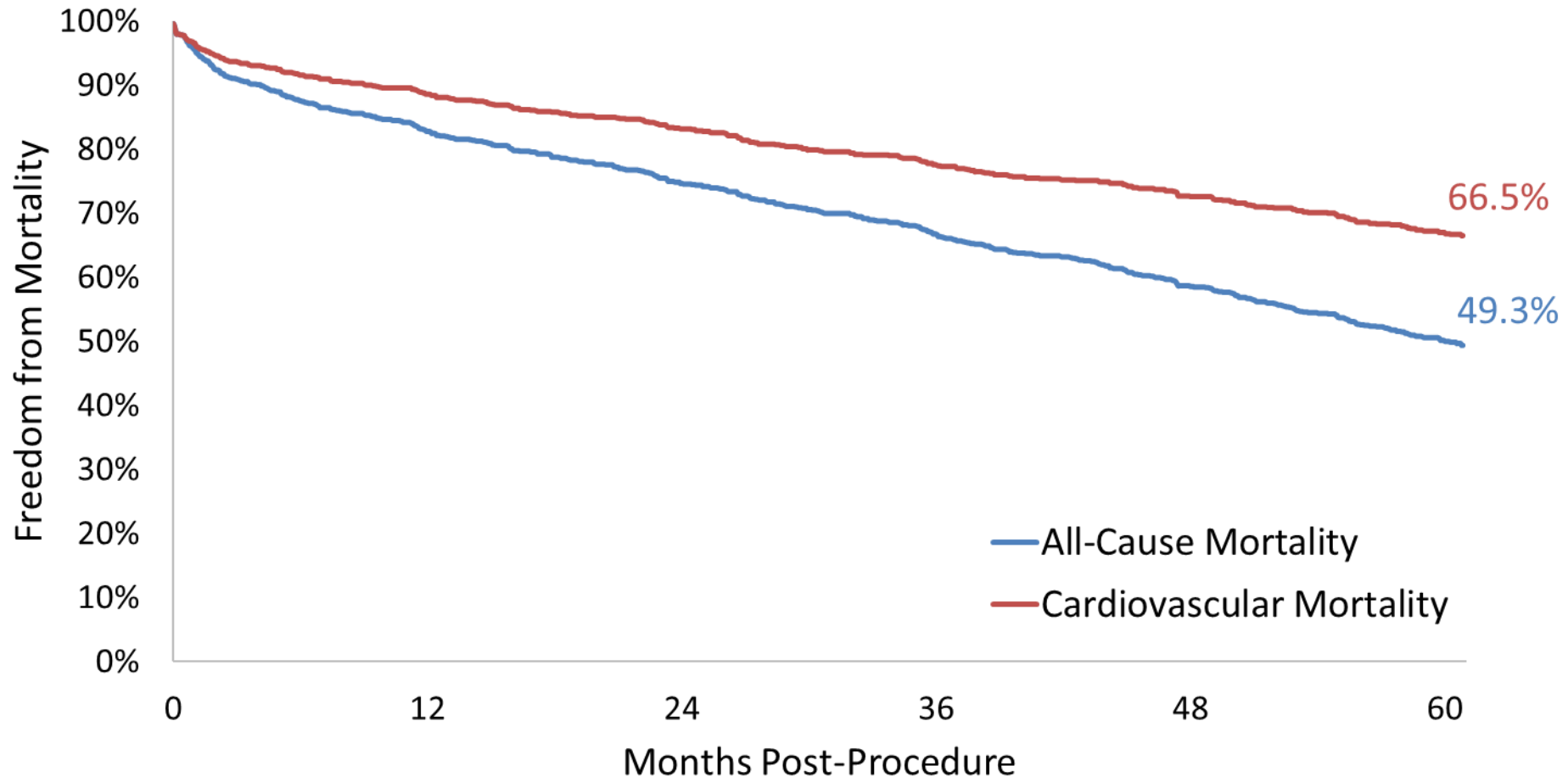
5 Years

	% (n)	95% CI
All-cause mortality*	50.7 (489)	[46.7%, 54.5%]
Cardiovascular mortality	33.5% (289)	[29.3%, 37.8%]
All-cause mortality or major stroke	51.8 (501)	[47.9%, 55.6%]
Stroke*	10.2 (78)	[7.2%, 13.7%]
Major stroke	5.4 (41)	[3.3%, 8.2%]
Myocardial infarction*	3.7 (27)	[2.0%, 6.1%]
New pacemaker implantation	33.7 (312)	[28.4%, 39.0%]
Emergent cardiac surgery or percutaneous reintervention*	2.8 (23)	[1.4%, 5.0%]
Acute kidney injury (stage III)	0.8 (7)	[0.2%, 2.4%]
Life-threatening/disabling bleeding	6.2 (57)	[3.9%, 9.2%]
Major bleeding	14.2 (129)	[10.7%, 18.2 5%]
MACCE	55.8 (541)	[51.9%, 59.5%]

*Components of MACCE, major adverse cardiac & cerebrovascular events

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All-cause and cardiovascular mortality



Number at risk:

996

808

721

639

560

407

996

808

721

639

560

407

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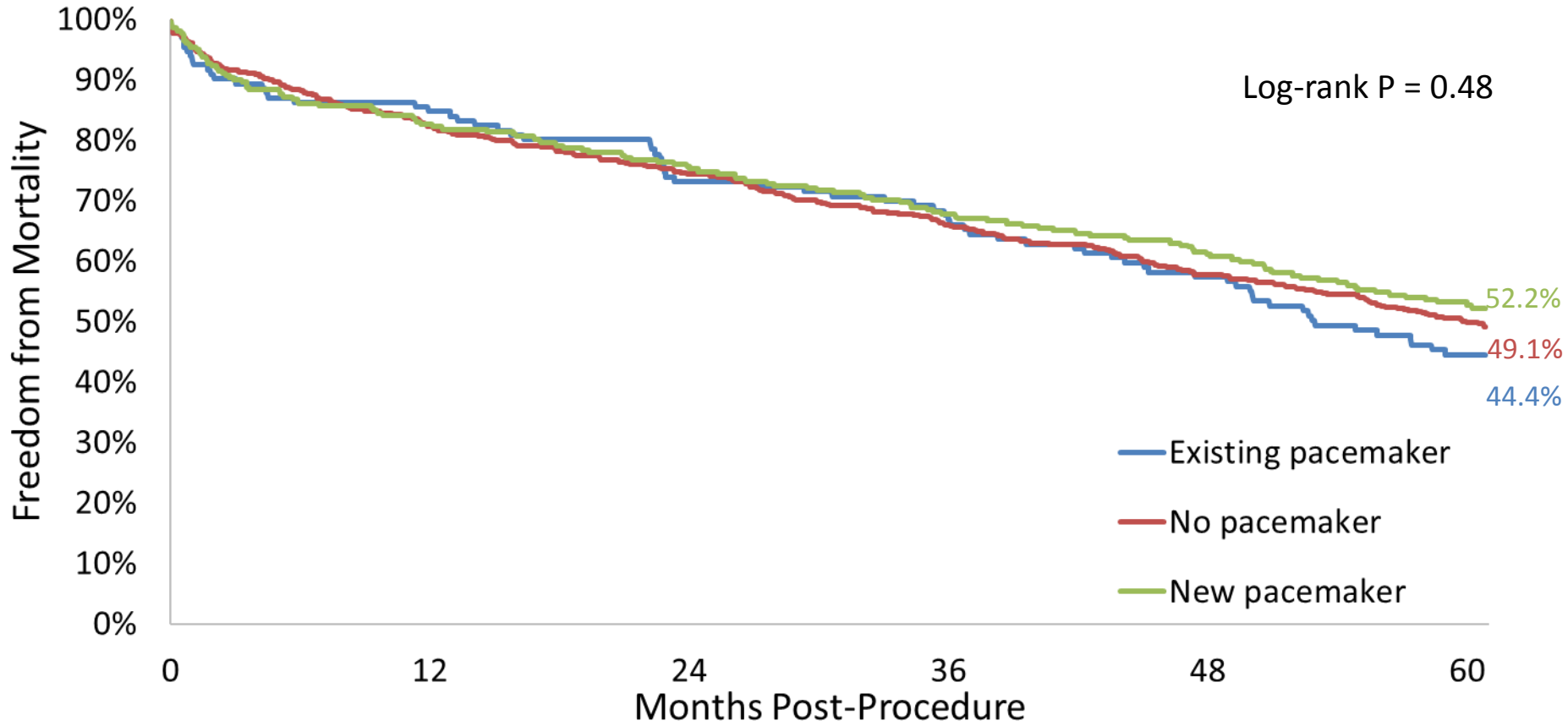
Multivariable predictors of mortality through 5 years

Characteristic	HR (95% CI)	P value
Age (Years)	1.03 (1.01, 1.05)	<0.001
Peripheral vascular disease	1.43 (1.11, 1.84)	0.006
Chronic obstructive pulmonary disease	1.32 (1.03, 1.70)	0.030
Creatinine (mg/dL)	1.22 (1.11, 1.35)	<0.001
Baseline left ventricular ejection fraction ≤50%	1.37 (1.11, 1.69)	0.008
Baseline mean AV gradient*	0.99 (0.98, 1.00)	0.029
Major bleeding	1.58 (1.19, 2.09)	0.001
Acute kidney injury (stage III)	14.31 (5.72, 35.79)	<0.001

*Higher baseline mean gradient was associated with a lower risk for mortality

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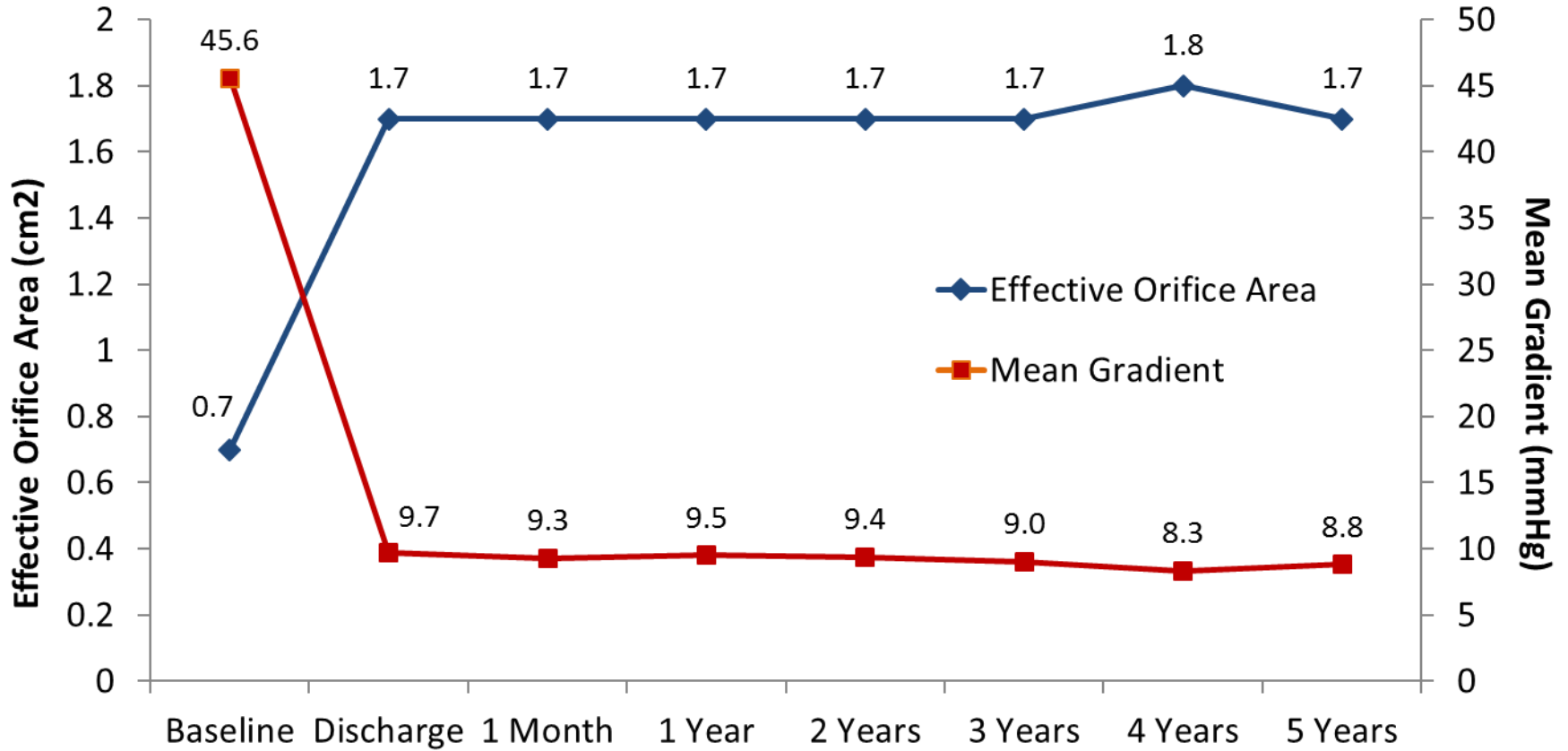
Survival by pacemaker use



Number at risk:

	0	12	24	36	48	60
New pacemaker	259	212	193	171	155	91
No pacemaker	606	484	433	378	330	183
Existing pacemaker	131	110	93	84	73	40

CoreValve ADVANCE Study Hemodynamics

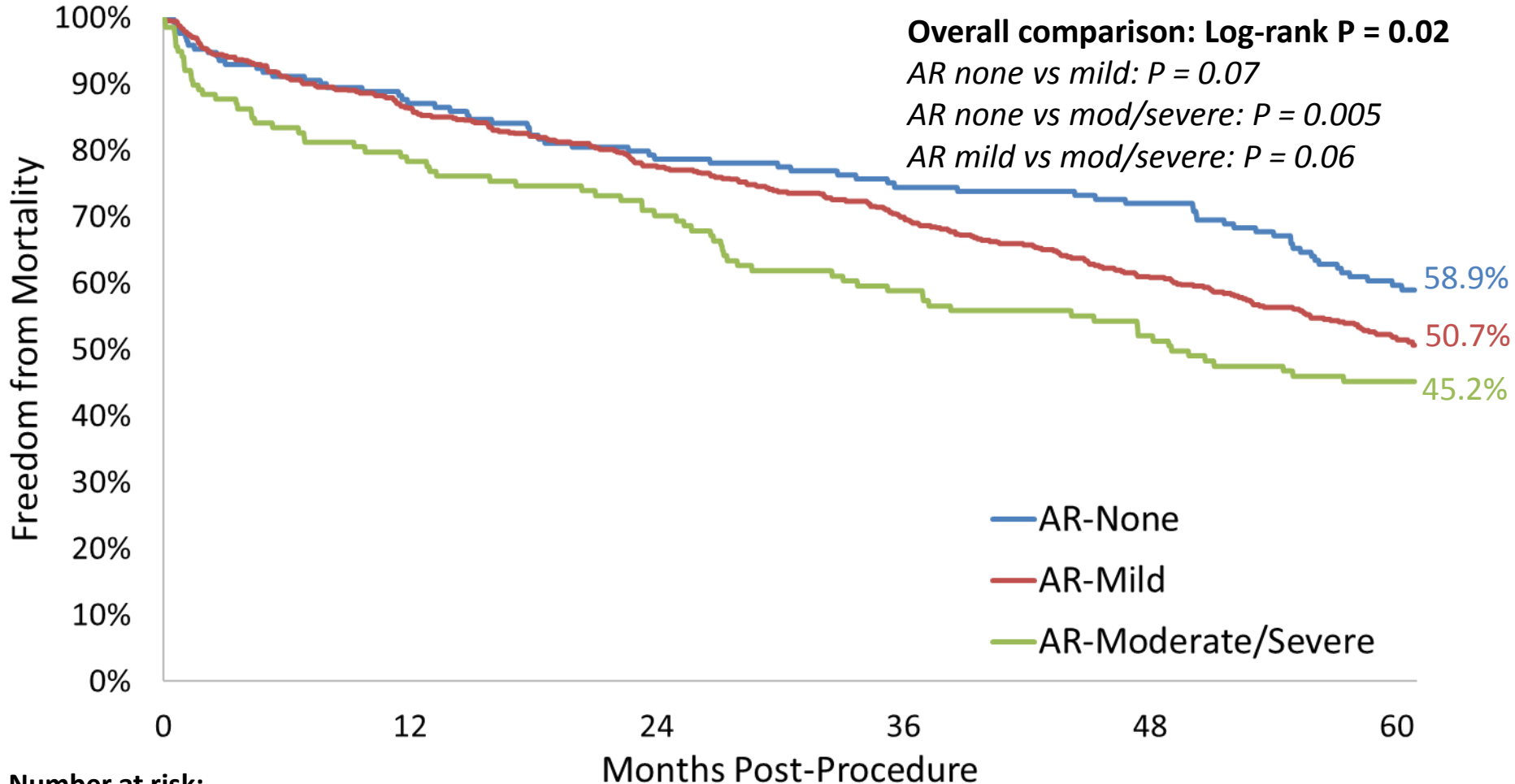


No. Echos

EOA:	795	512	388	394	351	253	210	146
Mean Gradient:	885	805	609	576	488	356	310	228

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Survival by aortic regurgitation

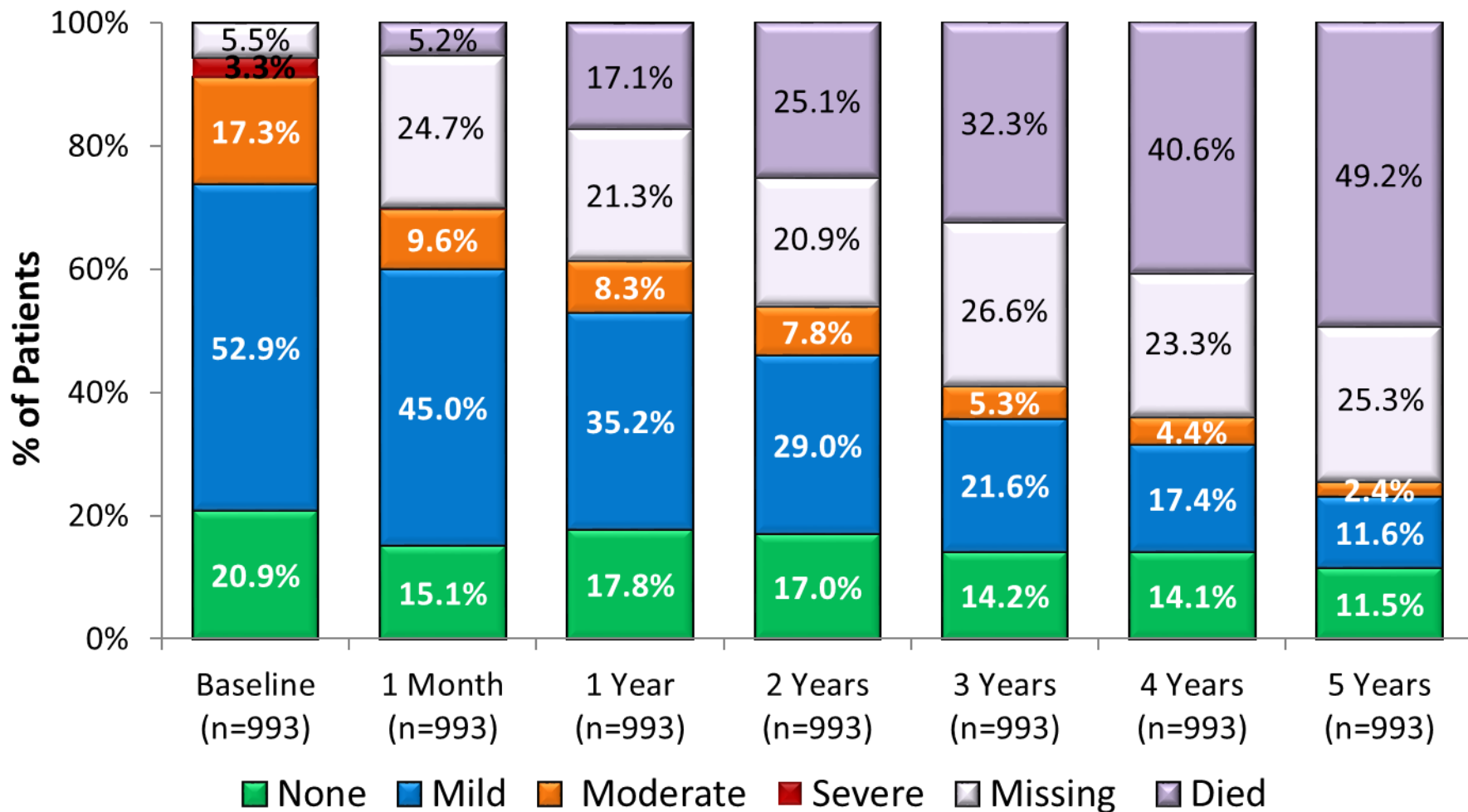


Number at risk:

139	108	93	78	68	36
561	477	426	378	331	185
172	145	131	122	118	64

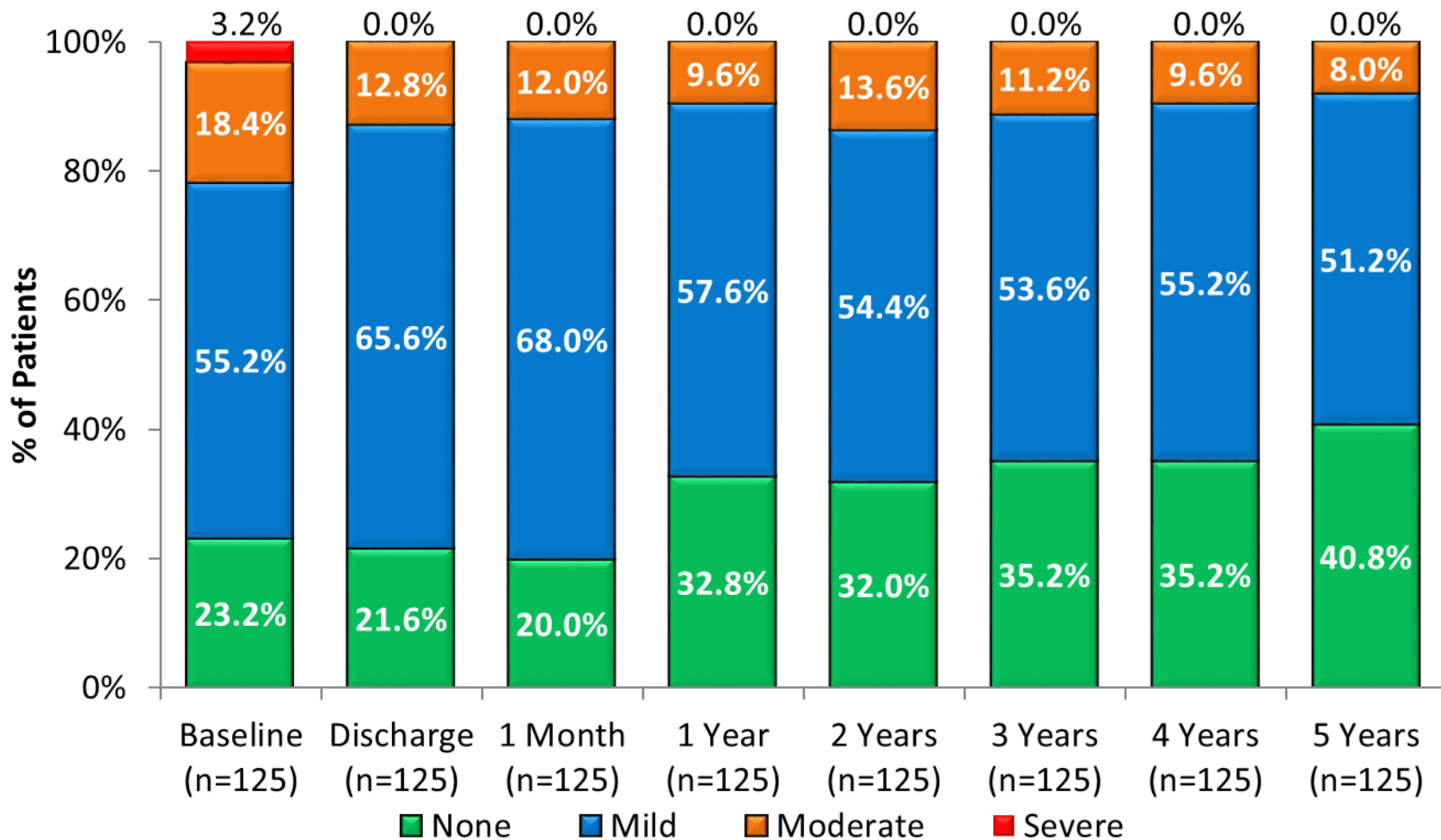
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Aortic regurgitation (all patients)



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Aortic regurgitation (paired)



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Valve durability through 5 years

Characteristic	N=860 ¹
Mean follow up (months)	36.0 ± 21.1
1 st and 3 rd quartile of follow-up time (months)	[13.5, 59.3]
Re-intervention after 30 days	10 (1.2%)
VARC-2 criteria ² for aortic valve stenosis	22 (2.6%)
moderate/severe AR	11 (1.3%)
AV mean gradient ≥20 mmHg or peak velocity ≥3 m/sec	11 (1.3%)
Re-intervention after 30 days or VARC-2 criteria	30 (3.5%)

¹ The analysis set included subjects with at least 1 echo post 30 days or a reintervention after 30 days; 267 subjects had 5 year follow-up

² VARC-2 definition: (AV mean gradient ≥20 mmHg or peak velocity ≥ 3 m/sec) and (EOA ≤0.9 cm² if BSA<1.6 or ≤1.1 cm² if BSA ≥1.6)
OR (≥mod/severe central aortic regurgitation)

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Conclusions

- Five year results in real-world, elderly, high-risk patients undergoing TAVI with a self-expanding bioprosthesis provide evidence for continued valve durability
 - rates of re-interventions and hemodynamic valve dysfunction were low
 - The excellent forward flow hemodynamic measures were consistent through 5 years
- Patients with no AR at discharge had a better rate of survival than patients with mild or moderate/severe AR
- There was no association between new pacemaker use and long-term mortality