EuroIntervention
2025;21:e411-e425
published online e-edition April 2025
DOI: 10.4244/EIJ-D-24-00341

ORIGINAL RESEARCH

Prognostic value of invasive versus echocardiography-derived aortic gradient in patients undergoing TAVI

Mark M.P. van den Dorpel[1], MD; Sraman Chatterjee[1], BSc; Rik Adrichem[1], MD; Sarah Verhemel[1], MD; Isabella Kardys[1], MD, PhD; Rutger-Jan Nuis[1], MD, PhD; Joost Daemen[1], MD, PhD; Claire Ben Ren[1], MD, PhD; Alexander Hirsch[1,2], MD, PhD; Marcel L. Geleijnse[1], MD, PhD; Nicolas M. Van Mieghem[1]*, MD, PhD

Corresponding author: Department of Cardiology, Thoraxcenter, Erasmus University Medical Center, office Nt-645, Dr. Molewaterplein 40, 3015 GD, Rotterdam, the Netherlands. E-mail: n.vanmieghem@erasmusmc.nl

This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-24-00341

ABSTRACT

BACKGROUND: Recent studies report a discordance between invasive and echocardiography-derived gradients after transcatheter aortic valve implantation (TAVI) with balloon-expandable (BEV) and self-expanding valves (SEV). There are limited data on the determinants and clinical implications of this discordance.

AIMS: We aimed to examine the prognostic value of invasive and echocardiography-derived gradients after implantation of SEV and BEV and to compare gradients for SEV versus BEV.

METHODS: We performed a retrospective, propensity score-matched study. Invasive measurements were obtained before and immediately after TAVI. Echocardiography was performed before and within 24 hours after TAVI, and at 1 year. Clinical outcomes were assessed at 30 days, 1 year, and 2 years.

RESULTS: The 1:1 propensity score matching resulted in 436 matched pairs (436 SAPIEN 3 and 436 Evolut). Invasive gradients post-TAVI independently predicted higher risk for all-cause mortality at 30 days, 1 year and 2 years as a continuous variable (hazard ratio [HR] 1.07, 95% confidence interval [CI]: 1.00-1.14; p=0.038; HR 1.06, 95% CI: 1.01-1.11; p=0.007; HR 1.05, 95% CI: 1.01-1.09; p=0.011, respectively) and by using >10 mmHg as a cutoff (HR 1.95, 95% CI: 1.13-4.78; p=0.028; HR 1.91, 95% CI: 1.11-3.65; p=0.030; HR 1.61, 95% CI: 1.03-2.96; p=0.021, respectively), but echocardiography-derived gradients did not (HR 1.13, 95% CI: 0.87-1.75; p=0.247; HR 1.02, 95% CI: 0.95-1.10; p=0.639; HR 0.99, 95% CI: 0.94-1.07; p=0.979, respectively). Mean gradients before and after TAVI were higher by echocardiography than by invasive measurements. The difference was more pronounced after implantation with BEV than SEV (7.0 [25th-75th percentile: 4.0-11.0] mmHg vs 5.0 [2.0-7.0] mmHg; p<0.001). Smaller valve size, higher ejection fraction and higher stroke volume amplified the discordance. Invasive mean gradients were similar after SEV and BEV (3.0 [0.0-6.0] mmHg vs 3.0 [0.0-6.0] mmHg; p=0.166), but echo-derived mean gradients were lower after SEV versus BEV (8.0 [6.0-11.0] mmHg vs 11.0 [8.0-14.0] mmHg; p<0.001).

CONCLUSIONS: Only invasively measured but not echocardiography-derived transvalvular mean gradients correlate with 30-day, 1-year and 2-year mortality. Aortic gradient measurements are higher by echocardiography than by invasive assessment and more so for BEV than SEV. Smaller valve size, higher ejection fraction and higher stroke volume increase this discordance between echocardiography and invasive assessment.

KEYWORDS: balloon-expandable valve; echocardiography; invasive; pressure gradient; self-expanding valve; TAVI

SUBMITTED ON 10/04/2024 - REVISION RECEIVED ON 1st 01/07/2024 / 2nd 03/09/2024 - ACCEPTED ON 24/09/2024

Transcatheter aortic valve implantation (TAVI) is a guideline-recommended treatment for selected patients with symptomatic severe aortic stenosis[1,2]. Randomised controlled trials have demonstrated equal haemodynamic valve performance for surgical and balloon-expandable valves (BEV) and consistently superior performance with self-expanding valves (SEV) characterised by larger valve areas and lower residual transvalvular pressure gradients up to 5 years[3-5].

There is increased interest in the evaluation of haemodynamic valve performance post-TAVI with different modalities. Recent studies reported equal transvalvular gradients measured invasively immediately after implantation with BEV and SEV but consistently higher gradients by predischarge echocardiography, and more so for BEV than SEV[6-16]. The scientific underpinning of this observation is limited and involves intrinsic limitations of echocardiography-derived measurements. There are limited data on the determinants for discordance between invasive and echocardiographic measurements.

It is also unclear whether these different gradient acquisitions may correlate differently with clinical outcome. Previous studies found weak correlations between invasive or echocardiographic mean gradients after TAVI and mortality, or they showed opposite results for echocardiographic and invasive measurements[6,8,17,18].

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OBJECTIVES OF THE STUDY

We aimed to examine the predictive value of invasive and echocardiography-derived transvalvular mean gradients post-TAVI for mortality and for the occurrence of bioprosthetic valve failure. Furthermore, we compared the difference between invasive and echocardiography-derived gradients for BEV versus SEV. The impact of different valve size, ejection fraction, indexed stroke volume and degree of aortic valve calcification on this discordance were also assessed.

Methods

We retrospectively included all consecutive patients who had undergone TAVI with a contemporary SAPIEN 3 (Edwards Lifesciences) or Evolut (Medtronic) valve for severe native aortic stenosis in our centre from January 2014 to March 2023. Exclusion criteria were TAVI in a failed surgical or transcatheter bioprosthesis and the need for more than one transcatheter heart valve (THV) due to initial malpositioning. Bicuspid valve patients were included in the analysis.

Echocardiography was performed before and within 24 hours after TAVI and at the 1-year follow-up visit. All echocardiography exams were performed according to the 2011 guidelines by the European and American Association of Echocardiography[19].

Invasive measurements were obtained minutes before and minutes after valve deployment. Invasive gradients were calculated as the difference between simultaneously measured pressures in the left ventricular outflow tract (LVOT) and the ascending aorta with 2 fluid-filled catheters (IMPULSE [Boston Scientific]) for simultaneous left ventricular (LV) and aortic pressure measurements. The LV catheter was positioned in the mid-ventricle at the level of the papillary muscles. The aortic catheter was positioned 2 cm above the stent frame for BEV and within the upper quadrant of the stent frame for SEV.

The Sensis Vibe haemodynamic system software program (Siemens Healthineers) was used for recording haemodynamic measurements. Measurements were first standardised with stable heartbeats, after which an average of 3 heartbeats in regular sinus or paced rhythm and 5 heartbeats in atrial fibrillation was used for the calculation of haemodynamic parameters. TAVI was performed under local anaesthesia with personalised close monitoring by trained nursing staff and without systematic intravenous administration of fluids, sedatives or anaesthetics. Patients remained wide awake, cooperative and communicative throughout the procedure.

The decision to predilate was per the operator's discretion and based on aortic root calcium content as determined by multislice computed tomography (MSCT). The trigger to predilate was typically lower for SEV than BEV. Non-circular frame expansion, more than mild paravalvular leakage or an invasive mean gradient >15 mmHg across the transcatheter valve were triggers for balloon post-dilatation.

Baseline demographics and clinical datapoints were captured in a dedicated electronic database. Clinical outcome was assessed at 30-day, 1-year, and 2-year follow-up visits. Clinical events, including the prevalence of bioprosthetic valve dysfunction, were defined according to Valve Academic Research Consortium (VARC)-3 criteria. The study was approved by the Medical Ethics Committee of the Erasmus University Medical Center (IRB: MEC-2023-0419), and the need for individual informed consent was waived because of the retrospective nature of the study.

To evaluate the impact of THV size on postprocedural gradients, THV size was classified into 4 categories: very small (SAPIEN 3 20 mm/Evolut 23 mm), small (SAPIEN 3 23 mm/Evolut 26 mm), medium (SAPIEN 3 26 mm/Evolut 29 mm) and large (SAPIEN 3 29 mm/Evolut 31/34 mm).

To evaluate the impact of LV ejection fraction (LVEF) and stroke volume index (SVI) on postprocedural gradients,

Impact on daily practice

In transcatheter aortic valve implantation (TAVI) patients, invasive but not echocardiographic gradients are a predictor of all-cause mortality. This highlights the clinical relevance of invasive-echocardiography discordance and the importance of invasive pressure acquisitions after TAVI. Aortic gradient measurements are higher by echocardiography than by invasive assessment, and this discordance is larger after TAVI with balloon-expandable than self-expanding valves.

Abbreviations

BEV balloon-expandable valve **SEV** self-expanding valve **TAVI** transcatheter aortic valve implantation

the most recent baseline echocardiogram prior to the TAVI procedure was used. To evaluate the impact of the aortic valve calcification degree, the computed tomography (CT) scan previously performed for TAVI planning was used.

A subanalysis of invasive and echocardiographic gradients and comparison of clinical outcomes was performed on patients with a small aortic annulus (<430 mm^2).

STATISTICAL ANALYSIS

Distributions of continuous variables were tested for normality using the Kolmogorov-Smirnov test. Continuous variables are expressed as median (25th-75th percentile); categorical variables are expressed as numbers and percentages. Comparison of continuous variables between (sub)groups was performed using the Mann-Whitney U and Kruskal-Wallis tests. Comparison of categorical variables between groups was performed with the chi-square test. Comparison of paired observations was performed with the Wilcoxon signed-rank test. Propensity scores were constructed using logistic regression. The THV platform (SEV or BEV) was used as the dependent variable, while baseline characteristics demonstrating significant differences between groups were the independent variables, along with other variables considered to be clinically relevant. We included the following variables into the propensity matching: age, sex, body mass index (BMI), body surface area (BSA), Society of Thoracic Surgeons (STS) score, hypertension, hypercholesterolaemia, atrial fibrillation, diabetes, estimated glomerular filtration rate (eGFR), LVEF, mean aortic valve gradient, peak aortic valve gradient, aortic valve area, valve size group, and aortic calcification degree. Using a 0.1 calliper setting and "nearest neighbour" matching without replacement, a propensity score-matched cohort with a 1:1 SEV versus BEV ratio was obtained. Standardised mean differences (SMD) were calculated for all variables to assess bias reduction. An SMD <0.2 was considered an indicator of adequate bias reduction. Comparison of continuous and categorical variables between matched groups were performed using the Wilcoxon signed-rank and McNemar tests. To test for the association between continuous variables and all-cause mortality, baseline variables of presumed prognostic importance and post-TAVI invasive and echocardiography-derived mean gradients (both continuous and dichotomised) were first analysed by univariable Cox proportional hazards regression. Afterwards, parameters with p-values of <0.10 were integrated into a multivariable Cox proportional hazards regression model. A separate Cox proportional hazards regression was performed to examine the association between continuous variables (including the gradients and variables of presumed prognostic importance) and the occurrence of bioprosthetic valve dysfunction at 1 year. Kaplan-Meier analysis was performed to compare clinical outcome between groups. P-values<0.05 were considered significant. Analyses were performed using SPSS, version 25.0 (IBM) and Rstudio version 4.3 (Posit Software, PBC).

Results

The flowchart of the study population is shown in **Supplementary Figure 1**. Overall, 1,227 patients underwent TAVI from January 2014 to March 2023 (Evolut: n=573; SAPIEN 3: n=654). Baseline characteristics are shown in **Table 1**. Propensity score matching resulted in 436 matched pairs. The median age was 80 (74-84) years for both groups, and the median STS score was 3.41 (2.40-5.02) for SEV versus 3.10 (2.01-4.99) for BEV; p=0.082. Baseline echocardiography displayed no differences between groups regarding LVEF (SEV: 57 [51-59]% vs BEV: 56 [48-59]%; p=0.108), moderate/severe mitral regurgitation (SEV: 13.5% vs BEV: 11.0%; p=0.216) or pulmonary hypertension (SEV: 9.6% vs BEV 10.8%; p=0.640). Seven patients were lost to follow-up at 30 days, 14 were lost to follow-up at 1 year, and 30 at 2 years.

Echocardiographic and invasive transvalvular gradient measurements before and after TAVI are shown in **Table 2**, **Figure 1A**, and **Figure 1B**. Baseline mean gradients were higher by echocardiography than by invasive measurements for both patients planned for SEV (39.0 [30.0-48.0] mmHg vs 36.0 [26.0-46.0] mmHg; p<0.001) and BEV (38.0 [30.0-48.0] mmHg vs 34.0 [27.0-42.0] mmHg; p<0.001). There were no differences between SEV and BEV for the baseline echocardiographic (39.0 [30.0-48.0] mmHg vs 38.0 [30.0-48.0] mmHg; p=0.379) or invasive measurements (36.0 [26.0-46.0] mmHg vs 34.0 [27.0-42.0] mmHg; p=0.311).

Invasive mean gradients post-TAVI were equal for BEV and SEV (3.0 [0.0-6.0] mmHg vs 3.0 [0.0-6.0] mmHg; p=0.166) **(Central illustration)**; however, the mean and maximum gradients by transthoracic echocardiography within 24 hours after TAVI were significantly lower in SEV as compared to BEV patients (8.0 [6.0-11.0] mmHg vs 11.0 [8.0-14.0] mmHg; p<0.001 and 14.0 [12.0-19.0] mmHg vs 19.0 [15.0-27.0] mmHg; p<0.001, respectively).

The mean gradients by echocardiography post-TAVI displayed higher values than invasive measurements, and the difference was more pronounced with BEV than SEV (7.0 [4.0-11.0] mmHg for BEV and 5.0 [2.0-7.0] mmHg for SEV patients; p<0.001) **(Figure 1C)**. A clinical example of this discordance between invasive and echocardiographic measurements is illustrated in **Supplementary Figure 2**. Of the 19 patients with a mean gradient of 20 mmHg or higher on post-TAVI echocardiography, only 5 had an invasive gradient of >20 mmHg.

Patients with a smaller THV exhibited a higher level of discordance between echocardiographic and invasive measurements, and this difference was more pronounced for BEV in each THV size category. With SEV, the difference between the invasive and echocardiographic mean gradient was 7.0 (2.0-10.0) mmHg for Evolut 23 mm versus 4.5 (2.0-6.5) mmHg for Evolut 31/34 mm; p=0.011. With BEV, the difference between invasive and echocardiographic mean gradients was 11.0 (5.5-17.0) mmHg for the SAPIEN 3 20 mm versus 7.0 (3.0-9.0) mmHg for the SAPIEN 3 29 mm; p=0.001 **(Table 3)**.

Patients with a higher LVEF exhibited a higher rate of discordance for the total group (7.0 [3.0-10.0] mmHg for LVEF >50% vs 5.0 [2.0-8.0] mmHg for LVEF <40%; p=0.041), and for BEV (8.0 [5.0-11.0] mmHg for LVEF >50% vs 6.0 [3.0-9.0] mmHg for LVEF <40%; p=0.021) **(Table 3)**. For each LVEF category (<40%, 40-50%, >50%), BEV exhibited a higher rate of discordance compared

Table 1. Baseline characteristics.

	Unmatched (n=1,227)				Matched (n=872)			
	SEV (n=573)	BEV (n=654)	*p*-value	SMD	SEV (n=436)	BEV (n=436)	*p*-value	SMD
Age, years	80 (74-84)	80 (74-84)	0.931	0.030	80 (74-84)	80 (74-84)	0.542	0.018
Male	248 (43.2)	428 (65.4)	<0.001	0.462	185 (42.4)	263 (60.0)	<0.001	0.370
BMI, kg/m^2	26.2 (23.1-30.1)	26.8 (24.1-30.5)	0.017	0.320	26.2 (23.1-30.1)	26.4 (23.9-30.1)	0.737	0.034
BSA, m^2	1.8 (1.7-2.0)	1.9 (1.8-2.0)	<0.001	0.320	1.68 (1.55-1.83)	1.76 (1.61-1.89)	0.070	0.251
STS score	3.25 (2.28-4.81)	2.94 (1.90-4.70)	0.007	0.160	3.41 (2.40-5.02)	3.10 (2.01-4.99)	0.082	0.013
Hypertension	436 (76.1)	487 (74.4)	0.454	0.036	337 (77.3)	321 (73.6)	0.216	0.085
Hypercholesterolaemia	349 (60.1)	384 (58.7)	0.602	0.015	271 (62.1)	259 (59.4)	0.690	0.004
Atrial fibrillation	190 (33.1)	210 (32.1)	0.270	0.107	147 (33.7)	141 (32.3)	0.767	0.004
Diabetes	182 (31.7)	204 (31.1)	0.721	0.011	136 (31.2)	143 (32.8)	0.611	0.004
Renal failure	187 (32.6)	227 (34.7)	0.338	0.043	134 (30.7)	156 (35.8)	0.293	0.018
Antiplatelet therapy			0.284	0.064			0.789	0.097
Aspirin	195 (34.0)	244 (37.3)			155 (35.5)	170 (39.0)		
Clopidogrel	116 (20.2)	134 (20.4)			85 (19.5)	97 (22.3)		
Dual therapy	48 (8.3)	52 (7.9)			37 (8.5)	42 (9.6)		
Anticoagulation			0.093	0.152			0.722	0.026
VKA	114 (19.9)	151 (23.1)			95 (21.7)	102 (23.4)		
NOAC	97 (16.9)	94 (14.4)			70 (16.1)	63 (14.5)		
NYHA Class			0.611	0.044			0.473	0.121
I	38/527 (7.2)	46/603 (7.6)			28/422 (6.6)	26/413 (6.3)		
II	186/527 (35.3)	212/603 (35.1)			149/422 (35.4)	151/413 (36.5)		
III	258/527 (48.9)	281/603 (46.6)			209/422 (49.5)	193/413 (46.7)		
IV	45/527 (8.5)	64/603 (10.6)			36/422 (8.5)	43/413 (10.4)		
Echo characteristics								
LVEF, %	58 (50-60)	55 (45-60)	<0.001	0.204	57 (51-59)	56 (48-59)	0.108	0.140
>50%	393 (68.6)	378 (57.8)	<0.001	0.228	311 (71.3)	290 (66.5)	0.093	0.154
40-50%	115 (20.0)	174 (26.6)	0.014	0.147	78 (17.9)	101 (23.2)	0.065	0.132
<40%	65 (11.4)	102 (15.6)	0.033	0.138	47 (10.8)	55 (12.6)	0.390	0.057
Preprocedural mean aortic gradient, mmHg	40.0 (31.0-50.0)	38.0 (30.0-48.0)	0.106	0.091	39.0 (30.0-48.0)	38.0 (30.0-48.0)	0.381	0.028
Preprocedural peak aortic gradient, mmHg	67.0 (55.0-81.0)	64.0 (49.0-81.0)	0.063	0.118	67.0 (52.0-81.0)	64.0 (52.0-81.0	0.374	0.037
AVA, cm^2	0.70 (0.60-0.90)	0.80 (0.62-0.90)	0.002	0.082	0.70 (0.6-0.8)	0.75 (0.6-0.80)	0.062	0.07
Moderate/severe mitral regurgitation	70 (12.2)	66 (10.1)	0.237	0.052	59 (13.5)	48 (11.0)	0.216	0.096
RVSP >40 mmHg	71 (12.4)	78 (11.9)	0.804	0.002	42 (9.6)	47 (10.8)	0.640	0.024
Valve types								
Evolut R[a]	309 (53.9)				228 (52.3)			
Evolut PRO(+)[a]	264 (46.1)				208 (47.7)			
SAPIEN 3[b]		378 (57.8)				248 (56.9)		
SAPIEN 3 Ultra[b]		276 (42.2)				188 (43.1)		
Valve size group			<0.001	0.593			0.106	0.129
Very small	33 (5.8)	13 (2.0)	<0.001	0.212	14 (3.2)	12 (2.8)	0.690	0.027
Small	207 (36.1)	142 (21.7)	<0.001	0.321	149 (34.2)	140 (32.1)	0.517	0.044
Medium	286 (49.9)	294 (44.9)	0.068	0.101	226 (51.8)	218 (50.0)	0.588	0.037
Large	47 (8.2)	205 (31.3)	<0.001	0.601	47 (10.8)	66 (15.1)	0.070	0.130

Table 1. Baseline characteristics (cont'd).

	Unmatched (n=1,227)				Matched (n=872)			
	SEV (n=573)	BEV (n=654)	*p*-value	SMD	SEV (n=436)	BEV (n=436)	*p*-value	SMD
Procedural characteristics								
Predilatation	292 (44.6)	132 (23.0)	<0.001	0.224	192 (44.0)	113 (25.9)	<0.001	0.398
Post-dilatation	164 (28.6)	158 (23.5)	0.074	0.106	136 (31.2)	116 (26.6)	0.096	0.102
Computed tomography measurements								
Annulus area, mm^2	462 (415-480)	495 (441-512)	<0.001	0.153	469 (421-472)	483 (440-497)	0.105	0.062
Valve morphology			0.282	0.081			0.271	0.070
Bicuspid	41 (7.0)	59 (9.0)	0.282	0.081	34 (7.7)	44 (10.1)	0.271	0.070
Tricuspid	532 (93.0)	595 (91.0)	0.282	0.081	402 (92.2)	392 (89.9)	0.271	0.070
Degree of calcification			0.042	0.141			0.542	0.064
Severe	488 (85.1)	586 (89.6)	0.019	0.139	360 (82.6)	377 (86.4)	0.338	0.074
Moderate	72 (12.6)	61 (9.3)	0.069	0.118	68 (15.6)	58 (13.3)	0.283	0.080
Mild	13 (2.3)	7 (1.1)	0.010	0.217	4 (0.9)	5 (1.1)	0.759	0.013
None	0 (0)	0 (0)	1.000	0.000	0 (0)	0 (0)	1.000	0.000

Values are median (25th-75th percentile), n (%) or n/N (%). [a]By Medtronic; [b]by Edwards Lifesciences. AVA: aortic valve area; BEV: balloon-expandable valve; BMI: body mass index; BSA: body surface area; LVEF: left ventricular ejection fraction; NOAC: non-vitamin K oral anticoagulants; NYHA: New York Heart Association; RVSP: right ventricular systolic pressure; SEV: self-expanding valve; SMD: standardised mean difference; STS: Society of Thoracic Surgeons; VKA: vitamin K antagonist

Table 2. Pre- and postprocedural invasive and echocardiographic gradient measurements.

	Unmatched (n=1,211)			Matched (n=861)		
	SEV	BEV	*p*-value	SEV	BEV	*p*-value
Echocardiography						
Pre-TAVI	(n=573)	(n=654)		(n=436)	(n=436)	
Mean PG, mmHg	40.0 (32.0-50.0)	38.0 (30.0-48.0)	0.106	39.0 (30.0-48.0)	38.0 (30.0-48.0)	0.379
Peak PG, mmHg	67.0 (55.0-81.0)	64.0 (49.0-81.0)	0.063	67.0 (52.0-81.0)	64.0 (52.0-81.0)	0.343
Predischarge	(n=567)	(n=644)		(n=436)	(n=431)	
Mean PG, mmHg	8.0 (6.0-11.0)	11.0 (8.0-14.0)	<0.001[&]	8.0 (6.0-11.0)	11.0 (8.0-14.0)	<0.001[&]
Peak PG, mmHg	14.0 (9.5-18.5)	19.0 (16.0-25.0)	<0.001[&]	14.0 (12.0-19.0)	19.0 (15.0-27.0)	<0.001[&]
1-year follow-up	(n=503)	(n=579)		(n=384)	(n=391)	
Mean PG, mmHg	8.0 (6.0-10.0)	10.0 (8.0-12.0)	<0.001[&]	8.0 (6.0-10.0)	9.0 (8.0-12.0)	<0.001[&]
Peak PG, mmHg	16.0 (12.0-19.0)	18.0 (14.0-23.0)	<0.001[&]	16.0 (12.0-19.0)	18.0 (14.0-23.0)	<0.001[&]
Invasive						
Pre-TAVI	(n=573)	(n=654)		(n=436)	(n=436)	
Mean PG, mmHg	36.5 (26.0-47.0)	34.0 (26.0-45.0)	0.240	36.0 (26.0-46.0)	34.0 (27.0-42.0)	0.311
Peak PG, mmHg	50.0 (33.0-66.0)	44.0 (31.0-63.0)	0.012[&]	49.0 (31.0-63.0)	44.0 (31.0-60.0)	0.023[&]
Post-TAVI	(n=573)	(n=654)		(n=436)	(n=436)	
Mean PG, mmHg	3.0 (0.0-6.0)	3.0 (0.0-6.0)	0.834	3.0 (0.0-6.0)	3.0 (0.0-6.0)	0.166
Peak PG, mmHg	2.0 (0.0-7.0)	2.0 (0.0-6.0)	0.212	2.0 (0.0-6.0)	2.0 (0.0-6.0)	0.570
Difference between gradients						
Pre-TAVI echo mean PG – pre-TAVI invasive mean PG, mmHg	3.5 (1.0-5.5) (p<0.001)*[&]	3.5 (1.5-5.0) (p<0.001)*[&]	0.664	3.5 (1.0-5.0) (p<0.001)*[&]	3.5 (1.5-5.0) (p<0.001)*[&]	0.302
Post-TAVI echo mean PG – post-TAVI invasive mean PG, mmHg	5.0 (2.0-7.0) (p<0.001)*[&]	7.0 (4.0-10.5) (p<0.001)*[&]	<0.001[&]	5.0 (2.0-7.0) (p<0.001)*[&]	7.0 (4.0-11.0) (p<0.001)*[&]	<0.001[&]
Pre-TAVI echo peak PG – pre-TAVI invasive peak PG, mmHg	17.0 (8.0-28.0) (p<0.001)*[&]	19.0 (8.0-32.0) (p<0.001)*[&]	0.296	17.0 (7.0-28.0) (p<0.001)*[&]	19.0 (8.0-32.0) (p<0.001)*[&]	0.281
Post-TAVI echo peak PG – post-TAVI invasive peak PG, mmHg	12.0 (8.0-17.0) (p<0.001)*[&]	18.0 (13.0-23.0) (p<0.001)*[&]	<0.001[&]	12.0 (8.0-16.0) (p<0.001)*[&]	17.0 (12.0-23.0) (p<0.001)*[&]	<0.001[&]
Number of patients displaying a mean PG >20 mmHg post-TAVI						
Echocardiography	9 (1.6)	20 (3.1)	0.085	6 (1.4)	13 (3.0)	0.099
Echocardiography + confirmed by invasive measurement >20 mmHg	0 (0)	5 (0.8)	0.022[&]	0 (0)	5 (1.1)	0.025[&]
Invasive	0 (0)	5 (0.8)	0.022[&]	0 (0)	5 (1.1)	0.025[&]

Values are median (25th-75th percentile) or n (%). *P-value applies to the difference between the echo-derived mean gradient and the invasive mean gradient within groups. [&]Indicates statistical significance. BEV: balloon-expandable valve; PG: pressure gradient; SEV: self-expanding valve; TAVI: transcatheter aortic valve implantation

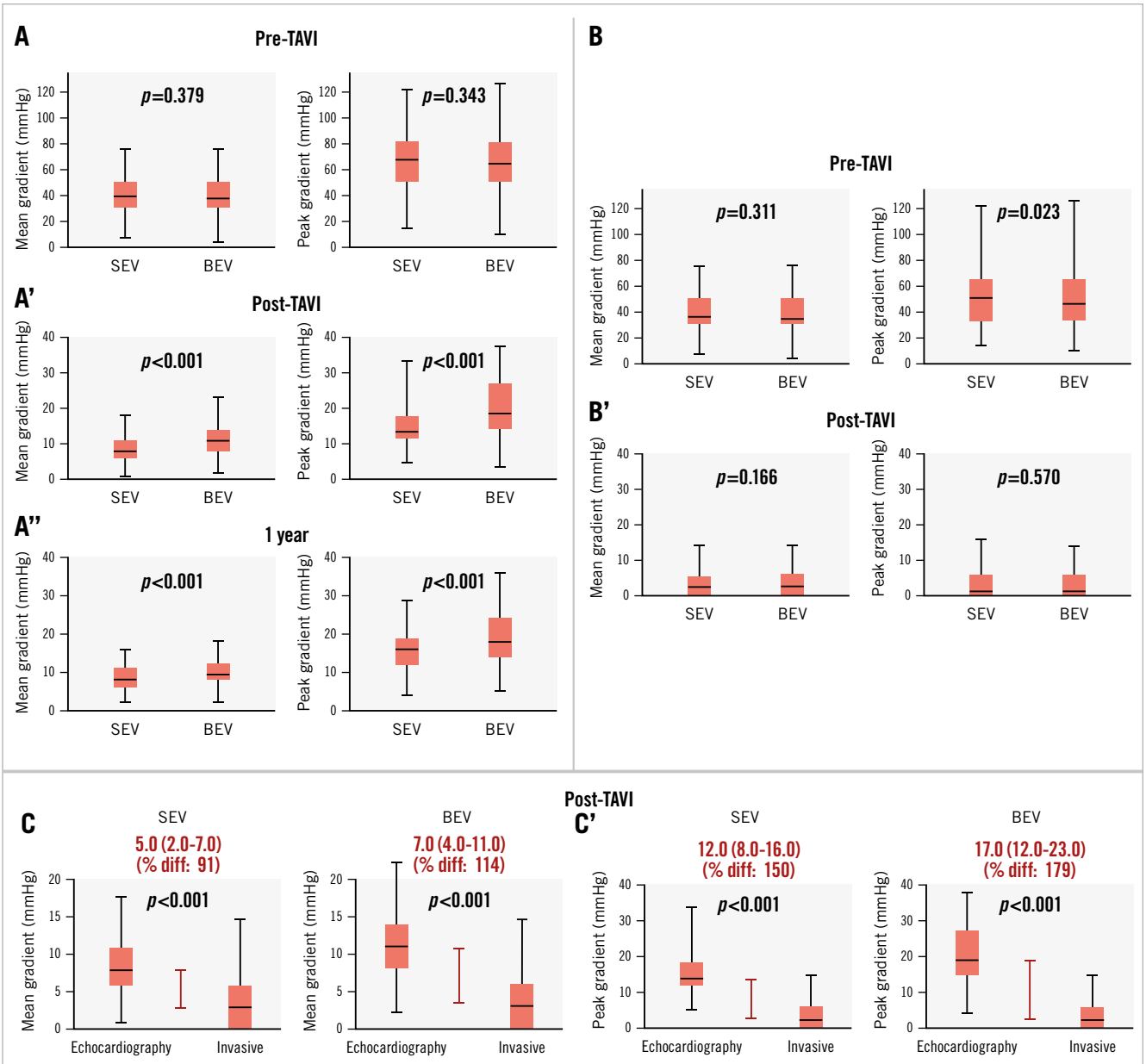


Figure 1. *Echocardiographic and invasive pressure gradient measurements in self-expanding valve and balloon-expandable valve patients. A) Echocardiographic mean and peak pressure gradients pre-TAVI. A') Echocardiographic mean and peak pressure gradients post-TAVI. A") Echocardiographic mean and peak pressure gradients at 1 year. B) Invasive mean and peak pressure gradients pre-TAVI. B') Invasive mean and peak pressure gradients post-TAVI. C) Difference between post-TAVI invasive and echocardiographic mean gradients. C') Difference between post-TAVI invasive and echocardiographic peak gradients. BEV: balloon-expandable valve; diff: difference; SEV: self-expanding valve; TAVI: transcatheter aortic valve implantation*

to SEV (8.0 [5.0-11.0] mmHg vs 5.0 [2.0-7.0] mmHg; p<0.001; 7.0 [5.0-10.0] mmHg vs 5.0 [1.0-7.0] mmHg; p<0.001; 6.0 [3.0-9.0] mmHg vs 5.0 [1.0-8.0] mmHg; p=0.227, respectively).

A high SVI increased the discordance for the total group (7.0 [3.0-9.0] mmHg for SVI >35 ml/m^2 vs 5.0 [3.0-8.0] mmHg for SVI <35 ml/m^2; p=0.048). This difference was statistically significant for BEV (9.0 [5.0-12.0] mmHg for SVI >35 ml/m^2 vs 6.0 [4.0-10.0] mmHg for SVI <35 ml/m^2; p=0.002) but not for SEV (5.0 [2.0-7.0] mmHg vs 5.0 [2.0-8.0]; p=0.730).

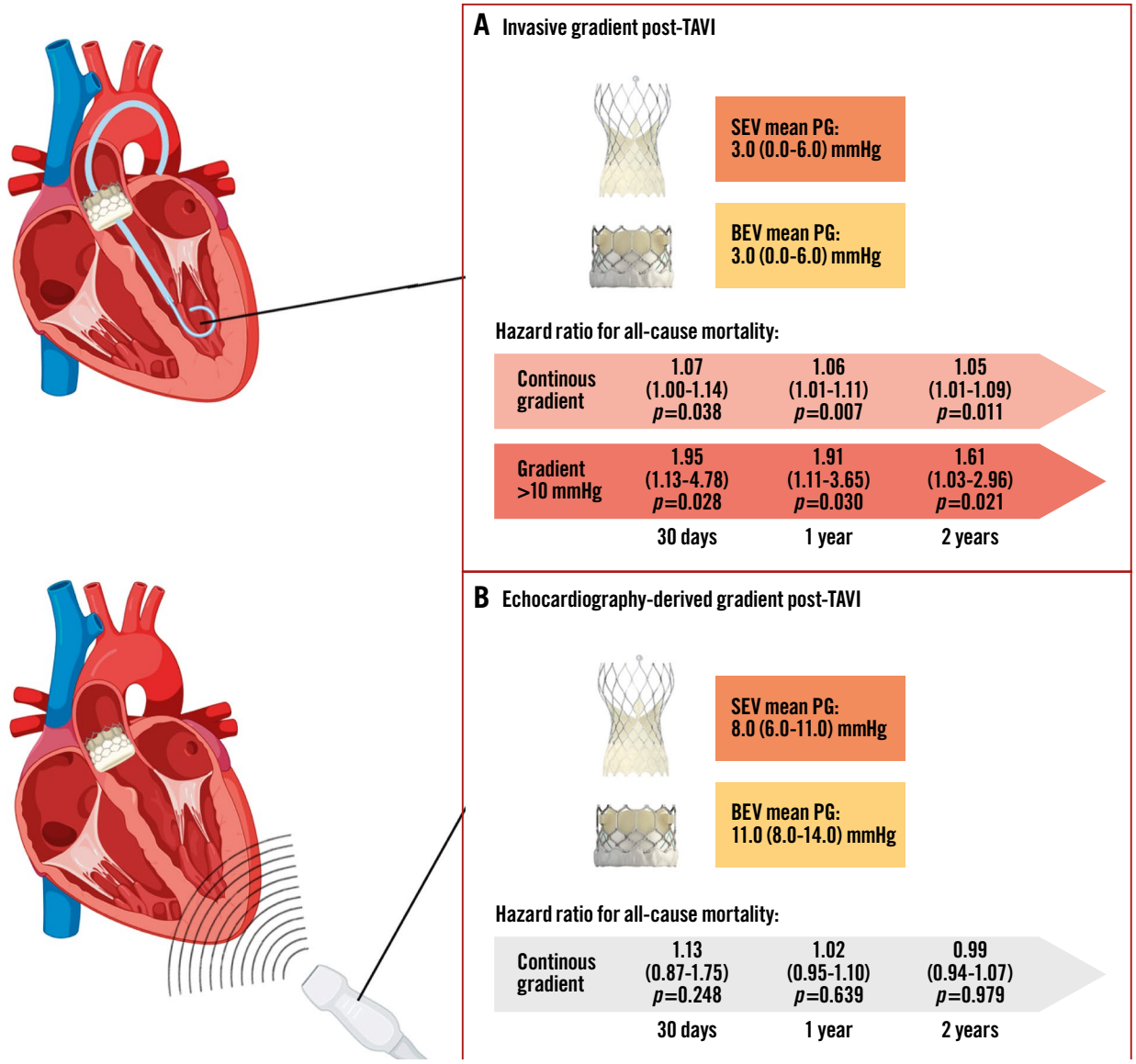
The degree of aortic valve calcification did not significantly affect the discordance between echo-derived and invasive measurements (7.0 [3.0-10.0] mmHg for severe calcification vs 7.0 [3.0-9.0] mmHg for mild calcification; p=0.638).

Clinical outcomes at 30 days, 1 year and 2 years are depicted in **Table 4**. Outcomes were similar after TAVI with SEV and BEV.

In small annulus patients (annulus area <430 mm^2), the mean gradients were lower for SEV than BEV by echocardiography (8.0 [6.0-11.0] mmHg vs 12.0 [9.0-16.0] mmHg; p<0.001) but not by invasive measurements

EuroIntervention — Central **Illustration**

Discordance between echocardiographic and invasive gradient measurements after TAVI using self-expanding and balloon-expandable valves.



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A) Invasive mean gradients post-TAVI were equal in SEV and BEV. Invasive mean gradients independently predicted a higher risk for all-cause mortality at 30 days, 1 year and 2 years as a continuous variable and by using >10 mmHg as the cutoff. B) Echocardiography-derived mean gradients post-TAVI were higher in BEV than SEV. Echocardiography-derived mean gradients showed no significant association with all-cause mortality. BEV: balloon-expandable valve; PG: pressure gradient; SEV: self-expanding valve; TAVI: transcatheter aortic valve implantation

(3.0 [0.0-5.0] mmHg vs 3.0 [0.0-6.0] mmHg; p=0.740) **(Supplementary Table 1)**. The median discordance between echo-derived and invasive mean gradients was larger for BEV than SEV (8.0 [5.0-12.0] mmHg vs 5.0 [2.0-8.0] mmHg; p<0.001). Clinical outcomes were similar for SEV and BEV except for a higher rate of bioprosthetic valve failure in BEV at 2 years (4.9% vs 11.1%; p=0.042). The clinical outcomes of small aortic annulus patients are displayed in **Supplementary Table 2**.

Invasive transvalvular mean gradients post-TAVI independently predicted a higher risk for all-cause mortality at 30 days, 1 year and 2 years (hazard ratio [HR] 1.07, 95% confidence interval [CI]: 1.00-1.14; p=0.038; HR 1.06, 95% CI: 1.01-1.11; p=0.007; and HR 1.05, 95% CI: 1.05-1.09;

Table 3. Median difference between echo-derived versus invasive mean gradients (mmHg) post-TAVI for different valve size categories, LVEF categories, stroke volume index categories and aortic valve calcification degrees.

	Unmatched (n=1,211)							Matched (n=861)						
	SEV +BEV	p-value	SEV (n=567) (ref=5.0)	*p*-value	BEV (n=644) (ref=7.0)	*p*-value	p-value (SEV vs BEV)	SEV +BEV	*p*-value	SEV (n=430) (ref=5.0)	*p*-value	BEV (n=431) (ref=7.0)	*p*-value	p-value (SEV vs BEV)
Valve size*														
Very small (VS)	9.0 (6.0-14.0)	ref	8.0 (4.0-13.0)	ref	12.0 (7.0-16.5)	ref	0.109	8.0 (4.0-14.0)	ref	7.0 (2.0-10.0)	ref	11.0 (5.5-17.0)	ref	0.370
Small (S)	7.0 (3.0-10.0)	0.004[&]	5.0 (2.0-8.0)	0.012[&]	9.0 (6.0-13.0)	0.681	<0.001[&]	6.0 (3.0-9.0)	0.003[&]	5.0 (2.0-8.0)	0.002[&]	9.0 (6.0-12.0)	0.124	<0.001[&]
Medium (M)	6.0 (3.0-9.0)	0.006[&]	4.0 (2.0-7.0)	0.001[&]	7.0 (4.0-10.0)	0.005[&]	<0.001[&]	6.0 (3.0-9.0)	<0.001[&]	5.0 (2.0-7.0)	<0.001[&]	7.0 (5.0-11.0)	0.008[&]	<0.001[&]
Large (L)	5.0 (4.0-8.0)	0.022[&]	4.0 (2.0-6.0)	0.039[&]	6.0 (4.0-9.0)	0.018[&]	0.013[&]	5.0 (3.0-8.0)	<0.001[&]	4.5 (2.0-6.5)	0.011[&]	7.0 (3.0-9.0)	0.001[&]	0.058
LVEF**														
>50%	7.0 (3.0-10.0)	ref	5.0 (2.0-8.0)	ref	8.0 (5.0-11.0)	ref	<0.001[&]	7.0 (3.0-10.0)	ref	5.0 (2.0-7.0)	ref	8.0 (5.0-11.0)	ref	<0.001[&]
40-50%	6.0 (3.0-9.0)	0.416	4.0 (0.0-7.0)	0.104	7.0 (4.0-9.0)	0.220	<0.001[&]	6.0 (3.0-9.0)	0.164	5.0 (1.0-7.0)	0.739	7.0 (5.0-10.0)	0.263	<0.001[&]
<40%	6.0 (2.0-8.0)	0.039[&]	5.0 (1.0-8.0)	1.000	6.0 (3.0-9.0)	0.020[&]	0.401	5.0 (2.0-8.0)	0.041[&]	5.0 (1.0-8.0)	0.616	6.0 (3.0-9.0)	0.021[&]	0.227
Stroke volume index***														
>35 ml/m^2	7.0 (3.0-10.0)	ref	5.0 (2.0-7.8)	ref	9.0 (5.0-12.0)	ref	<0.001[&]	7.0 (3.0-9.0)	ref	5.0 (2.0-7.0)	ref	9.0 (5.0-12.0)	ref	<0.001[&]
≤35 ml/m^2	6.0 (3.0-8.0)	0.044[&]	5.0 (2.0-8.0)	0.794	7.0 (4.0-9.0)	0.002[&]	<0.001[&]	5.0 (3.0-8.0)	0.048[&]	5.0 (2.0-8.0)	0.730	6.0 (4.0-10.0)	0.002[&]	<0.001[&]
AoV calcification****														
Severe	7.0 (3.0-9.0)	ref	5.0 (2.0-8.0)	ref	9.0 (5.0-11.0)	ref	<0.001[&]	7.0 (3.0-10.0)	ref	5.0 (2.0-7.0)	ref	9.0 (5.0-11.0)	ref	<0.001[&]
Moderate	7.0 (3.0-10.0)	0.697	5.0 (1.0-8.0)	0.794	8.0 (4.0-10.0)	0.367	<0.001[&]	7.0 (2.0-9.0)	0.521	5.0 (2.0-9.0)	0.450	8.0 (3.0-10.0)	0.502	<0.001[&]
Mild	6.5 (3.0-9.0)	0.246	6.0 (2.0-8.0)	0.107	8.0 (5.0-12.0)	0.301	<0.001[&]	7.0 (3.0-9.0)	0.638	5.0 (1.0-8.0)	0.477	8.0 (6.0-11.0)	0.230	<0.001[&]

Values are median (25th-75th percentile). [&]Indicates statistical significance. *For comparisons between valve size categories, "very small" is used as the reference. Other comparisons for the unmatched cohort: Total group: S vs M: p=0.357; S vs L: p=0.687; M vs L: p=0.706; SEV: S vs M: p=1.000; S vs L: p=1.000; M vs L: p=1.000; BEV: S vs M: p=0.0203; S vs L: p=0.000; M vs L: p=0.252. Other comparisons for the matched cohort: Total group: S vs M: p=0.169; S vs L: p=0.631; M vs L: p=0.423; SEV: S vs M: p=0.300; S vs L: p=0.837; M vs L: p=0.751; BEV: S vs M: p=0.005; S vs L: p≤0.001; M vs L: p=0.050. **For comparisons between LVEF tertiles, LVEF >50% is used as the reference category. Other comparisons for the unmatched cohort: Total group: LVEF <40% vs 40-50%: p=0.981; SEV: LVEF <40% vs 40-50%: p=0.720; BEV: LVEF <40% vs 40-50%: p=0.809. Other comparisons for the matched cohort: Total group: LVEF <40% vs 40-50%: p=0.840; SEV: LVEF <40% vs 40-50%: p=0.285; BEV: LVEF <40% vs 40-50%: p=0.216. ***For comparisons between stroke volume index category, SVI >35 ml/m^2 is used as the reference. ****For comparisons between calcification degrees, severe calcification is used as the reference. Other comparisons for the unmatched cohort: Total group: moderate vs mild: p=0.731; SEV: moderate vs mild: p=0.570; BEV: moderate vs mild: p=0.469. Other comparisons for the matched cohort: Total group: moderate vs mild: p=0.387; SEV: moderate vs mild: p=0.206; BEV: moderate vs mild: p=0.588. AoV: aortic valve; BEV: balloon-expandable valve; LVEF: left ventricular ejection fraction; ref: reference; SEV: self-expanding valve; SVI: stroke volume index; TAVI: transcatheter aortic valve implantation

p=0.011, respectively). Echocardiography-derived gradients did not show a significant association (HR 1.13, 95% CI: 0.87-1.75; p=0.248; HR 1.02, 95% CI: 0.95-1.10; p=0.639; and HR 0.99, 95% CI: 0.94-1.07; p=0.979, respectively) **(Table 5)**.

From a spline curve displaying post-TAVI invasive gradient and HR for all-cause mortality, the cutoff value for the invasive gradient to predict a clinically relevant outcome was identified as >10 mmHg **(Supplementary Figure 3)**. Additional Kaplan-Meier analysis by an invasive gradient <10 mmHg versus >10 mmHg demonstrated a significant difference in all-cause mortality at 1 year between the two groups (HR 1.83, 95% CI: 1.07-3.31; p=0.04) **(Supplementary Figure 4)**. In the multivariable regression, an invasive gradient >10 mmHg was an independent predictor at 30 days, 1 year and 2 years (HR 1.95, 95% CI: 1.13-4.78; p=0.028; HR 1.91, 95% CI: 1.11-3.65; p=0.030; and HR 1.61, 95% CI: 1.03-2.96; p=0.021, respectively) **(Table 5)**.

An invasive gradient >20 mmHg did not show a significant association with all-cause mortality at 30 days, 1 year or 2 years (HR 2.77, 95% CI: 0.37-20.69; p=0.320; HR 2.15, 95% CI: 0.53-8.77; p=0.287; and HR 1.48, 95% CI: 0.37-6.02; p=0.581, respectively). Conversely, a left ventricular ejection fraction below 30% was an independent predictor for all-cause mortality at 30 days, 1 year and 2 years (HR 3.69, 95% CI: 1.14-9.92; p=0.010; HR 3.02, 95% CI: 1.70-5.72; p<0.001; and HR 3.38, 95% CI: 1.73-5.85; p<0.001, respectively).

A subanalysis on the association between transvalvular mean gradients and mortality for SEV and BEV cohorts is displayed in **Supplementary Table 3**. Invasive gradients independently predicted a higher risk for all-cause mortality at

Table 4. Clinical outcomes.

30 days	Unmatched (n=1,211)			Matched (n=872)		
	SEV (n=573)	BEV (n=654)	Log-rank p	SEV (n=436)	BEV (n=436)	Log-rank p
All-cause mortality	15 (2.5)	14 (2.2)	0.581	13 (3.0)	8 (1.8)	0.240
Cardiovascular mortality	10 (1.7)	11 (1.7)	0.659	9 (2.1)	8 (1.7)	0.259
Rehospitalisation for heart failure	5 (1.0)	5 (0.7)	0.834	1 (0.2)	1 (0.2)	0.707
NYHA Class			0.411*			0.637
NYHA I	287/466 (61.6)	308/527 (58.4)		212/361 (58.7)	208/363 (57.3)	
NYHA II	136/466 (29.2)	170/527 (32.2)		116/361 (32.1)	121/363 (33.3)	
NYHA III	41/466 (8.8)	45/527 (8.5)		31/361 (8.6)	31/363 (8.5)	
NYHA IV	2/466 (0.4)	4/527 (0.8)		2/361 (5.5)	3/363 (0.8)	
Change in NYHA Class	–1.0 (–1.5 to –0.5)	–1.0 (–2.0 to 0.0)	0.950*	–1.0 (–1.0 to –0.5)	–1.0 (–2.0 to 0.0)	0.831
1 year						
All-cause mortality	49 (8.9)	51 (7.7)	0.628	41 (9.4)	39 (8.9)	0.215
Cardiovascular mortality	13 (2.2)	15 (2.3)	0.514	12 (2.8)	10 (2.3)	0.655
Rehospitalisation for heart failure	12 (2.2)	12 (1.9)	0.738	11 (2.5)	8 (1.8)	0.187
Bioprosthetic valve failure	17 (3.0)	23 (3.5)	0.254	13 (3.0)	17 (3.9)	0.389
NYHA Class			0.340*			0.612
NYHA I	135/247 (54.7)	193/335 (57.6)		121/231 (52.4)	137/234 (58.5)	
NYHA II	84/247 (34.0)	97/335 (28.9)		85/231 (36.8)	59/234 (25.2)	
NYHA III	26/247 (10.5)	40/335 (11.9)		23/231 (10.0)	34/234 (14.5)	
NYHA IV	2/247 (0.8)	5/335 (1.5)		2/231 (0.9)	4/234 (1.7)	
Change in NYHA Class	–1.0 (–2.0 to 0.0)	–1.0 (–2.0 to 0.0)	0.463*	–0.5 (–1.0 to 0.0)	–0.5 (–1.0 to 0.0)	0.391
2 years						
All-cause mortality	74 (12.9)	80 (12.2)	0.481	58 (13.3)	65 (14.9)	0.648
Cardiovascular mortality	24 (4.2)	22 (3.3)	0.101	20 (4.6)	16 (3.7)	0.914
Rehospitalisation for heart failure	26 (4.5)	22 (3.4)	0.077	20 (4.6)	21 (4.8)	0.378
Bioprosthetic valve failure	25 (4.4)	30 (4.6)	0.850	19 (4.4)	21 (4.8)	0.792
NYHA Class			0.317*			0.473
NYHA I	108/228 (47.3)	98/214 (45.8)		103/215 (47.9)	91/195 (46.6)	
NYHA II	96/228 (42.1)	83/214 (38.7)		92/215 (42.8)	78/195 (40.0)	
NYHA III	24/228 (10.5)	30/214 (14.0)		20/215 (9.3)	24/195 (12.3)	
NYHA IV	0/228 (0)	3/214 (1.4)		0/215 (0)	2/195 (1.0)	
Change in NYHA Class	–1.0 (–1.5 to 0.0)	–1.0 (–1.0 to 0.0)	0.349*	0.0 (–0.5 to 0.0)	–0.0 (–0.5 to 0.0)	0.293

Values are n (%) or n/N (%). *P-values for (change in) NYHA Class were calculated by the (McNemar) chi-square test. BEV: balloon-expandable valve; NYHA: New York Heart Association; SEV: self-expanding valve

30 days, 1 year and 2 years for both SEV (HR 1.05, 95% CI: 1.00-1.17; p=0.010; HR 1.04, 95% CI: 1.01-1.17; p=0.029; and HR 1.01, 95% CI: 1.00-1.10; p=0.041, respectively) and BEV (HR 1.07, 95% CI: 1.00-1.13; p=0.020; HR 1.16, 95% CI: 1.01-1.20; p=0.005; and HR 1.13, 95% CI: 1.01-1.18; p=0.029, respectively). Echocardiography-derived gradients did not show a significant association for SEV (HR 1.23, 95% CI: 0.91-1.66; p=0.175; HR 1.08, 95% CI: 0.91-1.11; p=0.946; and HR 0.97, 95% CI: 0.88-1.06; p=0.487, respectively) or BEV (HR 1.05, 95% CI: 0.93-1.19; p=0.436; HR 0.99, 95% CI: 0.89-1.09; p=0.822; and HR 0.96, 95% CI: 0.89-1.04; p=0.301, respectively).

Echocardiography-derived gradients showed no significant association with VARC-3 defined bioprosthetic valve failure at 1 year (HR 1.07, 95% CI: 0.98-1.17; p=0.136 [continuous], HR 1.11, 95% CI: 0.30-7.89; p=0.501 [>10 mmHg], and HR 1.29, 95% CI: 0.16-10.41; p=0.810 [>20 mmHg]). Invasive gradients also did not correlate with bioprosthetic valve failure at 1 year (HR 1.04, 95% CI: 0.98-1.10; p=0.127 [continuous], HR 1.99, 95% CI: 0.45-12.07; p=0.378

Table 5. Cox proportional hazards regression model for all-cause mortality.

Univariable	30 days		1 year		2 years	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age	1.00 (0.95-1.05)	0.798	0.98 (0.97-1.02)	0.140	0.99 (0.98-1.02)	0.787
Male	1.02 (0.96-1.09)	0.224	0.95 (0.60-1.49)	0.812	0.75 (0.51-1.12)	0.163
BMI	1.05 (0.98-1.12)	0.175	1.03 (0.99-1.07)	0.165	1.03 (0.99-1.07)	0.100
STS score	1.02 (0.96-1.09)	0.724	1.03 (1.00-1.05)	0.039[&]	1.04 (1.00-1.08)	0.034[&]
AVA	0.83 (0.51-1.15)	0.230	0.94 (0.82-1.12)	0.723	1.49 (0.79-2.81)	0.215
Diabetes	1.58 (0.66-3.71)	0.299	1.09 (0.69-1.73)	0.715	1.05 (0.71-1.56)	0.806
Hypertension	0.73 (0.30-1.77)	0.489	0.81 (0.50-1.29)	0.378	0.78 (0.52-1.17)	0.232
eGFR	0.99 (0.98-1.02)	0.661	0.99 (0.98-1.01)	0.641	1.00 (0.99-1.01)	0.717
eGFR <30 mL/min/1.73 m^2	1.80 (0.66-4.92)	0.251	1.48 (0.83-2.64)	0.185	1.23 (0.72-2.09)	0.450
Baseline LVEF	0.98 (0.95-1.02)	0.304	0.99 (0.97-1.01)	0.245	0.99 (0.97-1.00)	0.135
Baseline LVEF <30%	3.45 (1.34-8.92)	0.021[&]	1.91 (1.04-3.50)	<0.001[&]	3.16 (1.85-5.37)	<0.001[&]
Valve type (BEV/SEV)	0.49 (0.20-1.18)	0.112	0.89 (0.53-1.21)	0.284	0.91 (0.56-1.24)	0.279
Echo gradients						
Echo mean gradient post-TAVI (continuous)	1.13 (0.87-1.75)	0.248	1.02 (0.95-1.10)	0.639	0.99 (0.94-1.07)	0.979
Echo mean gradient post-TAVI >10 mmHg	1.07 (0.95-1.19)	0.189	1.76 (0.51-7.66)	0.309	1.32 (0.66-11.02)	0.573
Echo mean gradient post-TAVI >20 mmHg	1.05 (0.96-1.14)	0.205	2.37 (0.33-17.23)	0.394	2.33 (0.32-16.90)	0.404
Invasive gradients						
Invasive mean gradient post-TAVI (continuous)	1.08 (1.01-1.15)	0.034[&]	1.05 (1.00-1.10)	0.047[&]	1.05 (1.01-1.09)	0.009[&]
Invasive mean gradient post-TAVI >10 mmHg	2.94 (1.12-8.31)	0.030[&]	1.83 (1.07-3.31)	0.042[&]	1.71 (1.04-2.82)	0.036[&]
Invasive mean gradient post-TAVI >20 mmHg	2.77 (0.37-20.69)	0.320	2.15 (0.53-8.77)	0.287	1.48 (0.37-6.02)	0.581

Multivariable	30 days			2 years			2 years		
	B	HR (95% CI)	*p*-value	B	HR (95% CI)	*p*-value	B	HR (95% CI)	*p*-value
Model 1									
STS score		-		0.043	1.04 (0.99-1.10)	0.097	0.053	1.06 (0.99-1.12)	0.099
LVEF <30%	1.234	3.43 (1.17-10.12)	0.025[&]	1.075	2.93 (1.58-5.45)	<0.001[&]	1.171	3.23 (1.83-5.70)	<0.001[&]
Invasive mean gradient post-TAVI (continuous)	0.067	1.07 (1.00-1.14)	0.038[&]	0.060	1.06 (1.01-1.11)	0.007[&]	0.050	1.05 (1.01-1.09)	0.011[&]
Model 2									
STS score		-		0.157	1.17 (0.97-1.18)	0.365	0.048	1.05 (0.99-1.13)	0.096
LVEF <30%	1.306	3.69 (1.14-9.92)	0.010[&]	1.105	3.02 (1.70-5.72)	<0.001[&]	1.218	3.38 (1.73-5.85)	<0.001[&]
Invasive mean gradient post-TAVI >10 mmHg	0.667	1.95 (1.13-4.78)	0.028[&]	0.647	1.91 (1.11-3.65)	0.030[&]	0.476	1.61 (1.03-2.96)	0.021[&]

[&]Indicates statistical significance. AVA: aortic valve area; B: beta value; BEV: balloon-expandable valve; BMI: body mass index; CI: confidence interval; eGFR: estimated glomerular filtration rate; HR: hazard ratio; LVEF: left ventricular ejection fraction; SEV: self-expanding valve; STS: Society of Thoracic Surgeons; TAVI: transcatheter aortic valve implantation

[>10 mmHg], and HR 2.17, 95% CI: 0.27-17.19; p=0.463 [>20 mmHg]) **(Supplementary Table 4)**.

Discussion

The main findings of our comparative study of transprosthetic gradients by invasive measurement or echocardiography in TAVI with SEV or BEV are as follows: (1) only invasive mean gradients post-TAVI were associated with early, 1-year and 2-year mortality in both SEV and BEV; (2) invasive mean gradients post-TAVI were similar with SEV and BEV; (3) echocardiography-derived gradients were lower in SEV versus BEV patients; (4) there is a discordance between invasive and echocardiographic measurements before and after TAVI, with consistently lower invasive gradients; (5) this discordance is more pronounced with BEV than SEV; and (6) smaller THV size, higher LVEF and higher SVI increased the discordance.

Our data corroborate previous studies that showed a discordance between invasive and echocardiographic gradients. The randomised SOLVE-TAVI trial documented similar invasive gradients but higher gradients by echocardiography after BEV versus SEV[20]. Rodés-Cabau et al identified similar differences between BEV and SEV in valve-in-valve patients in the randomised LYTEN trial[8]. Abbas et al reported systematically higher gradients by echocardiography compared to invasive measurement and poor correlation between modalities[6,14]. Other authors have since reproduced these findings, both within the context of TAVI for native aortic valve stenosis as well as in degenerated bioprostheses[13,15].

Haemodynamic valve performance directly after valve implantation is assessed by invasive pressure recordings in the catheterisation laboratory and by echocardiography predischarge and at follow-up. It is vital to appreciate how both measurements are obtained. The invasive transaortic gradient is calculated as the net difference between left ventricular and aortic pressure and incorporates all contributing factors to flow, including pressure recovery. The technical limitations of invasive measurements are related to the need to calibrate the fluid-filled catheters and variation in catheter positioning in the ascending aorta (e.g., close to the sinotubular junction vs closer to the aortic arch). The ongoing DISCORDANCE TAVR (ClinicalTrials.gov: NCT04827238) study aims to evaluate the effects of catheter positioning on invasive pressure gradients[15]. Furthermore, catheters with multiple side holes may not capture the maximal gradient. Filling status, transient cardiac stunning and sedatives/anaesthesia may affect immediate flow post-TAVI, and changes in the hours following TAVI may result in different gradients over time[6,21]. These phenomena, however, would likely occur in both SEV and BEV groups, and our findings of equally low invasive gradients after TAVI in both groups corroborate this assumption. Moreover, in our centre, general anaesthesia is not applied, but instead, TAVI procedures are performed under local anaesthesia (with no sedation).

Echocardiography relies on Doppler flow velocities to determine transvalvular pressure gradients. However, echocardiography has intrinsic limitations **(Supplementary Table 5)**. Sample errors can occur when the ultrasound beam is not properly aligned with actual flow direction. There is also no consensus on where the Doppler beam should be positioned relative to the stent frame of different THV platforms[9,10].

Inherent limitations of the simplified Bernoulli formula may partly explain the discrepancies between invasive and echocardiographic gradients: the Bernoulli equation assumes laminar flow and a single level of stenosis and discards proximal LV velocity and pressure recovery, which may be accentuated after TAVI[22,23].

Pressure recovery relates to the phenomenon that the maximum speed of blood flow occurs at the narrowest point (vena contracta) and then decelerates entering the ascending aorta[9,24-27]. The loss of velocity occurs when kinetic energy is converted back to potential energy (e.g., blood pressure)[27,28]. Pressure recovery is taken into account with an invasive measurement that is assessed above the valve in the ascending aorta. Conversely, with echocardiography, the maximum velocity is measured at the level of the vena contracta where pressure recovery has not yet occurred **(Figure 2A)**.

We found lower echocardiographic maximum and mean gradients after TAVI with SEV versus BEV despite equal invasive gradients. The discordance between invasive and echocardiographic gradients was more pronounced with BEV than SEV in our series, which is consistent with previous research[6-10,14]. Furthermore, results from our subanalysis of patients with a small aortic annulus, which are in accordance with data from the recent SMART trial, yielded even greater discordance for BEV compared to SEV[29].

We speculate that the greater discordance in BEV versus SEV could be related to THV frame design: the SEV outflow expands into the aorta and is approximately twice the size of the BEV outflow. An earlier study on the haemodynamic effects of THV design illustrated that SEV exhibit a longer conduit upstream of the leaflets compared to BEV, which may contribute to an increase in turbulent flow distal to the valve, less conversion to potential energy and hypothetically less pressure recovery[10]. Because of the assumed blunted pressure recovery with SEV, the invasively measured gradient may be higher, and the discrepancy between invasive and (overestimated) echocardiographic pressure measurements may therefore be smaller for SEV. An exaggerated representation of this phenomenon is illustrated in **Figure 2B**-**Figure 2C**. It is important to note that in the setting of a normally functioning THV, the overall proportion of turbulent flow is very limited.

For the first time, we have demonstrated that THV size, LVEF and SVI further affect the discordance between invasive and echocardiographic measurements. Indeed, we found greater discordance with a smaller THV size, which seems consistent with the notion that pressure recovery is more pronounced in smaller anatomies[25]. This phenomenon occurred with BEV and SEV but was most pronounced in BEV. Abbas et al found higher echocardiographic gradients in small compared to large THV sizes in BEV but not in SEV patients[6,16].

Our data further suggest that a higher LVEF reinforces the discordance between invasive gradients and those derived by echocardiography. Although no specific studies on this phenomenon are available, we hypothesise that this is again related to limitations of the Bernoulli formula, which is not linear but contains a quadratic function. A higher transvalvular flow velocity with a higher LVEF will increase

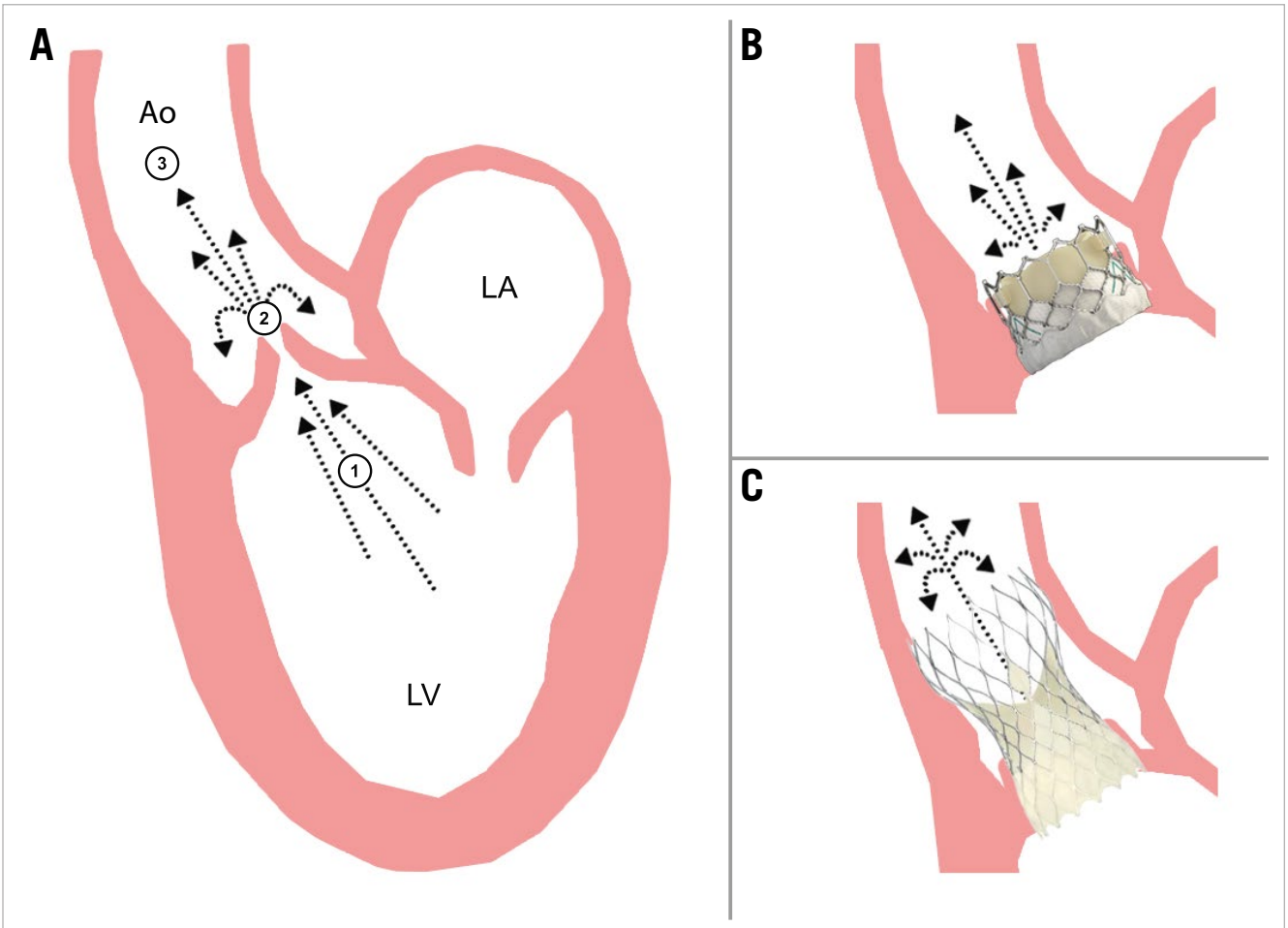


Figure 2. *Illustration of the pressure recovery phenomenon. A) Maximum speed of blood flow occurs at the narrowest point (vena contracta) and decelerates entering the ascending aorta. Velocity loss occurs when kinetic energy is converted back to potential energy (e.g., blood pressure). Invasive transvalvular gradients are measured between the LVOT (1) and the ascending aorta (3) by using double-lumen fluid-filled catheters for simultaneous LV and aortic pressure measurements. Echo-derived measurement requires manual alignment of the interrogating Doppler beam with the highest-velocity flow across the aortic valve at the level of the vena contracta (2). B) Illustration of a balloon-expandable (SAPIEN 3 [Edwards Lifesciences]) THV. C) Illustration of a self-expanding (Evolut [Medtronic]) THV. SEV exhibit a longer conduit upstream of the leaflets compared to BEV, which contributes to increased turbulent flow distal to the valve, possibly dampening pressure recovery. BEV therefore exhibit a higher rate of pressure recovery than SEV. Ao: aorta; BEV: balloon-expandable valve; LA: left atrium; LV: left ventricle; LVOT: left ventricular outflow tract; SEV: self-expanding valve; THV: transcatheter heart valve*

the transvalvular gradient in a quadratic proportion, which enhances the magnitude of the absolute echo versus invasive difference. This hypothesis is further supported by our finding that increasing SVI expands the magnitude of discordance, which was also shown by Stanová et al and Abbas et al[9,16].

For the first time, we have shown that invasive but not echocardiographic gradients post-TAVI are an independent predictor for all-cause mortality at 30 days, 1 year and 2 years. This may help explain why in the randomised CHOICE trial, even though gradients by echocardiography were higher with BEV, there was no difference in outcome at 1 year or 5 years between BEV and SEV[30]. Also in the SOLVE-TAVI trial, there was no difference in clinical outcome between contemporary BEV and SEV platforms[20]. Abbas et al found no association between invasive gradients (>10 mmHg) and 2-year mortality, while Khalili et al described lower mortality with low (<5 mmHg) invasive gradients relative to higher gradients (>20 mmHg)[6,18].

We hypothesise that invasive measurements ultimately provide the purest reflection of left ventricular load as they take pressure recovery into account (as opposed to echocardiography). This may explain why elevated echo gradients, which in some patients may be attributable to the intrinsic limitations of echocardiography rather than reflecting cardiac manifestations, are not predictors of all-cause mortality. Moreover, a substantial group of patients with elevated echo gradients relative to the median (e.g., 15.0-20.0 mmHg) demonstrated no mortality events during follow-up, which consequently further attenuates the association of echocardiographic gradients with mortality. In contrast, we

typically registered low mean gradients by invasive assessment (median 3.0 mmHg), but when elevated (>10 mmHg), the likelihood of mortality was higher **(Supplementary Figure 4)**. Collectively, our data underscore the value of invasive pressure acquisition immediately after TAVI and the importance for optimisation techniques (e.g., balloon post-dilatation) when a high residual gradient is invasively measured in the catheterisation laboratory. Echocardiography remains the standard for transprosthetic gradient follow-up over time, but the difference between predischarge echocardiography and invasive assessment should be documented to appropriately interpret an elevated gradient by echocardiography at a later follow-up. Furthermore, it seems reasonable to confirm any relevant gradient increments by invasive measurements before attributing clinical and therapeutic consequences.

Clinically relevant differences in pressure recordings between invasive and echocardiographic measurements are further demonstrated by our data – out of 19 patients with an elevated gradient (>20 mmHg) post-TAVI by echocardiography, only 5 patients (26.3%) had an invasive mean transaortic gradient >20 mmHg.

Future studies should further investigate differences in blood flow dynamics after implantation with BEV and SEV by using advanced imaging techniques, such as four-dimensional flow cardiovascular magnetic resonance.

Our findings highlight the importance of routine invasive assessment of transvalvular gradient after TAVI and suggest that a mean gradient >10 mmHg by invasive assessment should trigger further action.

Limitations

Limitations of this study include (1) its retrospective nature – consequently, no randomised comparison between THV platforms was feasible; (2) selection bias – the transcatheter platform selection was per operator discretion and based on the aortic root anatomy as determined by MSCT. Baseline characteristics between the SEV and BEV cohorts displayed statistical differences; however, it seems unlikely these differences were relevant for our findings since a propensity-matched analysis corroborated our main findings; (3) the absence of an independent core lab; and (4) the time interval between the immediate invasive measurements and the later echocardiographic measurements (up to 24 hours after implantation) may coincide with different haemodynamic loading conditions, LV recovery and ongoing (nitinol) frame expansion at the time of the respective gradient assessments.

Many previous studies comparing invasive and echocardiographic pressure measurements after TAVI had smaller sample sizes, were restricted to patient subsets, relied on suboptimal echocardiography in the catheterisation laboratory with the patient in supine position[8,14], or had longer intervals between invasive and echocardiography-derived measurements[8,9]. The relatively larger sample size, meticulous and methodological data acquisition and correlation with clinical outcome make our dataset robust.

Conclusions

Only invasively measured but not echocardiography-derived transvalvular mean gradients correlate with 30-day, 1-year and 2-year mortality. Aortic gradient measurements are higher by echocardiography than by invasive assessment, and more so for BEV than SEV. Smaller valve size, higher ejection fraction and higher stroke volume increase this discordance between echocardiography and invasive assessment.

Authors' affiliations

1. Department of Cardiology, Cardiovascular Institute, Thoraxcenter, Erasmus University Medical Center, Rotterdam, the Netherlands; 2. Department of Radiology and Nuclear Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands

Conflict of interest statement

N.M. Van Mieghem reports grants or contracts from Abbott, Boston Scientific, Biotronik, Edwards Lifesciences, Medtronic, PulseCath BV, Abiomed, and Daiichi Sankyo; consulting fees from JenaValve, Daiichi Sankyo, Abbott, Boston Scientific, and Medtronic; and payment or honoraria for lectures, presentations, speakers bureau, manuscripts and educational events from Abiomed, Amgen, and JenaValve. J. Daemen reports grants or contracts from AstraZeneca, Abbott, Boston Scientific, Acist Medical, Medtronic, MicroPort, Pie Medical, and Recor Medical; and consultancy and speaker fees from Abbott, Abiomed, Acist Medical, Boston Scientific, Cardialysis BV, CardiacBooster, Kaminari Medical, Recor Medical, PulseCath, Pie Medical, Sanofi, Siemens, and Medtronic. A. Hirsch reports grants and consultancy fees from GE HealthCare; speaker fees from GE HealthCare and Bayer; and he is also a member of the medical advisory board of Medis Medical Imaging Systems. The other authors have no conflicts of interest to declare.

References

1. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363:1597-607.

2. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364:2187-98.

3. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP; SURTAVI Investigators. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med.* 2017;376:1321-31.

4. Gleason TG, Reardon MJ, Popma JJ, Deeb GM, Yakubov SJ, Lee JS, Kleiman NS, Chetcuti S, Hermiller JB Jr, Heiser J, Merhi W, Zorn GL 3rd, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte JV, Mumtaz M, Oh JK, Huang J, Adams DH; CoreValve U.S. Pivotal High Risk Trial Clinical Investigators. 5-Year Outcomes of Self-Expanding Transcatheter Versus Surgical Aortic Valve Replacement in High-Risk Patients. *J Am Coll Cardiol.* 2018;72:2687-96.

5. Van Mieghem NM, Deeb GM, Søndergaard L, Grube E, Windecker S, Gada H, Mumtaz M, Olsen PS, Heiser JC, Merhi W, Kleiman NS, Chetcuti SJ, Gleason TG, Lee JS, Cheng W, Makkar RR, Crestanello J, George B, George I, Kodali S, Yakubov SJ, Serruys PW, Lange R, Piazza N, Williams MR, Oh JK, Adams DH, Li S, Reardon MJ; SURTAVI Trial

Investigators. Self-expanding Transcatheter vs Surgical Aortic Valve Replacement in Intermediate-Risk Patients: 5-Year Outcomes of the SURTAVI Randomized Clinical Trial. *JAMA Cardiol.* 2022;7:1000-8.

6. Abbas AE, Mando R, Kadri A, Khalili H, Hanzel G, Shannon F, Al-Azizi K, Waggoner T, Kassas S, Pilgrim T, Okuno T, Camacho A, Selberg A, Elmariah S, Bavry A, Ternacle J, Christensen J, Gheewala N, Pibarot P, Mack M. Comparison of Transvalvular Aortic Mean Gradients Obtained by Intraprocedural Echocardiography and Invasive Measurement in Balloon and Self-Expanding Transcatheter Valves. *J Am Heart Assoc.* 2021;10:e021014.

7. Bavry AA, Aalaei-Andabili SH, Okuno T, Kumbhani DJ, Stortecky S, Asami M, Lanz J, Windecker S, Pilgrim T. Transvalvular Gradients for Balloon-Expandable and Self-Expanding Valves. *J Invasive Cardiol.* 2020;32:E258-60.

8. Rodés-Cabau J, Abbas AE, Serra V, Vilalta V, Nombela-Franco L, Regueiro A, Al-Azizi KM, Iskander A, Conradi L, Forcillo J, Lilly S, Calabuig A, Fernandez-Nofrerias E, Mohammadi S, Panagides V, Pelletier-Beaumont E, Pibarot P. Balloon- vs Self-Expanding Valve Systems for Failed Small Surgical Aortic Valve Bioprostheses. *J Am Coll Cardiol.* 2022;80:681-93.

9. Stanová V, Rieu R, Côté N, Salaun E, Rodés-Cabau J, Pibarot P. In vitro Doppler versus catheter transvalvular pressure gradients in balloon-expandable versus self-expanding transcatheter aortic valves. *Catheter Cardiovasc Interv.* 2022;99:201-10.

10. Hatoum H, Hahn RT, Lilly S, Dasi LP. Differences in Pressure Recovery Between Balloon Expandable and Self-expandable Transcatheter Aortic Valves. *Ann Biomed Eng.* 2020;48:860-7.

11. Hase H, Yoshijima N, Yanagisawa R, Tanaka M, Tsuruta H, Shimizu H, Fukuda K, Naganuma T, Mizutani K, Yamawaki M, Tada N, Yamanaka F, Shirai S, Tabata M, Ueno H, Takagi K, Watanabe Y, Yamamoto M, Hayashida K; OCEAN-TAVI Investigators. Transcatheter aortic valve replacement with Evolut R versus Sapien 3 in Japanese patients with a small aortic annulus: The OCEAN-TAVI registry. *Catheter Cardiovasc Interv.* 2021;97:E875-86.

12. Abdelghani M, Mankerious N, Allali A, Landt M, Kaur J, Sulimov DS, Merten C, Sachse S, Mehilli J, Neumann FJ, Frerker C, Kurz T, El-Mawardy M, Richardt G, Abdel-Wahab M. Bioprosthetic Valve Performance After Transcatheter Aortic Valve Replacement With Self-Expanding Versus Balloon-Expandable Valves in Large Versus Small Aortic Valve Annuli: Insights From the CHOICE Trial and the CHOICE-Extend Registry. *JACC Cardiovasc Interv.* 2018;11:2507-18.

13. Ochiai T, Yoon SH, Sharma R, Miyasaka M, Nomura T, Rami T, Maeno Y, Chakravarty T, Nakamura M, Cheng W, Makkar R. Outcomes of Self-Expanding vs. Balloon-Expandable Transcatheter Heart Valves for the Treatment of Degenerated Aortic Surgical Bioprostheses - A Propensity Score-Matched Comparison. *Circ J.* 2018;82:2655-62.

14. Abbas AE, Mando R, Hanzel G, Gallagher M, Safian R, Hanson I, Almany S, Pibarot P, Dalal P, Vivacqua A, Sakwa M, Shannon F. Invasive Versus Echocardiographic Evaluation of Transvalvular Gradients Immediately Post-Transcatheter Aortic Valve Replacement. *Circ Cardiovasc Interv.* 2019;12:e007973.

15. Barker M, Abbas AE, Webb JG, Pibarot P, Sathananthan J, Brunner N, Wang DD, Wang J, Leon MB, Wood DA. Standardized Invasive Hemodynamics for Management of Patients With Elevated Echocardiographic Gradients Post-Transcatheter Aortic Valve Replacement at Midterm Follow-Up. *Circ Cardiovasc Interv.* 2022;15:e011243.

16. Abbas AE, Khalili H, Madanat L, Elmariah S, Shannon F, Al-Azizi K, Waggoner T, Pilgrim T, Okuno T, Bavry A, Ternacle J, Christensen J, Cabau JR, Mack M, Pibarot P. Echocardiographic Versus Invasive Aortic Valve Gradients in Different Clinical Scenarios. *J Am Soc Echocardiogr.* 2023;36:1302-14.

17. Alperi A, Robichaud M, Panagides V, Mesnier J, Nuche J, Paradis JM, Delarochelliere R, Kalavrouziotis D, Dumont E, Mohammadi S, Rodés-Cabau J. Impact of residual transvalvular gradient on clinical outcomes following valve-in-valve transcatheter aortic valve replacement. *Int J Cardiol.* 2022;366:90-6.

18. Khalili H, Pibarot P, Hahn RT, Elmariah S, Pilgrim T, Bavry AA, Maini B, Okuno T, Al-Azizi K, Waggoner TE, Mack M, Rodès-Cabau J, Abbas AE. Transvalvular Pressure Gradients and All-Cause Mortality Following TAVR: A Multicenter Echocardiographic and Invasive Registry. *JACC Cardiovasc Interv.* 2022;15:1837-48.

19. Zamorano JL, Badano LP, Bruce C, Chan KL, Gonçalves A, Hahn RT, Keane MG, La Canna G, Monaghan MJ, Nihoyannopoulos P, Silvestry FE, Vanoverschelde JL, Gillam LD. EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease. *Eur Heart J.* 2011;32:2189-214.

20. Thiele H, Kurz T, Feistritzer HJ, Stachel G, Hartung P, Eitel I, Marquetand C, Nef H, Doerr O, Lauten A, Landmesser U, Abdel-Wahab M, Sandri M, Holzhey D, Borger M, Ince H, Öner A, Meyer-Saraei R, Wienbergen H, Fach A, Frey N, König IR, Vonthein R, Rückert Y, Funkat AK, de Waha-Thiele S, Desch S. Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial. *Eur Heart J.* 2020;41:1890-9.

21. Naidu S, Chen T, Fiorilli P, Li RH, Desai N, Szeto WY, Giri J, Kobayashi T, Atluri P, Herrmann HC. Measuring TAVR Prosthesis Gradient Immediately Post-Procedure May Underestimate its Significance. *JACC Cardiovasc Interv.* 2022;15:120-1.

22. Firstenberg MS, Abel EE, Papadimos TJ, Tripathi RS. Nonconvective forces: a critical and often ignored component in the echocardiographic assessment of transvalvular pressure gradients. *Cardiol Res Pract.* 2012;2012:383217.

23. Herrmann HC, Pibarot P, Wu C, Hahn RT, Tang GHL, Abbas AE, Playford D, Ruel M, Jilaihawi H, Sathananthan J, Wood DA, De Paulis R, Bax JJ, Rodes-Cabau J, Cameron DE, Chen T, Del Nido PJ, Dweck MR, Kaneko T, Latib A, Moat N, Modine T, Popma JJ, Raben J, Smith RL, Tchetche D, Thomas MR, Vincent F, Yoganathan A, Zuckerman B, Mack MJ, Leon MB; Heart Valve Collaboratory. Bioprosthetic Aortic Valve Hemodynamics: Definitions, Outcomes, and Evidence Gaps: JACC State-of-the-Art Review. *J Am Coll Cardiol.* 2022;80:527-44.

24. Levine RA, Jimoh A, Cape EG, McMillan S, Yoganathan AP, Weyman AE. Pressure recovery distal to a stenosis: potential cause of gradient "overestimation" by Doppler echocardiography. *J Am Coll Cardiol.* 1989;13:706-15.

25. Niederberger J, Schima H, Maurer G, Baumgartner H. Importance of pressure recovery for the assessment of aortic stenosis by Doppler ultrasound. Role of aortic size, aortic valve area, and direction of the stenotic jet in vitro. *Circulation.* 1996;94:1934-40.

26. Razzolini R, Manica A, Tarantini G, Ramondo A, Napodano M, Iliceto S. Discrepancies between catheter and Doppler estimates of aortic stenosis: the role of pressure recovery evaluated 'in vivo'. *J Heart Valve Dis.* 2007;16:225-9.

27. Herrmann HC, Laskey WK. Pressure loss recovery in aortic valve stenosis: Contemporary relevance. *Catheter Cardiovasc Interv.* 2022;99:195-7.

28. Laskey WK, Kussmaul WG. Pressure recovery in aortic valve stenosis. *Circulation.* 1994;89:116-21.

29. Herrmann HC, Mehran R, Blackman DJ, Bailey S, Möllmann H, Abdel-Wahab M, Ben Ali W, Mahoney PD, Ruge H, Wood DA, Bleiziffer S, Ramlawi B, Gada H, Petronio AS, Resor CD, Merhi W, Garcia Del Blanco B, Attizzani GF, Batchelor WB, Gillam LD, Guerrero M, Rogers T, Rovin JD, Szerlip M, Whisenant B, Deeb GM, Grubb KJ, Padang R, Fan MT, Althouse AD, Tchétché D; SMART Trial Investigators. Self-Expanding or Balloon-Expandable TAVR in Patients with a Small Aortic Annulus. *N Engl J Med.* 2024;390:1959-71.

30. Abdel-Wahab M, Landt M, Neumann FJ, Massberg S, Frerker C, Kurz T, Kaur J, Toelg R, Sachse S, Jochheim D, Schäfer U, El-Mawardy M, Robinson DR, Richardt G; CHOICE Investigators. 5-Year Outcomes After TAVR With Balloon-Expandable Versus Self-Expanding Valves: Results From the CHOICE Randomized Clinical Trial. *JACC Cardiovasc Interv.* 2020;13:1071-82.

Supplementary data

Supplementary Table 1. Subanalysis of invasive and echocardiographic gradient measurements in patients with a small aortic annulus.

Supplementary Table 2. Subanalysis of clinical outcomes in patients with a small aortic annulus.

Supplementary Table 3. Cox proportional hazards regression model for all-cause mortality according to THV type.
Supplementary Table 4. Cox proportional hazards regression model for bioprosthetic valve failure.
Supplementary Table 5. Advantages and limitations of invasive and echocardiographic gradient measurements.
Supplementary Figure 1. Flowchart of the study population.
Supplementary Figure 2. Invasive and echocardiography-derived postprocedural gradient measurements in an individual patient.
Supplementary Figure 3. Spline curve for hazard ratio versus post-TAVI invasive gradient.
Supplementary Figure 4. Kaplan-Meier curve for all-cause mortality.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-24-00341

Supplementary data

Supplementary Table 1. Subanalysis of invasive and echocardiographic gradient measurements in patients with a small aortic annulus.

	Matched (n=315)		
	SEV	**BEV**	**P**
Echocardiography			
Pre-TAVI	**(n=162)**	**(n=153)**	
Mean PG (mmHg)	41.0 (32.0-50.0)	38.0 (30.0-48.0)	0.604
Peak PG (mmHg)	69.0 (55.0-85.0)	66.0 (58.0-84.0)	0.534
Pre-discharge	**(n=162)**	**(n=153)**	
Mean PG (mmHg)	8.0 (6.0-11.0)	12.0 (9.0-16.0)	**<0.001**
Peak PG (mmHg)	14.0 (11.0-19.0)	21.0 (16.0-29.0)	**<0.001**
12 months	**(n=159)**	**(n=145)**	
Mean PG (mmHg)	8.0 (6.0-11.0)	10.0 (8.0-15.0)	**0.010**
Peak PG (mmHg)	16.0 (12.0-19.0)	19.0 (14.0-27.0)	**0.008**
Invasive			
Pre-TAVI	**(n=162)**	**(n=153)**	
Mean PG (mmHg)	35.0 (27.0-29.0)	36.0 (25.0-45.0)	0.478
Peak PG (mmHg)	53.0 (32.0-65.0)	49.0 (35.0-64.0)	**0.046**
Post-TAVI	**(n=162)**	**(n=153)**	
Mean PG (mmHg)	3.0 (0.0-5.0)	3.0 (0.0-6.0)	0.740
Peak PG (mmHg)	2.0 (0.0-4.0)	2.0 (0.0-5.0)	0.345
Difference between gradients			
Pre-TAVI echo mean PG - pre-TAVI invasive mean PG (mmHg)	5.0 (2.0-8.0) **(p<0.001)***	3.0 (1.0-5.0) **(p<0.001)***	**0.019**
Post-TAVI echo mean PG - post-TAVI invasive meanPG(mmHg)	5.0 (2.0-8.0) **(p<0.001)***	8.0 (5.0-12.0) **(p<0.001)***	**<0.001**
Pre-TAVI echo peak PG - pre-TAVI invasive peak PG (mmHg)	19.0 (8.0-28.0) **(p<0.001)***	21.0 (12.0-34.0) **(p<0.001)***	0.179
Post-TAVI echo peak PG - post-TAVI invasive peakPG(mmHg)	12.0 (8.0-16.0) **(p<0.001)***	19.0 (14.0-25.0) **(p<0.001)***	**<0.001**
Number of patients displaying meanPG >20 mmHg post-TAVI			
Echocardiography	1 (0.6)	4 (2.6)	0.156
Echocardiography + confirmed by invasive measurement>20mmHg	0 (0)	2 (1.3)	0.144
Invasive	0 (0)	2 (1.3)	0.144

Values are median(25-75th percentile) or n (%). PG = pressure gradient; BEV=balloon-expandable valve; SEV=self-expanding valve. *P applies to the difference between echo-derived mean gradient and invasive mean gradient within groups.

Supplementary Table 2. Subanalysis of clinical outcomes in patients with a small aortic annulus.

	Matched (n=315)		
30 days	**SEV (n=162)**	**BEV (n=153)**	**Log rank P**
All-cause mortality	6 (3.7)	4 (2.6)	0.588
Cardiovascular mortality	4 (2.5)	3 (2.0)	0.286
Rehospitalisation for heart failure	1 (0.6)	2 (1.3)	0.529
NYHA Class			0.427*
o NYHA 1	85/137 (62.0)	72/124 (58.0)	
o NYHA 2	43/137 (31.4)	43/124 (34.7)	
o NYHA 3	9/137 (6.6)	7/124 (5.6)	
o NYHA 4	0/137 (0)	2/124 (1.6)	
12 months			
All-cause mortality	10 (6.2)	13 (8.5)	0.436
Cardiovascular mortality	5 (3.1)	6 (3.9)	0.589
Rehospitalisation for heart failure	2 (1.2)	4 (2.6)	0.368
Bioprosthetic valve failure	8 (4.9)	10 (6.5)	0.539
NYHA Class			0.628*
o NYHA 1	46/89 (51.7)	46/84 (54.8)	
o NYHA 2	31/89 (34.8)	23/84 (27.4)	
o **NYHA 3**	12/89 (13.5)	13/84 (15.5)	
o **NYHA 4**	0/89 (0)	2/84 (2.4)	
24 months			
All-cause mortality	14 (8.6)	22 (14.4)	0.114
Cardiovascular mortality	5 (3.1)	10 (6.5)	0.156
Rehospitalisation for heart failure	10 (6.2)	10 (6.5)	0.888
Bioprosthetic valve failure	8 (4.9)	17 (11.1)	**0.042**
NYHA Class			0.723
NYHA 1	41/79 (51.9)	39/77 (50.6)	
NYHA 2	30/79 (37.9)	26/77 (33.8)	
NYHA 3	8/79 (10.1)	10/77 (13.0)	
NYHA 4	0/79 (0)	2/77 (2.6)	

Values are n (%). BEV = balloon-expandable valve; SEV = self-expanding valve;

Supplementary Table 3. Cox proportional hazards regression model for all-cause mortality according to THV type.

	SEV						BEV					
Univariable	**30 days**		**12 months**		**24 months**		**30 days**		**12 months**		**24 months**	
	HR	**P**	**HR**	**P**	**HR**	**P**	**HR**	**P**	**HR**	**P**	**HR**	**P**
Age	0.98 (0.92-1.03)	0.412	1.09 (1.01-1.16)	**0.037**	1.04 (1.01-1.11)	**0.040**	1.00 (0.95-1.05)	0.798	0.95 (0.92-1.02)	0.140	0.99 (0.98-1.02)	0.787
Male	1.05 (0.91-1.11)	0.300	0.99 (0.92-1.60)	0.686	0.98 (0.76-1.35)	0.373	1.01 (0.93-1.15)	0.294	0.92 (0.46-1.81)	0.798	1.03 (0.63-1.70)	0.895
BMI	1.07 (0.99-1.15)	0.101	0.97 (0.93 - 1.03)	0.428	0.99 (0.94-1.04)	0.629	1.05 (0.94-1.17)	0.430	0.99 (0.92-1.07)	0.894	0.98 (0.93-1.03)	0.979
STS	1.11 (0.98-1.17)	0.124	1.14 (1.06-1.18)	**<0.001**	1.23 (1.18-1.29)	**<0.001**	1.08 (0.97-1.15)	0.188	1.17 (1.11-1.24)	**<0.001**	1.09 (1.03-1.19)	**0.026**
AVA	0.61 (0.44-1.21)	0.381	0.85 (0.29-2.64)	0.783	0.59 (0.21-1.77)	0.343	0.72 (0.56-1.46)	0.488	1.56 (0.58-3.24)	0.284	1.91 (0.59-6.24)	0.291
Diabetes	1.59 (0.61-4.19)	0.344	1.54 (0.86-2.75)	0.148	1.60 (0.94-2.69)	0.106	1.10 (0.94-1.30)	0.172	1.12 (0.55-2.27)	0.747	1.21 (0.77-2.10)	0.353
Hypertension	2.04 (0.47-6.91)	0.343	0.72 (0.37-1.35)	0.303	0.72 (0.40-1.28)	0.259	0.60 (0.46-1.28)	0.347	0.94 (0.67-1.37)	0.365	0.84 (0.31-1.11)	0.605
eGFR	0.99 (0.96-1.02)	0.509	0.99 (0.98-1.02)	0.371	0.99 (0.98-1.01)	0.357	0.98 (0.97-1.01)	0.218	0.98 (0.97-1.00)	0.111	0.97 (0.90-1.04)	0.450
eGFR<30	3.12 (1.55-6.49)	**0.026**	2.08 (1.43-4.89)	**0.034**	1.98 (0.91-3.45)	0.120	1.68 (0.21-13.72)	0.624	2.06 (0.79-5.32)	0.136	1.16 (0.73-2.55)	0.102
Baseline LVEF	0.97 (0.95-1.02)	0.244	0.97 (0.95-1.01)	0.301	0.98 (0.96-1.04)	0.389	1.00 (0.94-1.07)	0.925	1.01 (0.97-1.03)	0.946	0.98 (0.96-1.00)	0.126
Baseline LVEF <30%	4.65 (1.41-6.10)	**0.002**	5.07 (3.07-14.09)	**<0.001**	4.34 (2.52-9.28)	**<0.001**	3.16 (1.31-6.12)	**0.030**	1.55 (1.17-2.99)	**0.002**	2.05 (1.48-4.76)	**<0.001**
Echo gradients												
Echo mean gradient post-TAVI (continuous)	1.23 (0.91-1.66)	0.175	1.08 (0.91-1.11)	0.946	0.97 (0.88-1.06)	0.487	1.05 (0.93-1.19)	0.436	0.99 (0.89-1.09)	0.822	0.96 (0.89-1.04)	0.301
Echo mean gradient post-TAVI > 10 mmHg	1.10 (0.91-1.31)	0.261	1.54 (0.32-4.32)	0.429	1.60 (0.71-3.58)	0.316	1.06 (0.92-1.28)	0.3791	1.10 (0.53-1.41)	0.628	1.18 (0.70-1.89)	0.155
Echo mean gradient post-TAVI > 20 mmHg	1.09 (0.91-1.19)	0.281	2.19 (0.29-16.16)	0.439	1.63 (0.22-11.86)	0.630	1.17 (0.90-1.25)	0.157	2.86 (0.66-7.23)	0.186	2.02 (0.69-9.70)	0.551
Invasive gradients												
Invasive mean gradient post-TAVI (continuous)	1.12 (1.04-1.34)	**0.010**	1.09 (1.01-1.15)	**0.019**	1.02 (1.00-1.13)	**0.039**	1.03 (1.01-1.19)	**0.021**	1.02 (1.00-1.13)	**0.035**	1.17 (1.03-1.28)	**0.004**
Invasive mean gradient post-TAVI > 10 mmHg	2.21 (1.57-4.55)	**0.002**	1.43 (1.19-2.86)	**0.005**	1.40 (1.04-2.23)	**0.011**	2.80 (1.28-4.94)	**0.001**	2.06 (1.79-4.15)	**0.001**	1.79 (1.10-3.07)	**0.006**
Invasive mean gradient post-TAVI > 20 mmHg	2.61 (0.41-16.00)	0.296	2.35 (0.38-17.10)	0.459	2.02 (0.28-8.93)	0.475	3.15 (0.21-19.05)	0.166	2.94 (0.35-10.10)	0.130	1.67 (0.59-3.60)	0.266
Multivariable	**30 days**			**12 months**			**24 months**			**30 days**			**12 months**			**24 months**		
	B	**HR**	**P**	**B**	**HR**	**P**	**B**	**HR**	**P**	**B**	**HR**	**P**	**B**	**HR**	**P**	**B**	**HR**	**P**
Model 1																		
Age		-		0.068	1.07 (0.99-1.15)	0.131	0.166	1.18 (0.81-1.68)	0.286		-			-			-	

STS score		-		0.191	1.21 (0.90-1.70)	0.158	0.174	1.19 (0.95-1.55)	0.233		-		0.058	1.06 (0.97-1.18)	0.112	0.020	1.02 (0.95-1.21)	0.249
eGFR<30	1.047	2.85 (1.41-4.50)	**0.012**	0.531	1.70 (1.12-2.56)	**0.033**		-			-			-			-	
LVEF <30%	1.411	4.10 (1.85-5.99)	**<0.001**	1.656	5.24 (2.86-12.10)	**<0.001**	1.256	3.51 (1.90-7.15)	**<0.001**	1.275	3.58 (1.40-5.39)	**<0.001**	0.774	2.17 (1.19-4.94)	**0.001**	1.085	2.96 (2.07-6.32)	**<0.001**
Invasive mean gradient post-TAVI (continuous)	0.049	1.05 (1.00-1.17)	**0.010**	0.039	1.04 (1.01-1.17)	**0.029**	0.010	1.01 (1.00-1.10)	**0.041**	0.068	1.07 (1.00-1.13)	**0.020**	0.148	1.16 (1.01-1.20)	**0.005**	0.122	1.13 (1.01-1.18)	**0.029**
Model 2																		
Age		-		0.095	1.10 (0.95-1.81)	0.360	0.086	1.09 (0.91-2.30)	0.422		-			-			-	
STS score		-		0.148	1.16 (0.91-1.33)	0.203	0.086	1.09 (0.97-1.22)	0.386		-		0.104	1.11 (0.99-1.15)	0.215	0.148	1.16 (0.96-1.28)	0.190
eGFR<30	1.082	2.95 (1.32-5.67)	**<0.001**	0.916	2.50 (1.64-5.16)	**0.002**		-			-			-			-	
LVEF <30%	1.147	3.15 (1.32-7.26)	**<0.001**	1.004	2.73 (1.16-6.45)	**<0.001**	1.236	3.44 (1.59-7.50)	**<0.001**	1.306	3.69 (1.20-5.88)	**<0.001**	0.683	1.98 (1.30-3.67)	**<0.001**	1.280	3.60 (1.58-4.59)	**<0.001**
Invasive mean gradient post-TAVI > 10 mmHg	0.513	1.67 (1.20-3.86)	**0.010**	0.406	1.50 (1.09-2.35)	**0.011**	0.140	1.15 (1.04-1.52)	**0.025**	0.952	2.59 (1.19-6.13)	**<0.001**	0.631	1.88 (1.27-2.83)	**<0.001**	0.641	1.90 (1.07-3.20)	**0.016**

Values are hazard ratio (95% confidence interval)

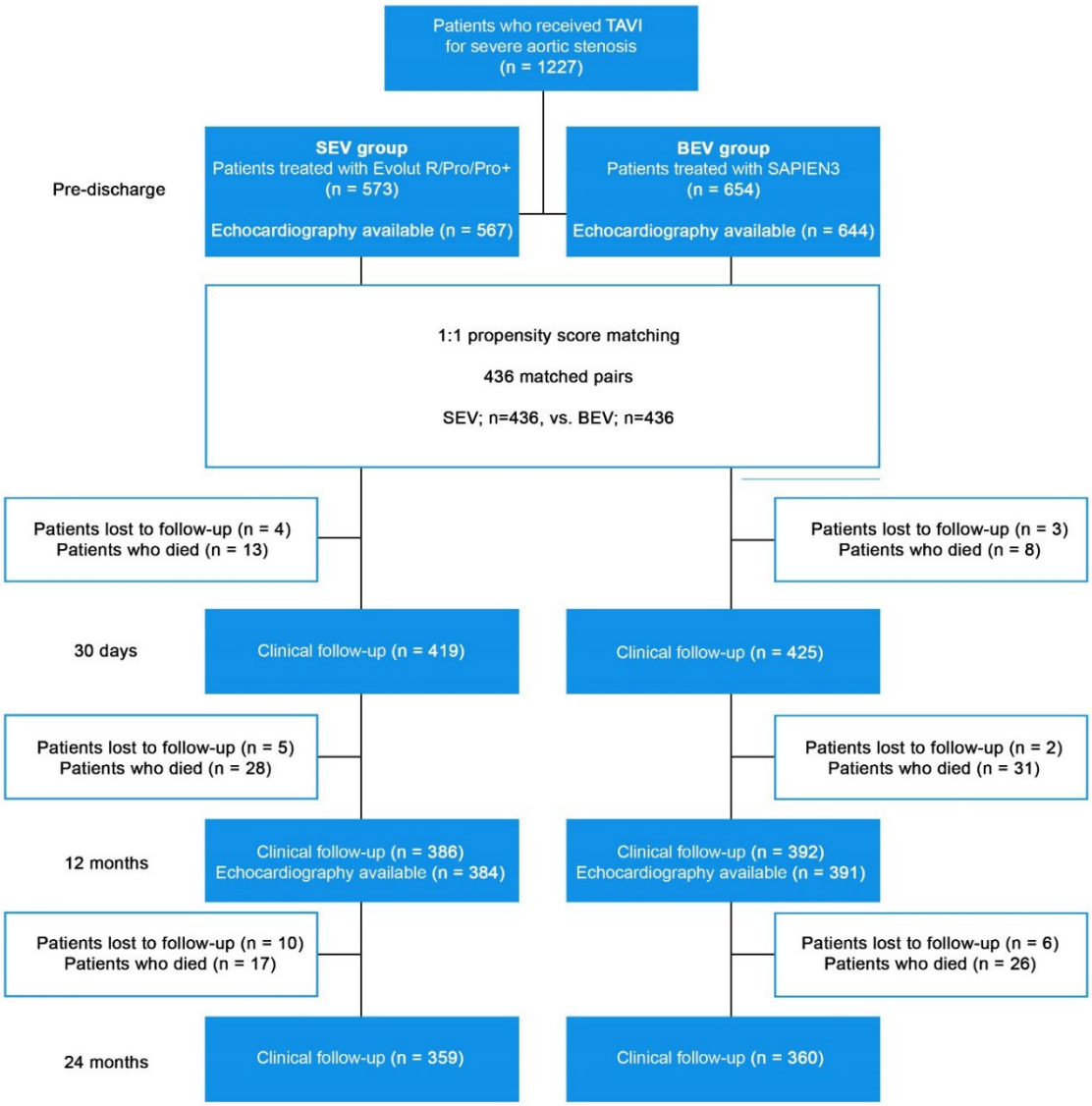
Supplementary Table 4. Cox proportional hazards regression model for bioprosthetic valve failure.

Univariable	**12 months**	
	HR	**P**
Age	0.99 (0.95-1.04)	0.757
Male gender	0.67 (0.31-1.41)	0.285
Smallest valve size	1.09 (0.63-1.79)	0.802
Predilatation	0.74 (0.32-1.81)	0.431
Oral anticoagulation use	0.73 (0.39-1.357)	0.315
Valve type (BEV/SEV)	1.27 (0.67-2.38)	0.463
Echo gradients		
Echo mean gradient post-TAVI	1.07 (0.98-1.17)	0.136
Echo mean gradient post-TAVI > 10 mmHg	1.11 (0.30-7.89)	0.501
Echo mean gradient post-TAVI > 20 mmHg	1.29 (0.16-10.41)	0.810
Invasive gradients		
Invasive mean gradient post-TAVI	1.04 (0.98-1.10)	0.127
Invasive mean gradient post-TAVI > 10 mmHg	1.99 (0.45-12.07)	0.378
Invasive mean gradient post-TAVI > 20 mmHg	2.17 (0.27-17.19)	0.463

Values are hazard ratio (95% confidence interval)

Supplementary Table 5. Advantages and limitations of invasive and echocardiographic gradient measurements.

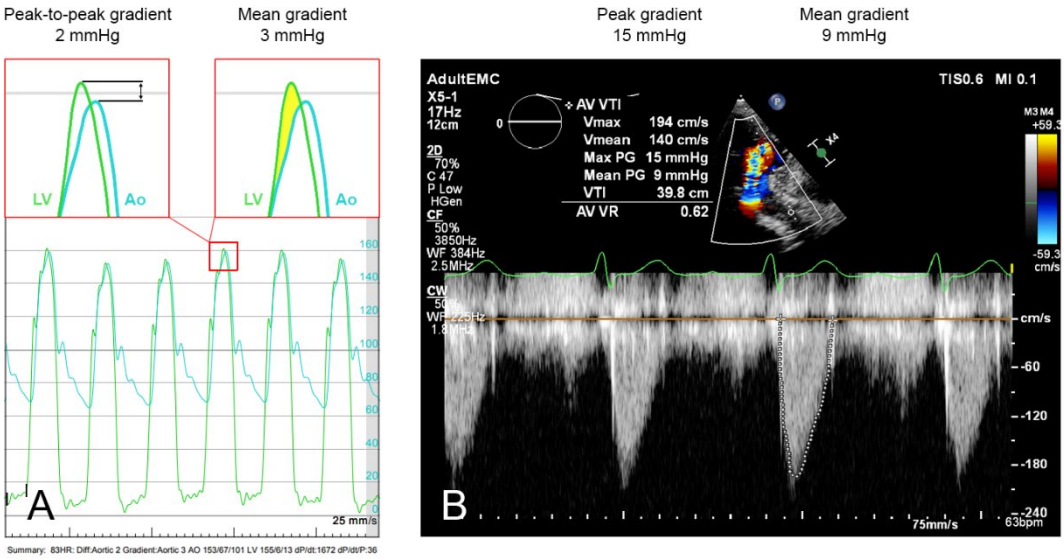
Echocardiography	
Advantages	**Limitations**
Widely accessible	Risk of measurement error in beam vs. flow misalignment
Noninvasive	Bernouilli formula relies on derivative variables (velocity) and assumes presence of laminar flow
No radiation exposure	Simplification of Bernouilli formula does not allow for the contribution of viscous forces, proximal LV velocity and pressure recovery
Invasive measurement	
Advantages	**Limitations**
Direct peak-to-peak pressure gradient	Need for calibration of fluid-filled catheter
Incorporates all contributing factors to flow	Variation in catheter positioning inside the ascending aorta
Not subject to derivative calculations	Invasive, exposure to radiation



Supplementary Figure 1. Flowchart of the study population.

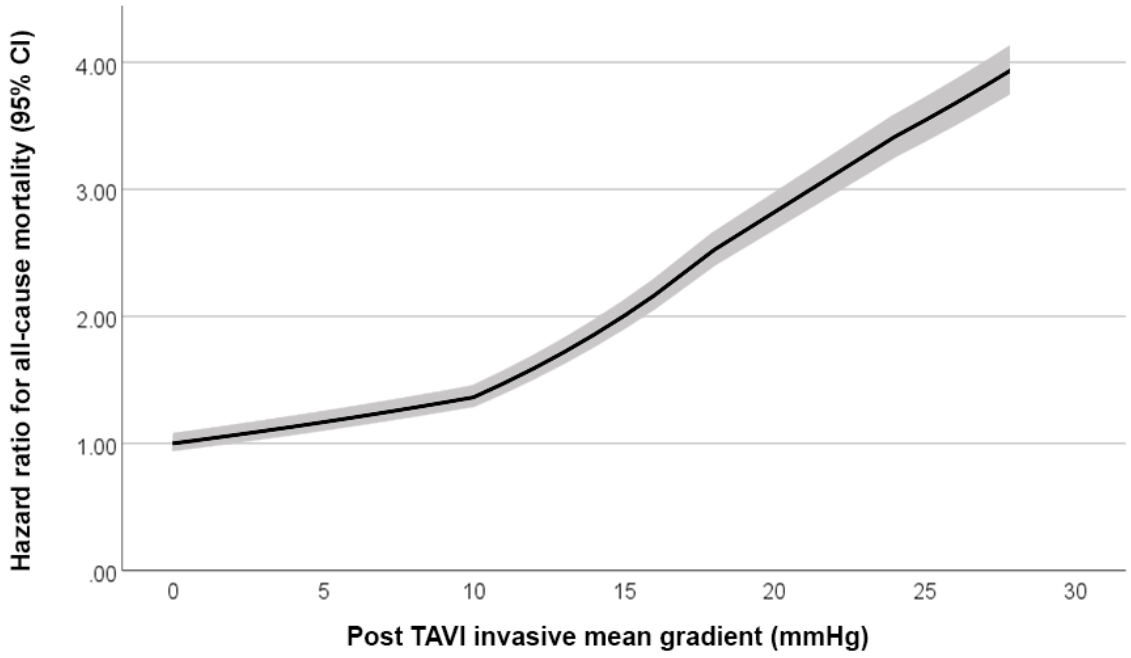
A total of 1227 patients underwent TAVI for severe aortic stenosis. After 1:1 propensity matching, 436 matching pairs were obtained. At 30 days, 7 patients were lost to follow-up and 21 patients had died. At 1 year, 14 patients were lost to follow-up and 80 patients had died. At 2 years, 30 patients were lost to follow-up and 113 patients had died.

SEV=self-expanding valve; BEV=balloon-expandable valve



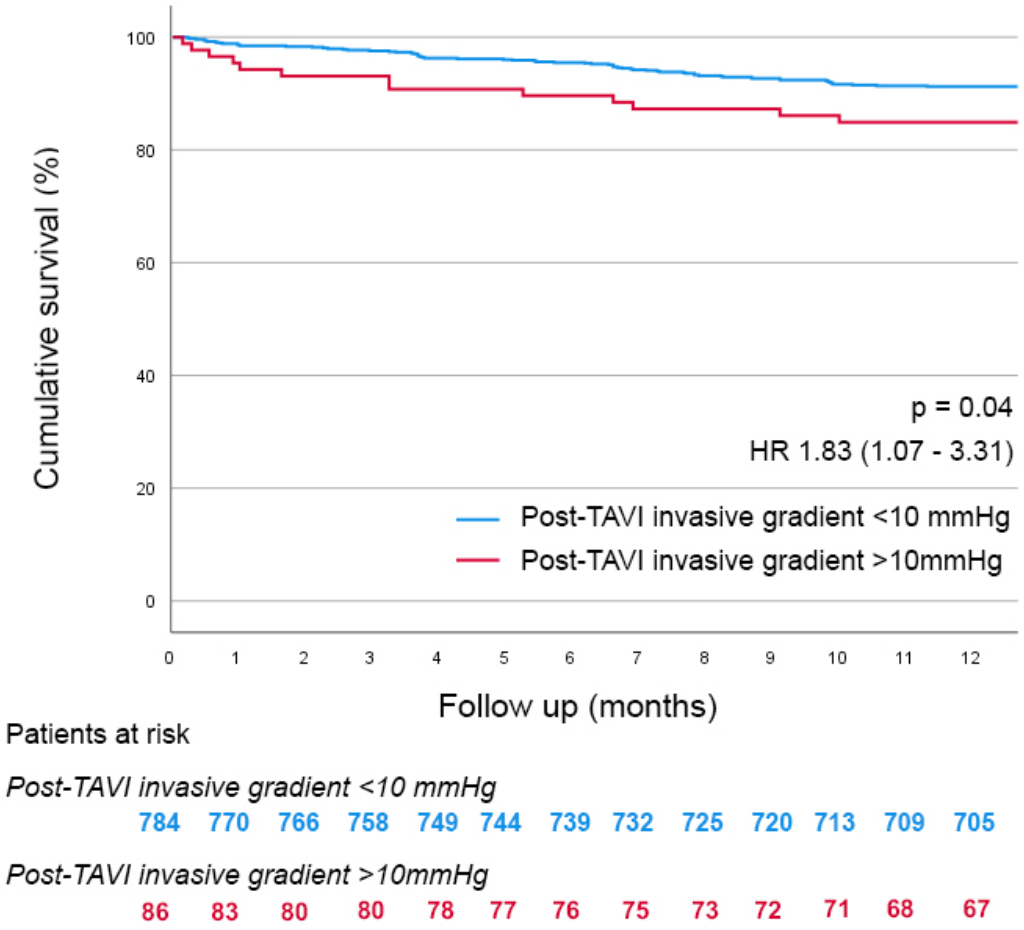
Supplementary Figure 2. Invasive and echocardiography-derived postprocedural gradient measurements in an individual patient.

A) Illustration of post-procedural invasive gradient acquisition. Peak-to-peak gradient is 2 mmHg. Mean gradient is 3 mmHg. B) Illustration of echocardiography-derived pressure gradient acquisition. Peak pressure gradient is 15 mmHg. Mean gradient is 9 mmHg.



Supplementary Figure 3. Spline curve for hazard ratio versus post-TAVI invasive gradient.

Spline curve displaying Hazard Ratio ±95% confidence interval for all-cause mortality versus post-TAVI invasive gradients. A relative increase in Hazard Ratio is observed starting from an invasive gradient of 10 mmHg.



Supplementary Figure 4. Kaplan-Meier curve for all-cause mortality.

Kaplan Meier curve displaying a significant difference in all cause mortality between patients with post-TAVI invasive gradients >10 mmHg and <10 mmHg (HR 1.83, 95%CI 1.07-3.31, p=0.04)