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Original Article

The hemodynamic performance of balloon-expandable aortic bioprostheses in the elderly: a comparison between rapid deployment and transcatheter implantation

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ABSTRACT

Background: Surgical aortic valve replacement with a rapid deployment valve (RDV) is a relatively recent treatment option. The aim of this study was to compare the hemodynamic performance of balloon-expandable (BE)-RDVs and BE-transcatheter heart valves (THVs) in a high surgical risk and frail-elderly population.
Methods: BE-THVs and BE-RDVs were implanted in 138 and 47 patients, respectively, all older than 75 years and with a Canadian Study of Health and Aging category of 5 or above. Echocardiographic assessment was performed at discharge and six months later.
Results: At discharge, transprosthetic pressure gradients and indexed effective orifice area (iEOA) were similar in both cohorts. At six-month follow-up, BE-RDVs showed lower peak (14.69 vs. 20.86 mmHg; $p < 0.001$) and mean (7.82 vs. 11.83 mmHg; $p < 0.001$) gradients, and larger iEOA (1.05 vs. 0.84 cm^2/m^2; $p < 0.001$). Similar findings were also shown considering only small-sized valves. Moderate-to-severe paravalvular leakage was more prevalent in BE-THVs at discharge (14.49 vs. 0.00%; $p = 0.032$) and, considering exclusively small prostheses, at six months too (57.69 vs. 15.00%; $p = 0.014$). Nevertheless, BE-THVs determined amelioration in left ventricular ejection fraction (53.79 vs. 60.14%; $p < 0.001$), pulmonary artery systolic pressure (35.81 vs. 33.15 mmHg; $p = 0.042$), and tricuspid regurgitation severity (40.58 vs. 19.57%; $p = 0.031$), from discharge to mid-term follow-up.
Conclusions: BE-RDVs showed better hemodynamic performance, especially when implanted in small annuli. Despite their worse baseline conditions, transcatheter patients still exhibited a greater improvement of their echocardiographic profile at mid-term follow-up.

Abbreviations: TAVI, transcatheter aortic valve implantation; SAVR, surgical aortic valve replacement; RDV, rapid deployment valve; THV, transcatheter heart valve; BE, balloon-expandable; PVL, paravalvular leakage; VARC, Valve Academic Research Consortium; iEOA, indexed effective orifice area; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; NYHA, New York Heart Association; EuroSCORE, European System for Cardiac Operative Risk Evaluation; EFVR, ejection fraction/velocity ratio.

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1. Introduction

Aortic valve stenosis is a progressive, age-related disease, representing one of the main causes of morbidity and mortality in the elderly, with a prevalence of approximately 10% in octogenarians[1]. It has faster progression in older patients who show poor prognosis and high cardiovascular mortality without interventions[2]. Comorbidities and "non-traditional" risk factors may explain the worst outcome. Frailty, defined as "a state of vulnerability characterized by decreased reserve and diminished resistance to external stressors",[3] is a very intriguing parameter in elderly people, as it generally plays a primary role in cardiovascular mortality[4,5] of a broad spectrum of conditions such as heart failure[6], ischaemic heart disease[7], cardiac surgery[8], and transcatheter aortic valve implantation (TAVI)[9].

Surgical aortic valve replacement (SAVR) has been for decades the gold standard for treating severe aortic stenosis[10]. Nevertheless, full sternotomy and protracted operative time confer significant risks, particularly for frail patients: about one third of high-risk patients were usually declared unsuitable for conventional SAVR[11,12].

Rapid deployment valves (RDVs) are new devices that could be considered as valid alternatives to both classical aortic surgical prostheses and transcatheter heart valves (THVs). Unlike previous surgical devices, RDVs are mounted on a self-expanding or a balloon-expandable (BE) stent designed to enable easy and rapid implantation, reducing or completely avoiding anchoring sutures to hold the valve in the appropriate location. They showed good hemodynamic performance, with reduction in cross-clamp and cardiopulmonary by-pass times as compared to SAVR[13-17]. In addition, surgical strategies allow for native valve excision and annulus decalcification, thus minimizing paravalvular leakage (PVL), which is a well-known risk factor for lower survival in TAVI patients[18,19].

RDVs might be considered as a valid alternative strategy in patients with intermediate-to-high operative risk too, since perioperative complications and in-hospital mortality are comparable to those of THVs[20,21]. However, data are controversial according to hemodynamic viewpoint: studies showed that RDVs have higher postoperative transvalvular gradients than THVs, although their performance was better[22-24]. The major difficulty in interpreting this data arises from the variability of THVs included and the recruitment of self-expanding RDVs[24]; very few studies indeed have compared the BE-RDVs to the BE-THVs[25-27], thus showing non-inferiority or even superiority regarding transvalvular gradients, both in the postprocedural setting and at mid-term follow-up of intermediate surgical risk patients.

The aim of the present study was to compare clinical outcomes as well as discharge and mid-term hemodynamic performances of both BE-RDVs and BE-THVs in a frail-elderly population of high surgical risk patients.

2. Methods

2.1. Study design and patient population

This is a post-hoc retrospective analysis which included 185 patients with severe aortic stenosis requiring SAVR or TAVI, admitted to three Italian heart centers, i.e., Policlinico University Hospital and "Santa Maria" Clinic of Bari, and "Montevergine" Clinic of Mercogliano, from March 2012 to December 2014. Such centers were involved into the "Magna Graecia" TAVI registry and the FOUNDATION registry, both approved by their Independent Ethical Committees in accordance with the Declaration of Helsinki. Only patients older than 75 years and with a Canadian Study of Health and Aging category of 5 or above have been selected[28]. We excluded those also requiring concomitant percutaneous or surgical cardiac procedures, finally considering two groups of patients: the first formed by patients who underwent TAVI with BE-THVs (n = 138) and the second composed by patients who underwent SAVR with BE-RDVs (n = 47). The decision about the type of procedure to perform was taken in each case after a multidisciplinary evaluation by the institutional Valve Heart Team. Postprocedural transthoracic echocardiography was carried out before hospital discharge and at mid-term follow-up, i.e., six months later. Data on events occurring after discharge and rehospitalizations for all causes were derived from follow-up outpatient visits or by telephonic interview.

2.2. Operative techniques and clinical outcomes

The only commercially available BE-RDVs were Intuity™ and Intuity Elite™ (Edwards Lifesciences LLC, Irvine, CA, USA); they are built on the Carpentier-Edwards Perimount platform (3 bovine pericardial leaflets), with a subannular BE skirt that serves for both anchoring and sealing. During their implantation, the 3 guiding annular sutures are tied and not removed, so these prostheses are not truly sutureless valves but they are rather described as RD devices. According to the surgeon's preference and expertise, they could be implanted traditionally or with a minimally invasive approach, i.e., right anterior thoracotomy or partial hemisternotomy. All of these minimally invasive AVRs were realized under moderately hypothermic (32°C) cardiopulmonary by-pass with aortic cross-clamping and cardioplegic arrest. A transverse aortotomy was performed a few centimeters above the aortic annulus, the native valve was removed, and the annulus was decalcified; then, the BE-RDV was installed in place.

On the other hand, in cases of transcatheter approaches, a Sapien XT™ or a Sapien 3™ (Edwards Lifesciences LLC, Irvine, CA, USA) through transfemoral, transapical, or transaortic access routes was implanted. Both valves consist of bovine pericardium sewn to a BE cobalt-chromium tubular frame.

Data on patients' characteristics and operative details were acquired retrospectively from patients' records. Postoperative length of stay, prosthesis function, and hemodynamic parameters were assessed. Moreover, device success, clinical outcomes, and mortality were defined according to the Valve Academic Research Consortium (VARC)-2 criteria[29].

2.3. Doppler echocardiography

Postoperative echocardiograms were carried out by experienced echocardiographers. According to VARC-2 consensus document, prosthesis assessment has included an evaluation of structure, function, and hemodynamics of both the prosthetic valve and the ventricle; follow-up echocardiograms were obtained at six months in order to assess the mid-term evolution of prosthesis performance and cardiac hemodynamics.

In detail, postoperative prosthetic transvalvular peak and mean gradients, as well as indexed effective orifice area (iEOA), were all measured. In TAVI patients, the left ventricular outflow tract diameter was measured immediately proximal to stent insertion for calculating the postoperative iEOA using the continuity equation.

PVL was also assessed, according to the American Society of Echocardiography and the European Association of Cardiovascular Imaging guidelines[30,31]: the severity of regurgitation was graded as none-to-trivial, mild, moderate, and severe.

Furthermore, parameters that are certainly modifiable by the treatment of aortic valvulopathy – i.e., left ventricular ejection fraction (LVEF), ejection fraction/velocity ratio (EFVR)[32], eventual concomitant mitral and tricuspid regurgitation, as well as pulmonary artery systolic pressure (PASP) – were studied according to most recent guidelines too. Particularly, taking into consideration

both LVEF and transvalvular peak pressure gradient, the EFVR is very useful in the evaluation of patients with aortic stenosis and left ventricular dysfunction.

2.4. Statistical methods

Statistical analysis was performed using SPSS 13.0 statistical software (IBM SPSS Inc., Chicago, IL, USA). Continuous variables with a normal distribution were expressed as mean ± standard deviation. Categorical data were summarized by absolute frequency distribution and percentage. The Kolmogorov' test was used to investigate the normality of variables collected; in case of small samples, the Shapiro-Wilk test was used. In the event of variable without normal distribution, the Mann-Whitney test to compare means was used. Fisher's exact test was used to compare proportions of a categorical or an ordinal variable between different independent groups. Statistical findings were considered significant if the p-value was less than 0.05.

3. Results

3.1. Patient characteristics

Table 1 shows demographic, clinical, and echocardiographic data of the patient population prior to any intervention. Among all 185 patients, 47 underwent SAVR with BE-RDVs, and 138 underwent TAVI with BE-THVs. Patients in the TAVI group were significantly older (83.41 ± 3.93 vs. 79.83 ± 2.40 years, $p < 0.001$) and showed both significantly higher New York Heart Association (NYHA) functional class ($p = 0.015$) and logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) (24.77 ± 18.99 vs. 19.46 ± 17.66%, $p = 0.033$).

Furthermore, TAVI cohort exhibited significantly higher aortic valve peak gradients (76.60 ± 22.30 vs. 67.02 ± 23.61 mmHg; $p = 0.038$) and lower EFVR (0.75 ± 0.33 vs. 0.88 ± 0.57; $p = 0.040$). Rates of moderate-to-severe mitral and tricuspid regurgitation were also significantly higher in transcatheter patients compared with surgical ones (56.52 vs. 29.79%, $p = 0.003$; and 42.03 vs. 17.02%, $p = 0.004$, respectively).

3.2. Procedural data

The proportion of transfemoral access was higher in the BE-THV cohort (89.13%) as compared to other access routes. Within BE-RDV cohort, full sternotomy was performed in 18 (38.30%) patients, while mini-sternotomy approach in 29 patients (61.70%); cardiopulmonary by-pass time was 85.55 ± 57.35 min, and valve implantation time accounted for 25.15 ± 17.59 min. The surgical group more often received smaller valves, i.e., prosthesis whose diameter was up to 23 mm, than the transcatheter one (85.11 vs. 56.52%, respectively, Table 2).

3.3. Clinical outcomes

Device success was similar in the BE-THV and BE-RDV groups (82.61 vs. 82.98%; $p = 0.869$), as well as in-hospital mortality (5.80 vs. 2.13%; $p = 0.537$) and 1-year all-cause mortality (8.70 vs. 4.26%; $p = 0.500$). Surgical patients exhibited higher rate of major bleedings (38.30 vs. 4.44%; $p < 0.001$) and longer hospital stay (13.62 ± 17.97 vs. 6.46 ± 3.96 days; $p < 0.001$) than transcatheter ones (Table 3).

3.4. Hemodynamic performance

Both groups had similar peak (19.93 ± 10.65 vs. 20.10 ± 7.25 mmHg; $p = 0.360$) and mean (10.15 ± 4.97 vs. 11.31 ± 4.34 mmHg; $p = 0.082$) transprosthetic gradients at the hemodynamic evaluation that was performed soon after the intervention. Conversely, peak (20.86 ± 6.97 vs. 14.69 ± 6.21 mmHg; $p < 0.001$) and mean (11.83 ± 4.12 vs. 7.82 ± 3.46 mmHg; $p < 0.001$) transprosthetic gradients were significantly higher in the BE-THV group at six-month follow-up. In detail, small prostheses

Table 1
Baseline characteristics of study population.

Variable	SAVR with BE-RDVs	TAVI with BE-THVs	ρ-value
No. of patients	47	138	
Age (years)	79.83 ± 2.40	83.41 ± 3.93	<0.001
Male	19 (40.43%)	47 (34.06%)	0.541
Body mass index (kg/m^2)	26.18 ± 3.45	26.63 ± 5.39	0.693
Hypertension	37 (78.72%)	120 (86.96%)	0.261
Diabetes mellitus	16 (34.04%)	41 (29.71%)	0.709
COPD	15 (31.91%)	39 (28.26%)	0.772
Peripheral artery disease	11 (23.40%)	30 (21.74%)	0.973
Prior revascularization	10 (21.28%)	23 (16.67%)	0.622
Previous PM/ICD/CRT implantation	2 (4.26%)	21 (15.22%)	0.087
New York Heart Association functional class III/IV	28 (59.57%)	109 (78.99%)	0.015
Logistic EuroSCORE (%)	19.46 ± 17.66	24.77 ± 18.99	0.033
Echocardiographic data			
Aortic valve peak pressure gradient (mmHg)	67.02 ± 23.61	76.60 ± 22.30	0.038
Aortic valve mean pressure gradient (mmHg)	42.74 ± 16.73	47.57 ± 15.11	0.093
AVA (cm^2)	0.64 ± 0.22	0.64 ± 0.20	0.997
iAVA (cm^2/m^2)	0.37 ± 0.12	0.42 ± 0.18	0.467
EFVR	0.88 ± 0.57	0.75 ± 0.33	0.040
LVEF (%)	54.13 ± 14.99	52.09 ± 11.80	0.159
≤35%	6 (12.77%)	14 (10.14%)	0.820
35 to 60%	23 (48.94%)	87 (63.04%)	0.126
≥60%	18 (38.30%)	37 (26.81%)	0.192
PASP (mmHg)	36.85 ± 9.44	39.97 ± 11.99	0.208
Mitral regurgitation (moderate-to-severe)	14 (29.79%)	78 (56.52%)	0.003
Tricuspid regurgitation (moderate-to-severe)	8 (17.02%)	58 (42.03%)	0.004

SAVR = surgical aortic valve replacement; BE-RDV = balloon-expandable rapid deployment valve; TAVI = transcatheter aortic valve implantation; BE-THV = balloon-expandable transcatheter heart valve; COPD = chronic obstructive pulmonary disease; PM = pacemaker; ICD = implantable cardioverter-defibrillator; CRT = cardiac resynchronization therapy; EuroSCORE = European system for cardiac operative risk evaluation; iAVA = indexed aortic valve area; EFVR = ejection fraction/velocity ratio; LVEF = left ventricular ejection fraction; PASP = pulmonary artery systolic pressure.

Table 2
Procedural data.

SAVR with BE-RDVs	Patients (n = 47)	TAVI with BE-THVs	Patients (n = 138)
Access		**Access**	
Mini-sternotomy	29 (61.70%)	Transfemoral	123 (89.13%)
Full sternotomy	18 (38.30%)	Transapical	8 (5.80%)
		Transaortic	7 (5.07%)
Valve model		**Valve model**	
Intuity	34 (72.34%)	Edwards Sapien XT	88 (63.77%)
Intuity Elite	13 (27.66%)	Edwards Sapien 3	50 (36.23%)
Prosthesis size		**Prosthesis size**	
19 mm	12 (25.53%)	23 mm	78 (56.52%)
21 mm	18 (38.30%)	26 mm	44 (31.88%)
23 mm	10 (21.28%)	29 mm	16 (11.60%)
25 mm	4 (8.51%)		
27 mm	3 (6.38%)		
Cardiopulmonary by-pass time (min)	85.55 ± 57.35		
Valve implantation time (min)	25.15 ± 17.59		

SAVR = surgical aortic valve replacement; BE-RDV = balloon-expandable rapid deployment valve; TAVI = transcatheter aortic valve implantation; BE-THV = balloon-expandable transcatheter heart valve.

exhibited significantly higher peak (22.21 ± 6.75 vs. 14.47 ± 5.53 mmHg; $p < 0.001$) and mean (12.46 ± 3.65 vs. 7.66 ± 3.25 mmHg; $p < 0.001$) transprosthetic gradients, while no significant differences between the two cohorts were found for large prostheses (see Table 4a).

At six-month follow-up, the iEOA was significantly larger in the BE-RDV group vs. BE-THV group (1.05 ± 0.19 vs. 0.84 ± 0.28 cm^2/m^2; $p < 0.001$), even considering only small prostheses (1.05 ± 0.19 vs. 0.73 ± 0.17 cm^2/m^2; $p < 0.001$). BE-THV patients exhibited, indeed, significant decrease in iEOA from discharge to mid-term follow-up ($p < 0.001$).

In addition, EFVR exhibited higher values in the BE-RDV cohort (4.61 ± 2.39 vs. 3.25 ± 1.12; $p < 0.001$) six months after the intervention, due to its considerable rise in the surgical group (from 2.90 ± 1.73 to 4.61 ± 2.39; $p < 0.001$).

Postprocedural moderate-to-severe PVL was more prevalent in the BE-THV group (14.49 vs. 0.00%; $p = 0.032$), while becoming comparable between the two cohorts at mid-term follow-up due to a significant increase of its rate in the BE-RDV group (from 0 to 14.89%; $p = 0.027$), see Table 4b and Fig. 1. However, considering only small-sized valves, the rate of PVL remained higher at six months in the BE-THV group (57.69 vs. 15.00%; $p = 0.014$).

Nevertheless, transcatheter patients showed a significant amelioration in LVEF, PASP, and tricuspid regurgitation, six months after the procedure (from 53.79 ± 11.90 to 60.14 ± 9.92%, $p < 0.001$; from 35.81 ± 9.22 to 33.15 ± 10.52 mmHg, $p = 0.042$; and from 40.58 to 19.57%, $p = 0.031$, respectively). PASP significantly worsened at six-month follow-up (from 18.84 ± 10.81 to 27.42 ± 9.40 mmHg; $p = 0.024$) in the surgical group (see Fig. 1).

4. Discussion

This is the first study that compares SAVR with BE-RDVs and TAVI with BE-THVs according to their hemodynamic performance, in a frail-elderly population of high surgical risk patients. The main results of this retrospective research are as follows: 1) although amelioration of hemodynamic profile was achieved through both approaches, BE-RDVs exhibited better performance because an amelioration of PVL in the immediate postprocedural period, and an amelioration in transprosthetic pressure gradients, iEOA, and EFVR at six-month follow-up; 2) the prostheses hemodynamics was clearly linked to their size, indeed, hemodynamic advantage in the BE-RDV group was greater among those patients with smaller aortic annulus; and 3) despite their worse baseline echocardiographic profile, patients implanted with BE-THVs exhibited a greater amelioration in LVEF, PASP, and tricuspid regurgitation at mid-term follow-up.

4.1. Clinical outcomes

Patients undergoing both TAVI and SAVR are exposed to an ineluctable risk for postprocedural bleeding and transfusion[33,34]. In particular, our study showed that major bleedings were 8-to-9 times more frequent in the SAVR group than in the TAVI one. Similar findings were reported by Généreux et al. in a high-risk population, with rates of bleeding complications of 11.3% and 22.7% after transfemoral TAVI and SAVR, respectively[33]. Although with lower events rate, also Tamburino et al. reported inferiority of

Table 3
Clinical outcomes.

Variable	SAVR with BE-RDVs (n = 47)			TAVI with BE-THVs (n = 138)	ρ-value
	Mini-sternotomy (n = 29)	Full sternotomy (n = 18)	All		
Acute kidney injury	0 (0.00%)	3 (16.67%)	3 (6.38%)	11 (7.97%)	0.801
New-onset atrial fibrillation	2 (6.90%)	1 (5.56%)	3 (6.38%)	11 (7.97%)	0.971
Stroke	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.725%)	0.571
Major bleeding	9 (31.03%)	9 (50.00%)	18 (38.30%)	6 (4.44%)	<0.001
Pacemaker implantation	2 (6.90%)	1 (5.56%)	3 (6.38%)	11 (7.97%)	0.961
Acute myocardial infarction	0 (0.00%)	1 (5.56%)	1 (2.13%)	2 (1.45%)	0.705
Vascular complications	5 (17.24%)	2 (11.11%)	7 (14.89%)	26 (18.84%)	0.804
Hospital stay (days)	11.16 ± 9.16	20.44 ± 31.76	13.62 ± 17.97	6.46 ± 3.96	<0.001
Device success	23 (79.31%)	16 (88.89%)	32 (82.98%)	114 (82.61%)	0.869
In-hospital mortality	1 (3.45%)	0 (0.00%)	1 (2.13%)	8 (5.80%)	0.537
1-year mortality	1 (3.45%)	1 (5.56%)	2 (4.26%)	12 (8.70%)	0.500

SAVR = surgical aortic valve replacement; BE-RDV = balloon-expandable rapid deployment valve; TAVI = transcatheter aortic valve implantation; BE-THV = balloon-expandable transcatheter heart valve.

Table 4
Early and mid-term postoperative echocardiographic data.

(a)

Variable	Postprocedural			Mid-term follow-up		
	SAVR with BE-RDVs	TAVI with BE-THVs	ρ-value	SAVR with BE-RDVs	TAVI with BE-THVs	ρ-value
Peak pressure gradient (mmHg)	20.10 ± 7.25	19.93 ± 10.65	0.360	14.69 ± 6.21	20.86 ± 6.97	<0.001
Small prostheses*	19.96 ± 7.19	22.21 ± 12.76	0.892	14.47 ± 5.53	22.21 ± 6.75	<0.001
Large prostheses*	22.61 ± 11.01	16.77 ± 5.46	0.263	17.13 ± 12.34	18.50 ± 6.93	0.783
Mean pressure gradient (mmHg)	11.31 ± 4.34	10.15 ± 4.97	0.082	7.82 ± 3.46	11.83 ± 4.12	<0.001
Small prostheses*	11.28 ± 4.37	10.84 ± 5.97	0.268	7.66 ± 3.25	12.46 ± 3.65	<0.001
Large prostheses*	11.82 ± 5.48	9.30 ± 3.26	0.614	9.57 ± 5.87	10.90 ± 4.71	0.766
PVL						
Small prostheses*	3/40 (7.50%)	22/78 (28.21%)	0.010	6/40 (15.00%)	45/78 (57.69%)	0.014
Large prostheses*	0/7 (0.00%)	18/60 (30.00%)	0.060	1/7 (14.29%)	20/60 (33.33%)	0.102
none-to-trivial	43 (91.49%)	90 (65.22%)	0.003	40 (85.11%)	73 (52.90%)	0.008
mild	4 (8.51%)	28 (20.29%)	0.056	0 (0.00%)	32 (23.19%)	0.006
moderate-to-severe	0 (0.00%)	20 (14.49%)	0.032	7 (14.89%)	33 (23.91%)	0.493
EFVR	2.90 ± 1.73	3.17 ± 1.55	0.106	4.61 ± 2.39	3.25 ± 1.12	<0.001
LVEF (%)	52.13 ± 9.32	53.79 ± 9.92	0.622	56.48 ± 6.96	60.14 ± 9.92	0.097
≤35%	3 (6.38%)	11 (7.97%)	0.926	0 (0.00%)	0 (0.00%)	–
35 to 60%	31 (65.96%)	86 (62.32%)	0.734	28 (59.57%)	62 (44.93%)	0.441
≥60%	13 (27.66%)	41 (29.71%)	0.920	19 (40.43%)	76 (55.07%)	0.441
PASP (mmHg)	18.84 ± 10.81	35.81 ± 9.22	<0.001	27.42 ± 9.40	33.15 ± 10.52	0.078
Mitral regurgitation (moderate-to-severe)	10 (21.28%)	59 (42.75%)	0.039	3 (6.38%)	12 (8.70%)	0.998
Tricuspid regurgitation (moderate-to-severe)	4 (8.51%)	56 (40.57%)	0.003	5 (10.64%)	27 (19.57%)	0.108
iEOA (cm^2/m^2)	–	1.20 ± 0.18	–	1.05 ± 0.19	0.84 ± 0.28	<0.001
Small prostheses*	–	1.54 ± 0.85	–	1.05 ± 0.19	0.73 ± 0.17	<0.001
Large prostheses*	–	2.04 ± 0.45	–	1.06 ± 0.08	0.95 ± 0.33	0.475

(b)

Variable	SAVR with BE-RDVs			TAVI with BE-THVs		
	Postprocedural	Mid-term follow-up	ρ-value	Postprocedural	Mid-term follow-up	ρ-value
Peak pressure gradient (mmHg)	20.10 ± 7.25	14.69 ± 6.21	<0.001	19.93 ± 10.65	20.86 ± 6.97	0.106
Mean pressure gradient (mmHg)	11.31 ± 4.34	7.82 ± 3.46	<0.001	10.15 ± 4.97	11.83 ± 4.12	0.010
PVL						
none-to-trivial	43 (91.49%)	40 (85.11%)	0.440	90 (65.22%)	73 (52.90%)	0.171
mild	4 (8.51%)	0 (0.00%)	0.259	29 (21.01%)	33 (23.91%)	0.702
moderate-to-severe	0 (0.00%)	7 (14.89%)	0.027	19 (13.77%)	32 (23.19%)	0.182
EFVR	2.90 ± 1.73	4.61 ± 2.39	<0.001	3.17 ± 1.55	3.25 ± 1.12	0.671
LVEF (%)	52.13 ± 9.32	56.48 ± 6.96	0.057	53.79 ± 11.90	60.14 ± 9.92	<0.001
≤35%	2 (4.26%)	0 (0.00%)	0.500	11 (7.97%)	0 (0.00%)	0.107
35 to 60%	32 (68.09%)	28 (59.57%)	0.623	86 (62.32%)	62 (44.93%)	0.051
≥60%	13 (27.66%)	19 (40.43%)	0.335	41 (29.71%)	76 (55.07%)	0.003
PASP (mmHg)	18.84 ± 10.81	27.42 ± 9.40	0.024	35.81 ± 9.22	33.15 ± 10.52	0.042
Mitral regurgitation (moderate-to-severe)	10 (21.28%)	0 (0.00%)	0.110	59 (42.75%)	38 (27.54%)	0.101
Tricuspid regurgitation (moderate-to-severe)	4 (8.51%)	5 (10.64%)	0.957	56 (40.58%)	27 (19.57%)	0.031
iEOA (cm^2/m^2)	1.05 ± 0.19	–	–	1.20 ± 0.18	0.84 ± 0.28	<0.001

SAVR = surgical aortic valve replacement; BE-RDV = balloon-expandable rapid deployment valve; TAVI = transcatheter aortic valve implantation; BE-THV = balloon-expandable transcatheter heart valve; EFVR = ejection fraction/velocity ratio; LVEF = left ventricular ejection fraction; PASP = pulmonary artery systolic pressure; iEOA = indexed effective orifice area.

* Small prostheses (RDVs 19, 21 and 23 mm; THV 23 mm); large prostheses (RDVs 25 and 27 mm; THVs 26 and 29 mm).

surgery in terms of bleeding complications (5.5% for TAVI and 9.0% for SAVR)[35].

Not surprisingly, the hospital length of stay was lower in the TAVI group, which was in line with literature[22,36,37]. These data might be explained by the less invasive nature of TAVI procedures (in particular, the absence of extracorporeal circulation) and the need of reduced duration of cardiac intensive care when patients underwent transfemoral approach.

According to their different age, NYHA functional class, EuroSCORE, mitral and tricuspid regurgitation grading, our transcatheter patients were in a significantly worse clinical and echocardiographic baseline status; in spite of that, their mortality, either in-hospital or 1-year, was comparable to that of surgical ones. In both groups, in-hospital mortality was higher than that reported in the most recent and numerous series[21], probably because we have included only frail-elderly patients who have been treated some years ago, whereas team experience is expected to be less and technologies older. On the other hand, 1-year mortality in our population was quite consistent with current literature[13,37].

4.2. Hemodynamic findings

As shown by other studies comparing BE-RDVs and BE-THVs performances soon after the intervention[25,26], we demonstrated comparable transprosthetic gradients between the two groups, but a significant reduction in their values at mid-term follow-up was observed only in the BE-RDV group. This is probably due to the structure of BE-RDVs, which are modelled, like BE-THVs, on a BE stent with subannular skirt that is expanded during valve implantation, favoring distension and reshaping of the outflow tract, therefore reducing turbulent flow[25,38]. However, transaortic gradients, especially if measured early after the intervention, might be influenced by procedural differences in valve replacement, and therefore they may not be directly connected with the authentic

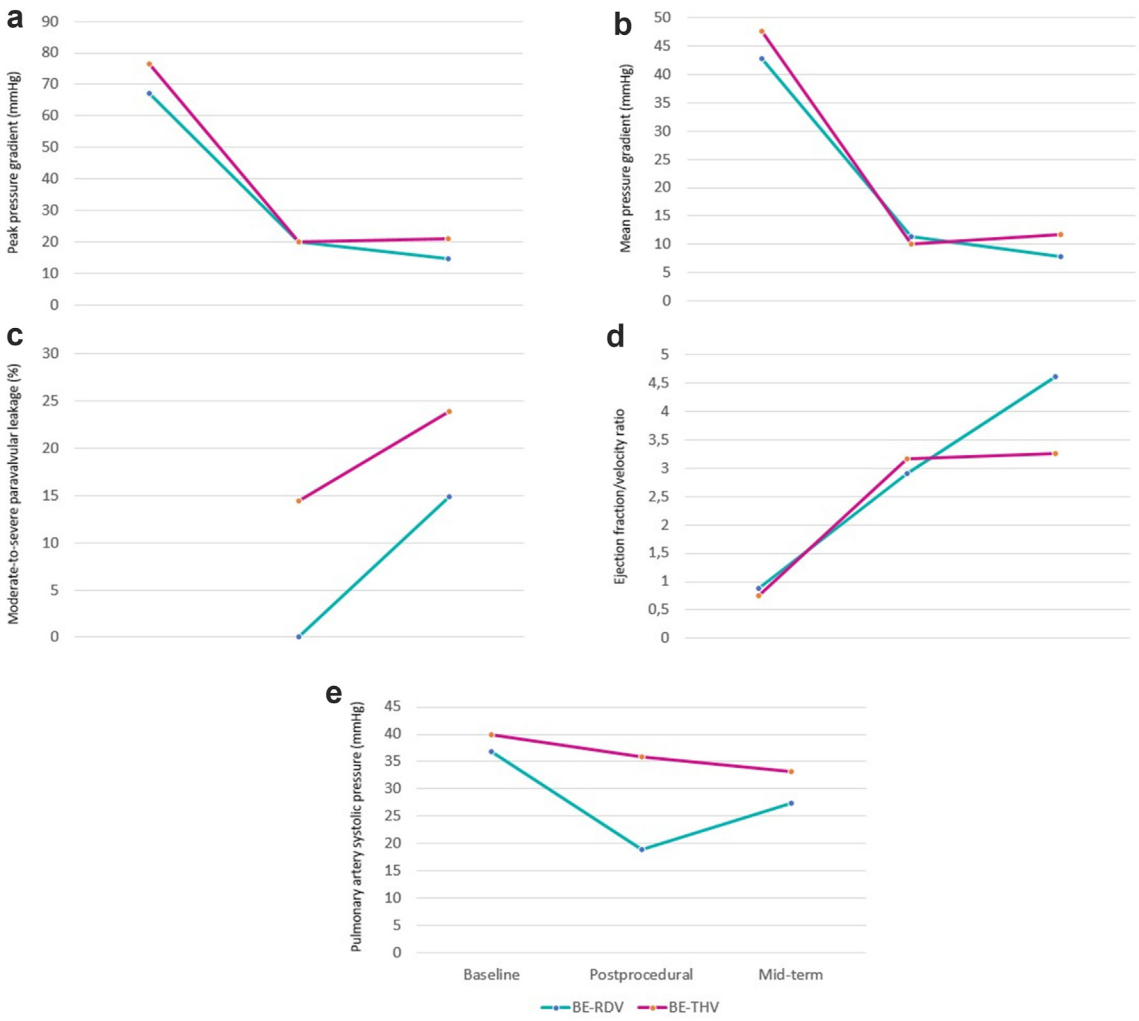

Figure 1. Transprosthetic peak (a) and mean (b) pressure gradients, moderate-to-severe paravalvular leakage (c), ejection fraction/velocity ratio (d), and pulmonary artery systolic pressure (e) trends. BE-RDV = balloon-expandable rapid deployment valve; BE-THV = balloon-expandable transcatheter heart valve.

hemodynamic performance of the implanted valve. In detail, postoperative anemia, hemodilution, and inflammation may have a role in the increased predischarge gradients usually found in the surgical group. In fact, Bruno and colleagues, in their comparation analysis between Intuity and TAVI, reported similar mean transprosthetic gradients at two-year follow-up, although they were significantly lower in the BE-THV group soon after the procedure[27].

As already stated by several authors[22,23,36,37], PVL rate was also lower in the RDV group. In fact, regurgitation after TAVI is usually due to an irregular compression of the calcified native valve against the aortic wall after deployment of the prosthesis. Indeed, the deposits of calcium avoid adequate stent expansion, allowing the creation of paravalvular spaces for possible leakage. In contrast, surgery, even with mini-sternotomy approach, allows for the excision of the calcified native valve in order to place the new prosthesis directly against the aortic annulus, thus minimizing the possibility of potential paravalvular spaces.

4.3. Pulmonary hypertension and left ventricular function in TAVI patients

RDV patients exhibited better basal echocardiographic profile in terms of PASP and rate of moderate-to-severe mitral and tricuspid regurgitation: in spite of that, the severity of such two valvulopathies became not significantly different between surgical and transcatheter groups at mid-term evaluation. Indeed, in TAVI patients, the elimination of severe aortic stenosis alone will have improved the degree of both mitral and tricuspid regurgitation too, especially if etiologically functional: the amelioration of all these valvulopathies realistically resulted in a significant decrease in PASP and an increase in LVEF both at discharge and at mid-term follow-up. These findings are of particular importance moreover in the elderly, for whom the aim of intervention is essentially to improve quality of life. In fact, previous studies have already shown that while decrease in pulmonary hypertension after TAVI was associated with improvement in clinical outcome and functional status[39,40], persistence or deterioration in PASP determined higher rate of rehospitalization and was an independent predictor of 1-year all-cause mortality[41].

4.4. Impact of small annulus size on valve hemodynamics

RDVs have led to a significant change in the surgical approach of severe aortic stenosis in patients with small annulus; in fact, unlike the traditional ones, these prostheses do not require the presence of a sewing ring for their anchorage, thus potentially optimizing EOA and, consequently, the rate of patient-prosthesis mismatch. Only one study compared self-expanding RDVs with BE-THV in

small annulus patients, showing similar findings in terms of iEOA and PVL, with lower pressure gradients in the TAVI group[42]. BE-RDVs have never been compared to BE-THVs in such setting of patients: in our study, all the main hemodynamic advantages of BE-RDVs respect to BE-THVs were led by the "small-sized valves" subgroup. In fact, we demonstrated a better hemodynamic performance not only in terms of PVL and iEOA but also regarding pressure gradients.

4.5. Limitations

The first limitation is that this is a post-hoc not prespecified analysis from two prospectively collected databases; therefore, we cannot exclude that potential confounding factors not considered in the models might have affected the results.

Another limitation concerns the low sample size; in fact, the level of evidence provided by this design is surely inferior to that stemming from randomized designs, and the results should be mainly considered hypothesis-generating findings rather than solid evidence: the possibility of selection bias cannot therefore be excluded, even though consecutive subjects of a real-world population were included in the current analysis.

Moreover, despite the fact that the prostheses groups were differently numerous and not really comparable, a propensity score match analysis to eliminate possible selection bias was not realized. Particularly, nearly two thirds of transcatheter patients received a small BE-THV, making any comparison regarding the prosthesis size very difficult.

Furthermore, the echocardiographic data were not assessed by a core laboratory, and therefore, they may not be standardized; also clinical events were not adjudicated by an independent committee and were site-reported.

Finally, many of our patients were referred to our tertiary referral centers for TAVI, but their long-term medical care was mostly continued at outside facilities. Accordingly, this study cannot reliably evaluate long-term procedural outcomes. Data from large, long-term trials are needed to confirm our results.

5. Conclusions

In summary, BE-RDVs ensured a hemodynamic advantage immediately after the operation, that was rather sustained at six months; conversely, patients implanted with a BE-THV did not improve very much that soon, but they still showed many echocardiographic ameliorations at mid-term follow-up. Moreover, such hemodynamic advantage has proven to be linked to aortic annulus size, with better pressure gradients, iEOA, and PVL exclusively among those patients with smaller aortic annulus. These findings suggest the importance of including aortic annulus size in the risk evaluation of such high-risk patients. PVL remains a disadvantage for BE-THVs; however, shorter hospitalization, lower rate of bleedings, and tricuspid regurgitation severity, surely balance the higher cost of such prosthesis and could favor early recovery of frail patients, for whom the aim of intervention is essentially to improve quality of life.

Conflict of interest

None.

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