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Prosthesis-patient mismatch after transcatheter aortic valve implantation with the Medtronic-Corevalve bioprosthesis

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Aims Prosthesis-patient mismatch (P-PM) is an important determinant of morbidity and mortality following open aortic valve replacement. The aims of this study were to report its incidence and determinants following transcatheter aortic valve implantation (TAVI) with the Corevalve bioprosthesis, which have—thus far—not been described.

Methods and results Patients with severe calcific aortic stenosis received TAVI with the Corevalve bioprosthesis via transfemoral route. Following TAVI, moderate P-PM was defined as indexed aortic valve effective orifice area (AVAi) $\leq$0.85 cm^2/m^2 and severe P-PM as AVAi $\leq$0.65 cm^2/m^2. Clinical, echocardiographic, and procedural factors relating to P-PM were studied. Optimal device position was defined on fluoroscopy as final position of the proximal aspect of the Corevalve stent frame 5–10 mm below the native aortic annulus. Between January 2007 and January 2009, 50 consecutive patients underwent TAVI in a single centre with the Corevalve bioprosthesis. Mean age was 82.8 years (SD 5.9; 70–93) and 48% were male. P-PM occurred in 16 of 50 cases (32%). Optimal position was achieved in 50% of cases. P-PM was unrelated to age, annulus size, LVOT size, Corevalve size, aortic angulation, ejection fraction, and sex. It was inversely correlated to optimal position (Spearman rho $r = -0.34$, $P = 0.015$). Those with optimal positioning had a 16% incidence of P-PM relative to 48% of those with suboptimal positioning (Pearson χ^2 $P = 0.015$).

Conclusion The incidence of P-PM following TAVI with the Corevalve bioprosthesis is compared favourably with that seen after AVR with conventional open stented bioprostheses and its occurrence is influenced by device positioning.

Keywords Prosthesis-patient mismatch • Patient-prosthesis mismatch • Transcatheter aortic valve implantation (TAVI) • Percutaneous aortic valve replacement (PAVR) • Medtronic-Corevalve

Introduction

Prosthesis-patient mismatch (P-PM) was first conceived by Rahimtoola in 1978.[1] Its conception was based on the premise that no valve prosthesis can fully approximate native valvular function and as such all valvular prostheses have at least mild P-PM. Subsequently, P-PM—when moderate or severe—has been shown to be an important determinant of morbidity, exercise capacity, and mortality following conventional open aortic valve replacement, occurring in 20–70%[2,3] of patients undergoing conventional open aortic valve replacement. Transcatheter aortic valve implantation (TAVI) has shown great promise in the treatment of severe aortic stenosis (AS) in patients regarded at high risk from or inoperable by conventional surgery.[4–11] The incidence and determinants of P-PM following TAVI has not been described. We sought to investigate the incidence of the phenomenon of P-PM after TAVI with the Medtronic-Corevalve bioprosthesis, which is designed for supra-annular positioning (*Figure 1*).[6] We also hypothesized that its occurrence could be predicted by clinical, echocardiographic, and procedural factors.

Methods

The study complies with the Declaration of Helsinki: a locally appointed Ethics Committee has approved the research protocol and informed consent was obtained from all subjects.

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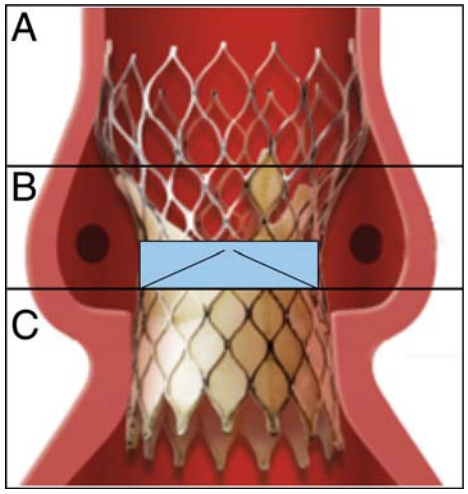

Figure 1 Medtronic-Corevalve. (*A*) Supra-annular device. The Medtronic-Corevalve transcatheter bioprosthesis is designed for prosthetic supra-annular positioning (depicted in blue) within the constrained portion (*B*) of the nitinol stent-frame. Within the left-ventricular outflow tract is the forcefully expansile portion of the stent-frame (*C*) which has a covered skirt to minimize paraprosthetic aortic regurgitation. The aortic portion (*A*) is designed to gently anchor the stent-frame to the aortic wall.

Clinical and anatomical selection criteria were in accord with the published investigational study for the third generation (18F) Corevalve device.[6,7] Patients were recruited in a single centre and received transcatheter aortic valve implantation (TAVI) with the Medtronic-Corevalve bioprosthesis via transfemoral route. All patients had severe calcific aortic stenosis (aortic valve area, AVA < 1 cm^2 or BSA indexed AVA, AVAi < 0.6 cm^2/m^2). They were symptomatic, considered at high risk from, or inoperable by, conventional surgery, had annuli of 20–27 mm and suitable peripheral vasculature (femoral artery diameter >6 mm). Patients with annuli of 20–23 mm received a 26 mm prosthesis (sized by its left-ventricular or 'inflow' diameter); those with annuli of 23–27 mm received a 29 mm prosthesis. The device was implanted as previously described.[6,7]

Echocardiographic aortic regurgitation (AR) was graded semiquantitatively using an established integrative approach[12] with parasternal long-axis view observations: none (grade 0), trivial or mild (grade 1+), moderate (grade 2+), moderate–severe (grade 3+), and severe (grade 4+).

The endpoint of prosthesis-patient mismatch (P-PM) was defined, according to previous convention,[3] as severe if the indexed aortic valve area [AVAi = (Effective Orifice Area/body surface area)] was ≤ 0.65 cm^2/m^2 and moderate if the AVAi was ≤ 0.85 cm^2/m^2 but >0.65 cm^2/m^2. Effective orifice area was calculated using the continuity equation (VTI method) and data derived from transthoracic echocardiography pre- and post-device implantation. Specifically, native LVOTd was measured on transthoracic echocardiography in the parasternal long-axis view in a selected zoomed mid-systolic frame, just below the hinge points of visible leaflets perpendicular to the aortic root wall; AVR LVOTd was measured in a zoomed mid-systolic frame in the parasternal long-axis view, just below hinge points of visible prosthetic leaflets, perpendicular to AVR long axis and from inner edges of the stent. The native aortic annulus was measured on transthoracic echocardiography in the parasternal long-axis view in a selected zoomed mid-systolic frame precisely from hinge point to hinge point. Candidate predictors (independent variables) of P-PM studied included age, sex, annulus size, LVOT size, bioprosthesis size, aortic angulation, and ejection fraction.

Depth of final device placement in the left-ventricular outflow tract (LVOT) was also studied. This was measured using a final fluoroscopic aortogram acquisition with the deployed bioprosthesis in a right anterior oblique (RAO) projection that displayed the aortic valve in optimal alignment with—as much as possible—all three leaflets visible in the same plane. The depth of delivery was defined as the distance from the native aortic annular margin on the side of the non-coronary cusp (leftward on the described projection) to—on the corresponding side—the most proximal edge (deepest in the left ventricle) of the deployed stent-frame. The pre-dilatation (Nucleus) balloon filmed in the same projection was used for calibration, its markers 20 mm apart. Importantly, its proximal markers spanning the LVOT were used for calibration, which is precisely the same vicinity where the final depth of implantation of the prosthesis was measured. Depth of delivery was also measured on transoesophageal echocardiography for a selected cohort, for comparison to the angiographic measure.

Since the trileaflet porcine pericardial valve is mounted onto the nitinol stent-frame ~12 mm above the left-ventricular edge of the stent (*Figure 1*), 'optimal' placement of the valvar component in the recommended supra-annular position was defined by the depth of the left-ventricular edge of the stent-frame in the LVOT relative to the annulus of the native non-coronary cusp of the aortic valve. The 'optimal' depth of 5–10 mm below the native non-coronary cusp as measured on fluoroscopy, would correlate to the prosthetic valve lying 2–7 mm above the native annulus. All other depths of delivery were defined as 'suboptimal'.

To correct for any potential distortion in the stent frame, either true or spurious, relative depth of implantation was derived from the absolute depth as a percentage of the full final measured length of the stent frame. As an optimal absolute depth of implantation of 5–10 mm was stipulated, optimal relative depth of implantation was represented as 5–10 mm of the full expected stent frame length supplied by the manufacturer. This proposed optimal absolute depth equates to a relative depth of 9.1–18.2% of 55 mm for the smaller 26 mm inflow Medtronic-Corevalve prosthesis (CRS-P3-640) and 9.4–18.9% of 53 mm for the larger 29 mm inflow prosthesis (CRS-P3–943).

Statistical methods

Statistical analysis was made using SPSS software (SPSS, Inc., Chicago, IL, USA). Differences were assessed using a paired sample *t*-test for normally distributed data or Wilcoxon signed rank two related samples analyses for other distributions. For comparison of independent non-parametric variables, a χ^2 statistic was used and for independent normally distributed variables an independent samples *t*-test. For correlations Pearson bivariate analysis with a two-tailed test for significance was used for parametric variables and Spearman rho correlations for non-parametric variables. Factors found to be related univariately to P-PM were studied in a multivariate binary logistic regression model.

Results

Between January 2007 and December 2008, 50 patients underwent TAVI. Baseline demographics are shown in *Table 1*. Mean age was 82.8 years (SD 5.9; 70–93) and mean logistic EuroSCORE was 22.2% (SD 13.1; 5.27–76.26). Forty-eight percent were male.

Procedural results

There was one periprocedural death secondary to heart failure aggravated by cardiac tamponade (2.9%) and subsequently a further four deaths within 30 days of the procedure. These were due to a subdural intracerebral haematoma following a fall, loss of temporary pacemaker capture with underlying asystole after successful implantation, an ischaemic stroke in a severely cachectic patient, and a perioperative death attributable to a low output state following an open surgical revision for severe paraprosthetic AR. Median post-procedural time in hospital, in those surviving to discharge, was 5 days (interquartile range 4–8).

Table 1 Baseline characteristics

	(*n* = 50)
Mean age, years ± SD	82.8 ± 5.9
Male gender, *n* (%)	24 (48)
Diabetes, *n* (%)	9 (18)
Hypertension, *n* (%)	21 (42)
Atrial fibrillation, *n* (%)	14 (28)
Ischaemic heart disease, *n* (%)	23 (46)
Prior MI, *n* (%)	7 (14)
Prior CVA/TIA, *n* (%)	7 (14)
Prior CABG, *n* (%)	9 (18)
Prior PCI, *n* (%)	15 (30)
Prior permanent pacemaker, *n* (%)	4 (8)
Peripheral vascular disease	5 (10)
Dialysis	2 (4)
Creatinine >200 μmol/L	2 (4)
Any renal impairment (eGFR <50 mL/min)	24 (48)
Pulmonary disease	16 (32)
Prior malignancy, *n* (%)	7 (14)
Active malignancy, *n* (%)	3 (6)
Declined outright for open surgery:	17 (34)
Multiple risk factors, log EuroSCORE >30	6 (12)
Severe respiratory disease	5 (10)
Porcelain aorta	3 (6)
Age >90	2 (4)
No contractile reserve on stress ECHO	1 (1)
Symptoms	
Dyspnoea, *n* (%)	50 (100)
Angina, *n* (%)	34 (68)
Syncope, *n* (%)	7 (14)
Emergent case/cardiogenic shock	1 (2.0)
NYHA I, *n* (%)	0
II, *n* (%)	24 (48)
III, *n* (%)	22 (44)
IV, *n* (%)	4 (8)
Biplane LVEF, %, mean ± SD	49.7 ± 13.5
Biplane LVEF ≤30%, *n* (%)	7 (14)
Biplane LVEF ≤40%, *n* (%)	15 (30)
Biplane LVEF ≤50%, *n* (%)	23 (46)
Logistic EuroSCORE, mean ± SD	22.2 ± 13.1
Logistic EuroSCORE >20%, *n* (%)	25 (50)
Peak pressure gradient, mmHg, mean ± SD	79.7 ± 30.4
Mean pressure gradient, mmHg, mean ± SD	47.4 ± 18.7
Aortic valve area, cm^2, mean ± SD	0.7 ± 0.2

MI, myocardial infarction; CVA, cerebrovascular accident; TIA, transient ischaemic attack; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; LVEF, left-ventricular ejection fraction.

Haemodynamic results

There were significant periprocedural reductions in peak (80.6 ± 29.9 to 15.9 ± 5.6 mmHg, $P < 0.001$) and mean (48.0 ± 18.4 to 8.1 ± 3.3 mmHg, $P < 0.001$) transvalvular gradients by echocardiography. There were substantial increases in aortic valve areas calculated by continuity effective orifice areas using Doppler velocity time integrals (CEOA VTI): 0.7 ± 0.2 to 1.7 ± 0.5 cm^2, $P < 0.001$.

Aortic regurgitation

There were no cases of transvalvular AR. On post-procedural transthoracic echocardiography, paravalvular AR was not present in 16%, grade 1 in 76%, grade 2 in 4% and grade 3–4 in 4% (*Table 2*). Optimal device position per se did not influence

Table 2 Haemodynamic and functional data

	Pre	Post	*P*-value
Peak aortic gradient, mmHg, mean ± SD	80.6 ± 29.9	15.9 ± 5.6	<0.001
Mean aortic gradient, mmHg, mean ± SD	48.0 ± 18.4	8.1 ± 3.3	<0.001
AVA, cm^2, mean ± SD	0.7 ± 0.2	1.7 ± 0.5	<0.001
AVAi, cm^2/m^2, mean ± SD	0.4 ± 0.1	1.0 ± 0.3	<0.001
Prosthetic AVAi ≤0.85 cm^2/m^2 (%)	—	16 (32)	—
Prosthetic AVAi ≤0.8 cm^2/m^2 (%)	—	14 (28)	—
Prosthetic AVAi ≤0.65 cm^2/m^2 (%)	—	1 (2)	—
AR grade			
0, *n* (%)	14 (28)	8 (16)	*P* = 0.196
1+, *n* (%)	32 (64)	38 (76)	
2+, *n* (%)	3 (6)	2 (4)	
3+, *n* (%)	1 (2)	1 (2)	
4+, *n* (%)	0	1 (2)	
Biplane LVEF, %, mean ± SD	49.9 ± 13.5	55.5 ± 9.4	0.001
Biplane LVEF ≤30%, n (%)	7 (14)	0	0.008
Biplane LVEF ≤40%, *n* (%)	15 (30)	6 (12)	0.005
Biplane LVEF ≤50%, *n* (%)	23 (46)	12 (24)	0.005
NYHA status			
I, *n* (%)	0	27 (54)	<0.001
II, *n* (%)	24 (48)	16 (32)	
III, *n* (%)	22 (44)	2 (4)	
IV, *n* (%)	4 (8)	0	

AVA, aortic valve area; AVAi, indexed aortic valve area; AR, aortic regurgitation; LVEF, left-ventricular ejection fraction.

Table 3 Differences between patients with optimal and suboptimal Medtronic-Corevalve positioning

	'Optimal' device position, $n = 25$	'Suboptimal' device position, $n = 25$	*P*-value
Depth of implantation, cm (SD)	0.8 (0.1)	1.3 (0.3)	<0.001
Age, years (SD)	84.2 (4.9)	81.4 (6.5)	0.082
Male sex, *n* (%)	11 (44)	13 (52)	0.571
Annulus size, cm (SD)	2.3 (0.2)	2.3 (0.2)	0.504
LVOT size, cm (SD)	2.2 (0.3)	2.1 (0.3)	0.105
STJ size, cm (SD)	2.8 (0.5)	2.8 (0.4)	0.566
Aortic angulation, degrees from midline (SD)	−27.8 (10.5)	−28.1 (10.3)	0.901
Prosthetic AVA, cm^2 (SD)	1.8 (0.5)	1.7 (0.5)	0.337
BSA, m^2 (SD)	1.7 (0.2)	1.8 (0.2)	0.376
Prosthetic AVAi, cm^2/m^2 (SD)	1.1 (0.3)	1.0 (0.3)	0.21
P-PM, *n* (%)	4 (16)	12 (48)	0.015
Aortic regurgitation			0.261
Grade 0, *n* (%)	4 (16)	4 (16)	
Grade 1+, *n* (%)	19 (76)	19 (76)	
Grade 2+, *n* (%)	2 (8)	0	
Grade 3+, *n* (%)	0	1 (4)	
Grade 4+, *n* (%)	0	1 (4)	

AVA, aortic valve area; AVAi, indexed aortic valve area; LVOT, left-ventricular outflow tract; BSA, body surface area; P-PM, prosthesis-patient mismatch; STJ, sinotubular junction.

degree of AR (*Table 3*), suggesting factors other than positioning to be important in the pathogenesis of this phenomenon. However, the incidence of very deep delivery (>15 mm) was rare ($n = 2$, 4%), and using a Spearman rho correlation, clinically significant paravalvular AR (grade 2 or more on post-procedural echocardiography) was related to very deep depth of delivery ($r = 0.313$, $P = 0.032$).

Left-ventricular systolic function and NYHA status

There was an acute improvement in biplane ejection fraction on the pre-discharge echocardiogram, relative to baseline, from 49.9 ± 12.6 to 55.5 ± 9.4% ($P = 0.001$). This improvement was more marked in those with at least moderate LV impairment at baseline (EF < 40%), EF increasing from a mean of 31.5 to 47.5% ($P = 0.001$).

For the 45 patients surviving beyond 30 days, NYHA status improved from a mean of 2.58 at baseline to 1.44 pre-discharge ($P < 0.001$). There was 1 case with a deterioration in NYHA status (2%), 4 (8%) with no change, and 40 with an improvement (80%) (*Table 2*).

Table 4 Characteristics of those with and without prosthesis-patient mismatch (AVAi ≤ 0.85 cm^2/m^2)

	No P-PM, $n = 34$	P-PM, $n = 16$	*P*-value
Depth, cm (SD)	1.0 (0.3)	1.1 (0.4)	0.357
Age, years (SD)	82.6 (5.8)	83.3 (6.1)	0.683
Male sex, *n* (%)	14 (41.2)	10 (62.5)	0.159
Aortic annulus size, cm (SD)	2.3 (0.2)	2.3 (0.2)	0.659
LVOT size, cm (SD)	2.2 (0.3)	2.0 (0.3)	0.127
STJ size, cm (SD)	2.8 (0.5)	2.8 (0.3)	0.945
Aortic angulation, degrees (SD)	−28.9 (9.9)	−26.0 (11.1)	0.366
Biplane LVEF pre-procedure, % (SD)	49.1 (14.5)	50.9 (11.6)	0.651
'Optimal' implant position, *n* (%)	21 (61.8)	4 (25.0)	0.015
AVA, cm^2 (SD)	1.9 (0.4)	1.3 (0.2)	<0.001
BMI, kg/m^2	24.0 (2.4)	25.1 (3.1)	0.289
BSA, m^2 (SD)	1.7 (0.2)	1.8 (0.3)	0.095
AVAi, cm^2/m^2 (SD)	1.2 (0.2)	0.7 (0.1)	<0.001

AVA, aortic valve area; AVAi, indexed aortic valve area; LVOT, left-ventricular outflow tract; BSA, body surface area; STJ, sinotubular junction; BMI, body mass index.

Incidence and predictors of prosthesis-patient mismatch

Prosthesis-patient mismatch occurred in 16/50 cases (32%) (*Table 4*). It was unrelated to age, sex, native AV annulus dimension (*Figure 2*), LVOT dimension, device size, aortic angulation, and baseline biplane ejection fraction.

Depth of implantation was on average 10.5 ± 3.4 mm, measured fluoroscopically in all cases. Depth of implantation measured in 26 patients on transoesophageal echocardiography correlated well to the fluoroscopic measure (Pearson correlation coefficient $r = 0.728$, $P < 0.001$).

Optimal position (defined here as 5–10 mm below the native aortic annulus measured fluoroscopically) was inversely correlated to P-PM (Spearman rho $r = -0.34$, $P = 0.015$). However, despite this clear correlation optimal position was unrelated to AVA, BSA, and AVAi per se, suggesting a nonlinear relationship between optimal position and AVAi, with a degree of overlap between optimal and suboptimal implants in the lower range of AVAi which are not clinically significant (i.e. AVAi > 0.85 cm^2/m^2, not P-PM, *Figure 3*). The variable of optimal relative depth of implantation (depth of implantation as a proportion of measured stent frame length) remained inversely correlated to P-PM (Spearman rho correlation coefficient $r = -0.364$, $P = 0.01$), suggesting that the data presented here for absolute depth is robust.

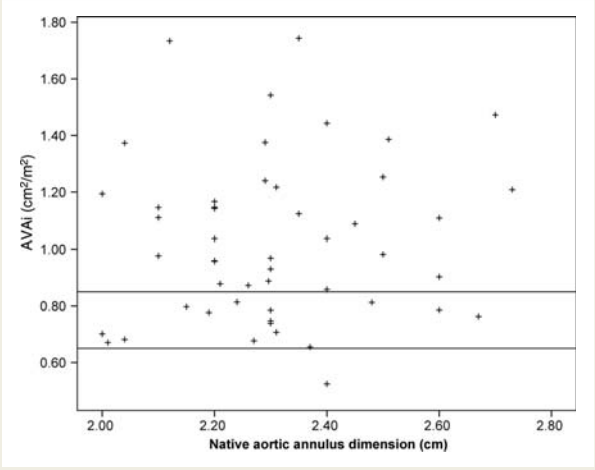

Figure 2 Indexed aortic valve area according to annulus size. In contrast to open aortic valve replacement, there was a lack of association between aortic annulus size and bioprosthesis indexed aortic valve area (AVAi), even for smaller (20–21 mm) annuli; cut-offs for moderate (AVAi ≤ 0.85 cm^2/m^2; $n = 15$) and severe (<0.65 cm^2/m^2; $n = 1$) prosthesis-patient mismatch (P-PM) are shown.

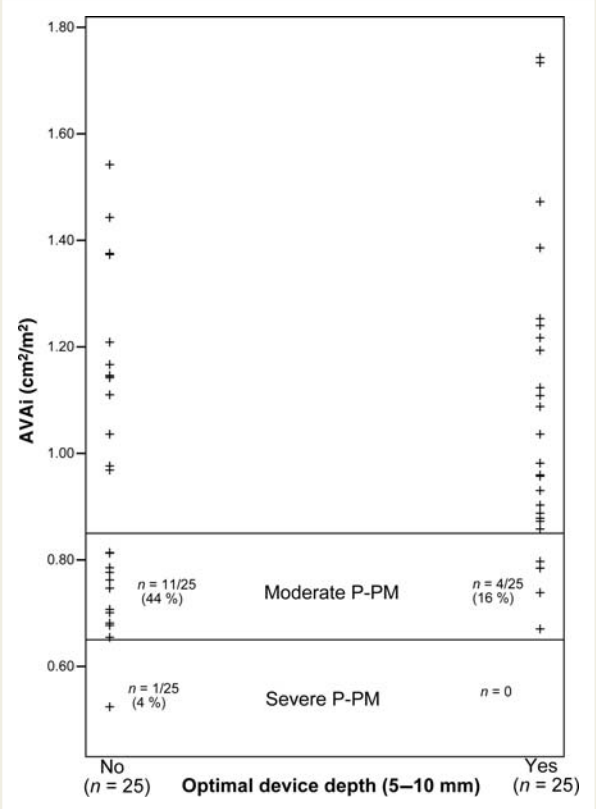

Figure 3 The relationship between optimal deployment and prosthesis-patient mismatch. Scatter plot showing indexed aortic valve area for patients with optimal vs. non-optimal device final deployment position. Considerably fewer cases of prosthesis-patient mismatch were seen if final position was optimal (defined as 5–10 mm from the annulus). There was only one case of severe prosthesis-patient mismatch seen, in a case with suboptimal positioning.

As expected, depth of implantation influenced the position of the new prosthetic annular margin visible on contrast fluoroscopy, which became supra-annular, annular, or infra-annular depending on final position (*Figure 4*). 'Optimal' implants were achieved in 25/50 cases (50%), with a mean AVAi of 1.07 cm^2/m^2 and incidence of P-PM of 16% (4/25). 'Shallow' implants (0–5 mm) were seen in 2/50 (4%), with a mean AVAi of 0.69 cm^2/m^2 (incidence of P-PM 100%) and 'deep' (10–15 mm) implants in 20/50 (40%), with a mean AVAi of 0.99 cm^2/m^2 (P-PM in 9/20 = 45%). Three of the 50 cases (6%) were 'very deep' (>15 mm) with mean AVAi 1.0 cm^2/m^2 (P-PM in 1/3 = 33.3%). In one case, there was a valve-in-valve procedure after the first implant was deployed very deep (19 mm), the second was optimally placed and this resulted in an optimal AVAi of 1.2 cm^2/m^2.

Discussion

P-PM is present when the effective orifice area of the inserted prosthetic valve is too small in relation to body size.[1,2] Haemodynamically, the consequence is to generate higher than expected gradients through normally functioning prosthetic valves.[3] This study demonstrates for the first time an incidence of P-PM following TAVI with the Medtronic-Corevalve bioprosthesis (32%), which is slightly less than that seen after conventional open AVR with stented bioprostheses.

The Medtronic-Corevalve device is a long device and allows for a wide range of implant depths. It does appear, however, that position of implantation is important in optimizing the indexed aortic valve area and hence minimizing the phenomenon of P-PM, with the prescribed supra-annular position of the bioprosthesis within the stent-frame achieving optimal haemodynamics and a low incidence of P-PM (16%). It is important to emphasize that the term 'supra-annular'—when referring to conventional aortic valve replacement—describes a prosthesis type that has no stent material obstructing the outflow area.[13] The term 'supra-annular', used here in the context of Corevalve implantation is another entity, describing the position of the prosthetic valve within the Corevalve stent frame relative to the native aortic annulus.

Interestingly, optimal position, while related to P-PM, was unrelated to AVAi and to the individual components of AVAi (AVA and BSA), suggesting a nonlinear haemodynamic relationship. One might hypothesize that suboptimal position may influence Corevalve stent expansion which—in turn—may be nonlinearly related to AVAi. Importantly in this context, it is not AVAi per se but its lower threshold of ≤ 0.85 cm^2/m^2 which defines P-PM. Moreover, it is P-PM rather than the continuous variable of AVAi from which P-PM is derived that is predictive of adverse outcome after open AVR.

Of note, P-PM was unrelated to small aortic root geometry, with no relation to annular, LVOT, and STJ dimension. This is perhaps related to the fact that the Corevalve case selection requires native aortic valve annuli of 20–27 mm and hence excludes very small annuli. It appears that the device allows consistent valve area in both males and females, and over a wide range of annuli.

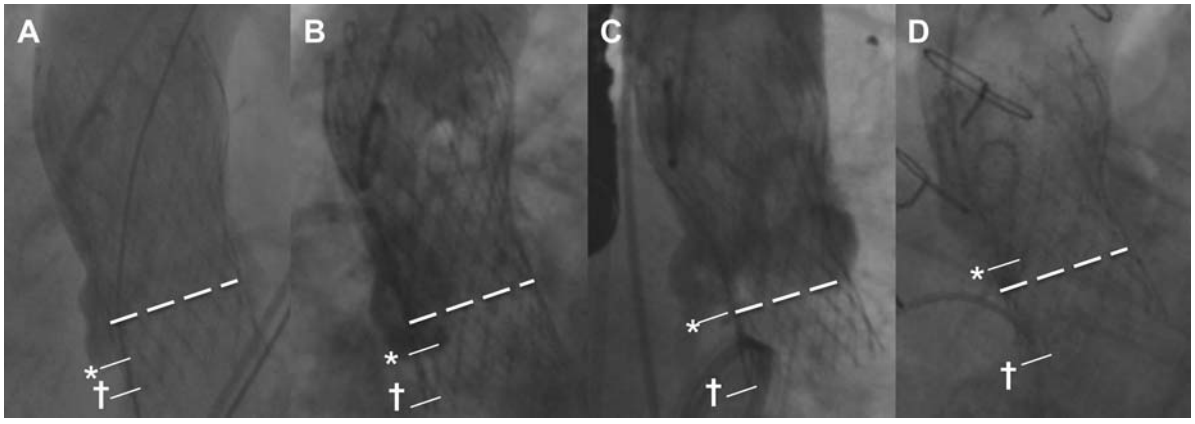

Figure 4 Supra-annular positioning is not always achieved. Fluoroscopic illustration of depth of implantation and its influence on the new annular position (shown) and indexed aortic valve area. Native annular margin is shown (asterisk), as is depth of inflow portion of device (dagger). The new bioprosthetic aortic annulus is identified by the dashed line for each case shown. (*A*) A shallow implant (depth = 4.7 mm, AVAi = 0.68 cm^2/m^2)—new valve very supra-annular. (*B*) An optimal implant (depth = 8.4 mm, AVAi = 1.7 cm^2/m^2)—new valve supra-annular. (*C*) A deep implant (depth = 12.7 mm, AVAi = 1.1 cm^2/m^2)—new valve annular. (*D*) A very deep implant (depth = 18.4 mm, AVAi = 0.7 cm^2/m^2)—new valve infra-annular.

Controversy over the effect of prosthesis-patient mismatch on clinical outcomes

Prosthesis-patient mismatch has been the subject of much controversy of late. Vicchio *et al.*[14] recently reported that—in an elderly cohort—both moderate and severe mismatch had no bearing on survival, ventricular mass, and quality of life. Similar studies failed to show its influence on short and long-term survival.[15–18]

In contrast, Bleiziffer *et al.*[19] reported in a series of 312 patients (34.3% of whom had P-PM) a significant difference in exercise capacity measured objectively at follow-up with stress testing, in favour of those without P-PM. Also recently, Florath *et al.*[20] demonstrated that severe P-PM was an independent risk factor of survival time.

Several authorities have attributed the apparent discrepancies in the significance of P-PM to the choice of parameter used to define this phenomenon.[2,19,21] Most discordant studies have identified P-PM by use of either the *in vitro* effective orifice area (EOA), provided by the manufacturer of the prosthesis, or the geometric orifice area calculated from the internal diameter of the prosthesis stent, rather than by direct measurements.[2] Hence the overwhelming body of evidence, both historical and contemporary, supports P-PM as an important determinant of morbidity[22,23] and both short and long-term mortality.[24–30] One postulates that the importance of P-PM would hold regardless of the mode of implantation, although clearly this must be demonstrated in longitudinal studies of patients following TAVI.

Patient groups susceptible to the effects of prosthesis-patient mismatch

There is recent evidence that patients under 65 years of age have more adverse effects from P-PM than older sedentary patients.[2,3] This may be indicative of the fact that younger patients have higher cardiac output requirements, in relation to higher basal metabolism and increased physical activity, than older individuals. Younger patients have, by definition, a longer life expectancy and may thus be exposed to the 'chronic' effects of P-PM for a longer period of time. Moreover, older patients have more frequent and more severe comorbidities that may compete with or mask the adverse effects of P-PM.

While not relevant to the TAVI population at present, should the technology demonstrate long-term efficacy, it may be expected to penetrate younger and more active patient groups. There is already established evidence that patients with left-ventricular dysfunction are more susceptible to the adverse effects of even moderate P-PM.[28–30] This represents an important subset of patients presently undergoing TAVI and it may be that in such cases—given the data presented in here—one should strive aggressively for 'optimal' implantation.

Prevention of prosthesis-patient mismatch in open aortic valve replacement

Studies have demonstrated that the risk of P-PM can be accurately predicted at the time of AVR from the 'projected indexed EOA', by dividing the normal reference values of EOA for the different models/sizes of prostheses, by the patient's body surface area.[31] In the case of anticipated P-PM, a different prosthesis, with a more optimal haemodynamic profile for a particular patient can be chosen.[2,31,32] A more radical solution, particularly for small annuli, is aortic root enlargement, to accommodate a larger prosthesis of the same model of AVR.[2,33,34] This has yielded variable results with some operators reporting no increased surgical risk and others reporting a slight excess of procedural mortality.[33,34]

Prevention of prosthesis-patient mismatch in transcatheter aortic valve implantation

This study showed Medtronic-Corevalve final deployed position to be associated with P-PM. Deep delivery may preclude complete expansion of the section of the stent housing the valve. There were only two cases with a very shallow implant, but both displayed P-PM. If this is indeed a true relationship, it might be explained by the influence of final stent morphology on the function of the valve prosthesis it carries: the stent frame, when optimally deployed, displays a slight conical configuration in its lower portion which houses the valve, with a flute like flaring of its proximal (inflow) portion in the LVOT. One observation is that shallow implants appear to result in a loss of this configuration in favour of a more cylindrical one, which could theoretically result in the leaflets of the bioprosthesis being pushed closer together, thereby impeding function. Investigating this relationship is clearly beyond the scope of this paper but may be borne out in future larger studies.

Comparison with the published experience with the Edwards–Sapien valve

As yet, limited choices exist for choice of TAVI prosthesis, with only two sizes of prosthesis offered for each of the two transcatheter aortic devices in widespread clinical use: the Medtronic-Corevalve and the Edwards–Sapien device.[4,6] The Edwards–Sapien device is a short balloon-expandable device and precise positioning is mandatory for deployment, with the use of rapid pacing.[4] Clavel *et al.*[35] recently compared haemodynamic performance in a series of 50 Edwards–Sapien TAVI cases to a matched population of stented and stentless surgical bioprostheses. They reported that 12% of Edwards–Sapien TAVI cases had no AR on discharge, 80% trivial or mild AR, and 8% moderate AR. Although cross-series comparisons are especially difficult for this endpoint, we observed similar results with Medtronic-Corevalve TAVI: no AR in 16%, trivial or mild AR in 76%, moderate AR in 4%, and more AR in 4%.

The same study reported improved indexed effective orifice area and less P-PM with the TAVI device, relative to the surgical prostheses. Moreover, they found that, whilst for surgical prostheses P-PM was even greater with smaller annuli, native annular dimension appeared unrelated to P-PM in TAVI. With Medtronic-Corevalve, we observed an indexed effective orifice area of 1 ± 0.3 cm^2/m^2, with a mean transthoracic gradient of 8.1 ± 3.3 mmHg and severe P-PM in only 2%, whereas in Clavel's series with Edwards–Sapien TAVI, the indexed effective orifice area on discharge was 0.9 ± 0.26 cm^2/m^2, with a mean transthoracic gradient of 10 ± 4 mmHg and severe P-PM in 11% of cases. It should be noted that these are indirect comparisons and a direct haemodynamic comparison is an important future direction.

With the relatively long self-expanding stent-frame of the Medtronic-Corevalve prosthesis,[6] we demonstrate that, although several positions of prosthesis are feasible, optimization of AVAi and minimization of P-PM seem to occur within a relatively narrow window of final placement depth. Some degree of flexibility in positioning exists when the device is partially deployed and established centres should strive to optimize the final device position; transoesophageal echocardiography can complement fluoroscopy to achieve this.[36]

Even when final deployment is very deep in the left ventricle, other options exist to improve valve haemodynamic function. Within our series, we report one case with Medtronic-Corevalve valve-in-valve at the same sitting and, although this was for severe paraprosthetic AR, this resulted in an excellent AVAi. Other operators have dealt with the problem of deep final deployment with the use of a snare to pull back the deployed device, although this is more technically challenging and slightly unpredictable as the prosthesis is often firmly anchored to the calcified native leaflets.[37] This makes the excessive force required on pull-back with a snare difficult to regulate.

With regard to paraprosthetic AR (another important component of valve haemodynamic function), we found very deep implantation to be an important factor. Numbers with very deep implantation, just as with very shallow implantation, were few. Severe AR ensued since the covered skirt with very deep implantation is situated below the native annulus in this scenario, allowing blood to regurgitate through the large holes of the uncovered portion of the stent frame. These holes are designed to preserve coronary flow if the Medtronic-Corevalve is optimally placed. The aetiology of paraprosthetic AR is a complex one governed by multiple factors, which should be the subject of further study.

Conclusion

The clinical relevance of P-PM following TAVI remains unproved and requires further elucidation in longitudinal series. Nevertheless, just as for open AVR, one should strive to reduce this complication. Its incidence (32% in the series presented here) appears to compare at least as favourably to that seen following conventional AVR, and perhaps even more favourably (16%) when device positioning is 'optimal'. This study demonstrates that the operator can significantly influence valve haemodynamic function by differences in positioning of the Medtronic-Corevalve stent frame.

Study limitations and future indications

This is a small study and its findings and hypotheses generated must be validated and tested in larger series. Early echocardiography after a significant intervention may skew haemodynamic results but, even though the echocardiograms were performed pre-discharge for this study, one might expect the stent frame dimensions and haemodynamics to have stabilized at this time. It could be argued that later echocardiography introduces the added confounder of potential valve deterioration, although we have not witnessed this to date. The limited size of the study makes multivariate analyses difficult. Future studies should probe the clinical relevance of P-PM in the setting of TAVI, the influence of device design and the impact of the phenomenon on longer-term clinical outcomes.

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