Sizing strategy is a major determinant of postoperative pressure gradients in commonly implanted stented tissue valves

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INTRODUCTION

Aortic valve replacement is one of the most commonly performed cardiac operations worldwide, with more than 200 000 implantations per year [1]. There is a dramatic shift in recent years towards the use of primarily stented tissue valves [1]. In the US alone, the fraction of biological valves of all implanted aortic prostheses increased from 44 to 78% within a 10-year period (1997–2006) [1].

Since the majority of these biological prostheses are stented tissue valves, heated debates have developed revolving around the haemodynamic performance of these prostheses. The debate is based on the fact that stented tissue valves generally have smaller geometric orifice areas (GOAs) than their appropriate mechanical counterpart [2]. The difference is owing to the almost complete opening of mechanical leaflets so that the GOA for mechanical valves are almost identical to the area comprised of the inner stent. It is, therefore, only logical to select the size of a mechanical prosthesis based on matching the inner stent diameter to the diameter of the outflow tract/annulus (intra-annular sizing).

Most stented biological valves have the actual valve apparatus mounted on the outside of the stent and the actual opening area of the cusps (pericardial or porcine) is much smaller than the inner stent area [3]. Thus, a suprannular position has been suggested to be haemodynamically superior because, with placement of the valve above the annulus, a bigger valve may be implanted, allowing the ‘concealment’ of some of the dead space located inside the stent in the aortic root and resulting in a larger GOA being placed over the left ventricular outflow tract [3].

However, the developments in this area have become highly confusing because the competing companies did not adhere to a common nomenclature with respect to size labelling of their valves and sizing strategies. We and others previously reported differences in valve-size nomenclature [4, 5] and we illustrated how these differences make reliable, direct comparisons of the...
haemodynamic properties of different valve prostheses practically impossible [5].

In addition, companies have changed the design of stented tissue valves to improve their haemodynamic performance. Improvement of the relative valve opening has been suggested, by designing pericardial valves (e.g. the Sorin Mitroflow or the new SJM Trifecta) where the cusps are wrapped around the stent, allowing a greater opening than with cusps placed on the inside of the stent (e.g. any porcine valve or the Carpentier-Edwards Perimount). But these newly designed valves differ again in their suggested sizing strategies and their valve size/sizer relation.

We, therefore, aimed to compare the haemodynamic properties of the Mitroflow with those of the Perimount. Comparative data of these two valves are scarce [6–8], but the two valves are ideal to investigate the above-described considerations because one valve has the pericardial cusps on the insides of the stent (Perimount) and the other has the cusps wrapped around its stent (Mitroflow). Being also aware of the differences in sizing strategy, we speculated that the improvement in the valve design of the Mitroflow may get lost by using a less aggressive sizing strategy.

METHODS

Patient selection and characteristics

Between January 2007 and November 2010, we selected all patients who received a Carpentier-Edwards Perimount Prosthesis (model 2900) or a Sorin Mitroflow prosthesis (model LXA) as the only valve procedure during their cardiac operations. Perimount was implanted in 670, and Mitroflow in 224 patients. In the same time period, 806 more aortic valves were replaced, but either with a different prosthesist or as part of a multivalve procedure and were therefore not included in the current report. For the purpose of haemodynamic comparison of the two prostheses, we analysed only discharge echocardiograms performed by the same single examiner. Thus, 537 of the patients who received a Perimount and 164 of those who received a Mitroflow were used for the final comparative analysis. The study was approved by the Institutional Review Board (No. 3279-10/11) and was consistent with the Declaration of Helsinki. The need for individual informed consent was waived on the condition that the study is retrospective and the patients’ identities were hidden before analysing the data. All preoperative, operative and postoperative data were collected prospectively in our surgical database, QIMS (Quality and Information Management System).

Valve dimensions and assessment of haemodynamic properties

We obtained external and internal valve diameters from the manufacturers, and measured sizer dimensions with a caliper [9]. Haemodynamic properties of the prostheses were assessed by analysing peak and mean gradients as well as flow velocity from routinely performed discharge echocardiograms. These transthoracic echocardiograms were generally performed 1 week postoperatively. Pressure gradients and velocities were measured using continuous-wave Doppler with the modified Bernoulli equation:

\[ P = 4V^2, \]

where \( P \) is the pressure gradient across the valve and \( V \) is the flow velocity across the valve [10]. Information on ejection fraction and ventricular dimensions was also obtained in the context of the routine discharge echocardiography and used for the comparison of baseline data.

Statistical analysis

Baseline patient characteristics were reported as mean ± standard deviation for quantitative variables or as frequencies and percentages for discrete variables. Statistical differences between the two groups were analysed by Student’s t-test for quantitative data and Fisher’s exact test for discrete data. To assess the effect of both valve types, different size labels, and the interaction between them as well as preoperative patient characteristics on pressure gradients, and multivariate analyses using linear models were applied. To assess multiplicity, we used Holm–Bonferroni adjustment. Differences were considered significant at \( P < 0.05 \). All statistical calculations were performed using the SAS 9.3 and SPSS 20 software (SPSS, Inc., Chicago, IL, USA).

RESULTS

Due to the retrospective nature of the study and the fact that we analysed only discharge echocardiograms, all patients in this analysis had survived the operation. Table 1 shows the demographic data of the two patient groups. Patients receiving Mitroflow were slightly older, were more often female and had slightly better ejection fractions. EuroSCORE was also slightly higher, and body surface area (BSA) was ~5% smaller in the Mitroflow group. The fractions of patients in the four New York Heart Association class categories were similar. Equal fractions of patients were operated on urgent and emergent bases. The number of patients with concomitant replacement of the ascending aorta was higher in the Perimount group.

Figure 1 shows the distribution of selected valve sizes for the patients having received Perimount or Mitroflow prosthesis. The majority of implanted valves were sizes 23 and 25 for the Perimount and 23 and 21 for the Mitroflow, possibly reflecting the fact that the Mitroflow group contained more women and smaller BSA. Valves labelled 19 or 29 were only occasionally implanted and are therefore excluded from further analysis.

Figure 2 illustrates the presumed haemodynamic advantage of the Mitroflow. For the same outer diameter, the maximal valve opening area (the geometric orifice area (GOA)) is larger for the Mitroflow than for the Perimount. However, the Mitroflow with the same outer diameter as the Perimount has a two sizes-greater size label (i.e. a Mitroflow size label 27 equals the outer diameter of a 23 Perimount). Figure 2B shows company-suggested sizing strategies for the Mitroflow (upper panel) and Perimount (lower panel). Considering a patient with an annulus diameter of 23 mm, a 21 Mitroflow and a 23 Perimount will most likely be selected. Figure 2C then, illustrates a comparison of the most likely selected valves based on the sizing strategies illustrated in Fig. 2B. Following the company-suggested sizing strategy therefore results in the implantation of the Perimount that may be 6–8 mm larger than the Mitroflow.

Figure 3 shows the haemodynamic outcomes of the two groups as assessed by discharge echocardiography. Comparisons were made by the manufacturer’s size label. For the two valves,
maximal flow velocity across the valve ($V_{\text{max}}$) is shown in Fig. 3A and peak and mean pressure gradients are shown in Fig. 3B and C, respectively. Pressure gradients were highest for the 21 valves compared with the other size labels ($P < 0.05$), but differences were small. Most relevant for our study, comparing the two prostheses by size label showed no significant difference between the Mitroflow and the Perimount.

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Perimount n=536</th>
<th>Mean ± SD</th>
<th>Mitroflow n=163</th>
<th>Mean ± SD</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>70.0 ± 7.5</td>
<td></td>
<td>75.1 ± 7.8</td>
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<td>Male sex</td>
<td>70.6</td>
<td></td>
<td>42.7</td>
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<td>LVEF (%)</td>
<td>57.0</td>
<td></td>
<td>57.9 ± 13.6</td>
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<td>0.071</td>
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<tr>
<td>NYHA class</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>I</td>
<td>26</td>
<td>4.8</td>
<td>6</td>
<td>3.7</td>
<td>0.620</td>
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<tr>
<td>II</td>
<td>171</td>
<td>31.8</td>
<td>47</td>
<td>28.7</td>
<td></td>
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<tr>
<td>III</td>
<td>306</td>
<td>57.0</td>
<td>103</td>
<td>62.8</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>34</td>
<td>6.3</td>
<td>8</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>178/536</td>
<td>33.2</td>
<td>72/163</td>
<td>44.2</td>
<td>0.012</td>
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<td>Hypertension</td>
<td>441/534</td>
<td>82.6</td>
<td>146/164</td>
<td>89.0</td>
<td>0.051</td>
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<td></td>
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<td>Urgent</td>
<td>64</td>
<td>11.9</td>
<td>24</td>
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<td>Elective</td>
<td>458</td>
<td>85.3</td>
<td>134</td>
<td>81.7</td>
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<td>Surgery</td>
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<td></td>
<td></td>
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<tr>
<td>AVR</td>
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<td>56.8</td>
<td>91</td>
<td>55.8</td>
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<td>CABG</td>
<td>183</td>
<td>34.1</td>
<td>67</td>
<td>41.1</td>
<td></td>
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<tr>
<td>AAR</td>
<td>49</td>
<td>9.1</td>
<td>5</td>
<td>3.1</td>
<td></td>
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<tr>
<td>EuroSCORE</td>
<td>537</td>
<td>7.1 ± 2.6 (Median: 7.0 IQR: 5.0–9.0)</td>
<td>164</td>
<td>8.4 ± 2.4 (Median: 8.0 IQR: 7.0–10.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>537</td>
<td>1.93 ± 0.19</td>
<td>164</td>
<td>1.84 ± 0.20</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; BSA: body surface area; AAR: ascending aorta replacement; IQR: inter-quartile range; AVR: aortic valve replacement; CABG: coronary artery bypass graft.

*Based on Mann–Whitney–U test.

DISCUSSION

We demonstrated in this study that the potential haemodynamic advantage of the Mitroflow is lost due to a ‘defensive’ sizing strategy. Our results underscore the importance of an optimal sizing strategy, possibly by replica sizing.

This is not the first comparison of the haemodynamics of stented tissue valves, but we attempted, for the first time, a comparison based on reproducible true valve dimensions in relation to the suggested and practiced sizing strategies. We also did not aim to compare different prostheses based on effective orifice area (EOA) values. We used pressure gradients and flow velocities because they most closely reflect clinical relevance for the patient. Although the EOA accurately reflects haemodynamic relevance for the individual patient, we consider the EOA a potentially misleading parameter because its denomination (given as cm²) may lead to the erroneous assumption that the EOA is the actual opening of the tissue valve. However, we and others [5, 11, 12] have demonstrated previously that the EOA and the actual opening area of the valve may differ significantly. We suggested that the EOA is a result of the interplay between the maximal opening area of the prosthesis and the
patient’s anatomy (specifically the area of the left ventricular outflow tract) [5]. Thus, for the proper comparison of two different tissue valves, haemodynamic performance cannot be compared based on the assessment of the EOA alone. It is striking to note in this context that the directly measured values for the maximal opening area of stented tissue valves have never been published in a systematic fashion and all published information attempting to arrive at a true valve opening area are calculations and therefore influenced by methodological confounders [12].

As mentioned above, no information is available for the actual GOA for the Mitroflow or for the Perimount. Therefore, a truly quantitative comparison of the potential haemodynamic properties cannot be made, assuming that EOAs closely reflect GOAs or are associated with the same amount of systematic error. Nevertheless, in an effort to make a principal comparison of haemodynamics, we took published EOA values for the two valves from the literature, being well aware of the possibly significant difference to the GOA values. However, it is interesting to note that the EOA for the 23 Mitroflow as published by Yankah et al. [13] reflects about one-third of the space occupied by the sewing ring, while the EOA published by Pibarot and Dumesnil [14] for the 23 Perimount reflects ~20% of the space occupied by the sewing

Figure 2: Schematic illustration of the presumed haemodynamic design advantage for the Mitroflow compared with the Perimount. (A) comparison of the two valve prostheses with the outer diameter of 31 mm; (B) most likely selection of final valve size according to company suggested sizing strategies. (C) Comparison of the most likely selected valves based on sizing strategies illustrated in (B). The outer diameters and sizing strategies were obtained from the valve packages. Note that a company-suggested sizing strategy will result in the selection of a smaller prosthesis for the Mitroflow.
Figure 3: Maximal flow velocity across valve prostheses ($V_{\text{max}}$, A), peak (B) and mean pressure gradients (C) for sizes 21 through 27 of the Perimount (black bars) and the Mitroflow (white bars). Values are mean ± 95% confidence interval based on multivariate analyses. *P < 0.05.

Our illustration made in Fig. 2 and our results shown in Fig. 3 demonstrate and explain why the haemodynamic design advantage of the Mitroflow is, however, practically not relevant.

Our results allow another important conclusion. It is the general notion that implanting a small prosthesis is associated with higher pressure gradients. However, our results suggest that this impression is not backed by real-life data. This is due to the fact that the average pressure gradients (peak and mean) were identical between most sizes. Furthermore, although the actual differences between sizes 21 and 23 or 25 were statistically significant, they were smaller than one would have expected. These numbers presented by us are also not new and find support from other surgeons [17–24] both in absolute numbers as well as in the small differences between valve sizes. For instance, Botzenhardt et al. [24] demonstrated mean pressure gradients of 11.5 ± 3.8 mmHg for Size 21 Perimount and even higher mean gradients for Size 25 Perimount (12.7 ± 5.0 mmHg). However, what appears new is the recognition that haemodynamic performance is not primarily influenced by valve size, but much more so by sizing strategy and therefore the selection of a given valve size in relation to the patient’s anatomy. Since the relationship should be similar for all valve sizes, it is not surprising to observe the lack of great differences in pressure gradients between different valve sizes. From a haemodynamic perspective, this interpretation means that implanting a valve size 27 should be just as challenging as implanting a valve size 21.

The last conclusion may cause irritation because every surgeon knows cases where implanting a small valve may result in at times prohibitively high pressure gradients. Continuing our thinking from above, possible explanations for these situations may be a suboptimal position (tilting) of a valve (resulting in obstruction of flow) or the selection of a valve smaller than the sizing strategy would suggest. Thus, if a patient with a 23 annulus receives a valve size 21 or even 19, the pressure gradients are bound to be higher than if a 23 valve were implanted. Importantly, the high pressure gradient is then due to a difference in size selection and not primarily due to the implanted prosthesis.

The previous paragraph compared different prostheses of the same make. Comparing prostheses of different makes with each other reveals that the Mitroflow valve is the smallest of biological stented valves [5]. In addition, the sizing strategy for the Mitroflow, as applied by many surgeons, is intra-annular despite the potential for supra-annular sizing and placement. Although the valve sizer may be used as a replica and a much larger valve may potentially fit into the root (see Fig. 2B), this suggestion has not been emphasized in the past, either by the company, or by the surgeon. From a practical stand point, such ‘aggressive sizing’ for the Mitroflow may be even dangerous because the valve is mounted on a flexible stent and ‘forcing’ an ‘oversized valve’ into the root may result in geometric distortion and valve dysfunction [25]. In other words, the currently practiced sizing strategy may indeed be the best for the respective valve types, which means that the design improvement in the Mitroflow will not be able to live up to its expectations in real life.

It is important for us to stress at this point that we do not suggest, with this analysis, routine ‘oversizing’. Selecting a larger valve also bears a greater risk of causing damage, specifically to the aorta around the aortotomy. When selecting a larger prosthesis, it may be necessary to take the valve off the holder and tilt it for proper introduction into the root. In any case, we believe that it is important that every surgeon who implants tissue prostheses develops a profound understanding of this context, in order not to
be limited in his or her surgical options. If a surgeon decides to ‘oversize’, we recommend the use of a replica (which is available for most of the new generation of Prostheses), because it is usually identical in shape and size to the corresponding prosthesis.

The practical experience with the Perimount demonstrates that in most patients, a larger valve than the Mitroflow can be implanted. However, the Perimount is also known for a greater need for root enlargement by patch placement than other valves [22]. Such complications are almost not reported for the Mitroflow, which apparently is due to the smaller total diameter. Thus, we believe that understanding these differences in valve design, dimensions and sizing strategies provides the surgeon with a much greater spectrum of options for achieving haemodynamically superior results. From a practical stand point, we suggest that such results may be achieved best by applying sizing strategies based on the use of valve replicas, because replicas should represent the prostheses’ actual shape and size and allow fitting the biggest prosthesis to the patient’s anatomy (which may often be bigger than the size selected based on company suggested sizing strategy).

Conclusion

We conclude that the potential haemodynamic advantage of the Mitroflow is lost due to the different sizing strategies. The results underscore the importance of an optimal sizing strategy, possibly by replica sizing.

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