Significant intra-valvular pressure loss across EPIC SUPRA and perimount magna supra-annular designed aortic bioprostheses in patients with normal aortic size

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1. Introduction

Supra-annular designed stented aortic valve bioprostheses provide superior hemodynamics due to low profile, low stent base and sleek commissure posts. The St Jude Medical Epic heart valve (St Jude Medical, Inc, St Paul, MN) is a tri-composite glutaraldehyde-preserved porcine bioprosthesis designed for complete supra-annular implantation. Hemodynamic performance of the St. Jude Medical Epic Supra bioprosthesis in aortic position has been extensively studied. Trans-prosthetic mean gradients have averaged 12.5 mmHg and 15.5 mmHg in two studies for 21# EPIC heart valve and effective valve area of 1.6 cm².1,2 Perimount Magna bioprosthesis (Edwards Lifesciences, Irvine, CA, USA) is also a true supra-annular design heart valve designed to provide 25% better hemodynamics compared to standard stented tissue valves.3 Average mean gradients across Perimount Magna in aortic position are less than 20 mmHg on moderate exercise (resting average mean gradient 10.8 mmHg), mean effective valve area is 1.6 cm² and valve performance index averages 45%.4–6 Marked pressure recovery to a varying extent is common to all prosthetic heart valves including bioprostheses. Pressure recovery-related differences are usually small except in patients with bileaflet metallic prosthesis, wherein high-pressure local jets across central orifice have been documented since long back and also in patients with narrow aortic root. We describe two patients with normally functioning stented aortic bioprostheses with supra-annular design (EPIC SUPRA and PERIMOUNT MAGNA), wherein very high trans-prosthetic gradients and critically reduced estimated effective valve orifice areas in presence of normal aortic size were consistently recorded over long periods of follow-up. The valve leaflets, however had normal excursion, were thin, opened with a triangular or oblong shape and had expected geometric valve area (1.7 and 1.6 cm² respectively) measured by 3D trans-oesophageal echocardiographic planimetry. Pressure recovery upstream the valves accounted for 20% and 12% of total pressure gradients respectively. Dominant site for pressure drop was intra-valvular (75–85%). Such a phenomenon has not been reported in vivo for these two valve designs.

2. Case report I

This 72-year-old male underwent 3-vessel coronary bypass surgery along with aortic valve replacement and subsequently (Epic Supra in one and Perimount Magna in the other) who consistently showed high trans-prosthetic gradients and critically reduced estimated effective valve orifice areas in presence of normal aortic size were consistently recorded over long periods of follow-up. The valve leaflets, however had normal excursion, were thin, opened with a triangular or oblong shape and had expected geometric valve area (1.7 and 1.6 cm² respectively) measured by 3D trans-oesophageal echocardiographic planimetry. Pressure recovery upstream the valves accounted for 20% and 12% of total pressure gradients respectively. Dominant site for pressure drop was intra-valvular (75–85%). Such a phenomenon has not been reported in vivo for these two valve designs.

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**ABSTRACT**

Doppler-derived trans-prosthetic gradients are higher and the estimated effective valve area is smaller than the catheter-derived and directly measured hemodynamic values, mostly due to pressure recovery phenomenon. Pressure recovery to a varying extent is common to all prosthetic heart valves including bioprostheses. Pressure recovery-related differences are usually small except in patients with bileaflet metallic prosthesis, wherein high-pressure local jets across central orifice have been documented since long back and also in patients with narrow aortic root. We describe two patients with normally functioning stented aortic bioprostheses with supra-annular design (EPIC SUPRA and PERIMOUNT MAGNA), wherein very high trans-prosthetic gradients and critically reduced estimated effective valve orifice areas in presence of normal aortic size were consistently recorded over long periods of follow-up. The valve leaflets, however had normal excursion, were thin, opened with a triangular or oblong shape and had expected geometric valve area (1.7 and 1.6 cm² respectively) measured by 3D trans-oesophageal echocardiographic planimetry. Pressure recovery upstream the valves accounted for 20% and 12% of total pressure gradients respectively. Dominant site for pressure drop was intra-valvular (75–85%). Such a phenomenon has not been reported in vivo for these two valve designs.

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**Abbreviations:** LV, left ventricle; LA, left atrium; RVOT, right ventricular outflow tract; Ao, aorta; LVOT, left ventricular outflow tract.

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bioprosthesis (St Jude Medical, Inc., St Paul, MN, USA) was implanted in aortic position. He has remained asymptomatic ever since then and routine echocardiographic evaluation performed immediately after surgery and annually has shown peak trans-prosthetic gradients varying from 57 to 74 mmHg (mean gradients 35–44 mmHg) and effective valve orifice area between 0.72 and 0.9 cm². Mean diastolic LV wall thickness has been 10 mm. His last echocardiographic examination was performed in February 2016 which showed peak and mean trans-prosthetic gradients of 74 and 43 mmHg respectively (velocity time integral of 110 cm) with estimated effective orifice area by continuity equation of 0.72 cm² at a heart rate of 54 beats/min and normal flow rate of 300 mL/s (Table 1, Fig. 1). The left ventricular outflow tract diameter and sino-tubular junction of aorta measured 21 mm and 31 mm respectively. Peak sub-valvular velocity measured was 100 cm/s. Dimensionless valve index was 0.22. Geometric valve area measured using cross-sectional and 3D trans-esophageal echocardiography averaged 1.7 cm² (Figs. 2–4). The leaflets of the bioprosthesis were thin and moved normally. There was no pannus or thrombus. Basal and mid inferior walls were akinetic, estimated left ventricular ejection fraction was 40% and the left ventricular mass index was 104 Gm/M². He also had moderate mitral regurgitation.

Table 1 shows estimates of pressure recovery using effective orifice area and aortic diameter at sinotubular junction. 75% of the estimated pressure recovery was intra-valvular when estimated by combined use of the modified Gorlin formula and the energy loss index.7,8 Valve performance index was 21% using effective orifice area and 49% using geometric orifice area. Trans-valvular flow rate was 300 mL/s.

3. Case #2

This 58-year female had aortic valve replacement in March 2010 for bicuspid aortic valve with severe aortic stenosis. Her pre-operative echocardiogram showed left ventricular hypertrophy (mean diastolic wall thickness of 14.5 mm), LV ejection fraction of 47%, mean trans-aortic gradient of 60 mmHg and effective valve orifice area of 0.6 cm². A Perimount Magna #21 bioprosthesis (Edwards Lifesciences, Irvine, CA, USA) was implanted in supra-annular location. She has remained asymptomatic since the time of operation. However, annual echocardiographic examination has shown consistently high trans-prosthetic gradients with mild aortic and mitral regurgitation and estimated left ventricular ejection fraction of 45% and mean diastolic wall thickness of 11 mm. Her latest echocardiographic examination performed in September, 2015 showed peak and mean trans-prosthetic pressure gradients of 64 and 36 mmHg (velocity time integral of 85 cm) and effective valve orifice area by continuity equation of 0.8 cm² (Table 1 and Fig. 5). Dimensionless valve index was 0.23 and trans-valvular flow rate was 232 mL/s. The valve leaflets were normal and opened seamless with an inter-leaflet distance of 20 mm during systole when examined by cross-sectional echocardiography (Fig. 6). The left ventricular outflow tract below the valve was patent and had a peak velocity of 90 cm/s. Average geometric orifice area by planimetry was 1.6 cm² when measured from 3D multiplanar reconstructed images and cross-sectional images during early systole (Fig. 7).

| Case #1, EPIC SUPRA #21 | Case #2, PERIMOUNT MAGNA#21 |
|--------------------------|-----------------------------|
| HR (BPM) | 54 | 64 |
| BP (mmHg) | 140/90 | 130/84 |
| Peak gradient (mmHg) | 74 | 64 |
| Mean gradient (mmHg) | 43 | 36 |
| Stroke volume (mL) | 80 | 75.4 |
| Geometric valve area (cm²) | 4.32 | 4.82 |
| Indexed | 1.7 | 1.6 |
| Expected mean gradient (mmHg) by Gorlin formula | 6.4 | 9 |
| Sino-tubular junction (cm) | 3.1 | 4.0 |
| EOA (cm²) by continuity equation | 0.72 | 0.8 |
| Pressure recovery (using EOA) mmHg | 15/8.7 (20%) | 7.5/4.2 (12%) |

Fig. 1. (Case #1): Panel A shows continuous-wave interrogation of the aortic prosthesis in apical 5-chamber view. Panel B shows pulsed-wave Doppler spectrum of the left ventricular outflow tract. Panel C shows trans-esophageal long axis view for measuring the left ventricular outflow tract. The estimated aortic valve area by continuity equation was 0.72 cm².
Using the corrected Gorlin formula and energy loss index, of the total 36 mmHg trans-thoracic mean gradient, 75% was due to pressure recovery and of this, 85% pressure recovery was intra-valvular and 15% was due to non-valvular factors7,8 (Table 1). Valve performance index was 23% using effective orifice area and 47% using geometric valve orifice area.

4. Discussion

The patients after cardiac valve replacement are routinely followed by Doppler echocardiography to study the opening and closing characteristics of the prosthetic valve, its morphology and hemodynamic performance. The non-invasive evaluation of prosthetic valve function is challenging. The effects of flow rate, valvular geometry, leaflet motion, jet direction and pressure recovery all impact the Doppler evaluation of prosthetic performance.8 Differentiating prosthesis obstruction from pressure recovery in patients who have high Doppler velocities across an aortic valve prosthesis is crucial for appropriate management. High gradients after aortic valve replacement can be due to measurement error (e.g. ignoring high sub-valvular velocity in modified Bernoulli equation), prosthetic stenosis, acquired subvalvular obstruction, localized high velocity jets due to valve design (intra-valvular flow turbulence) and pressure recovery, a physical phenomenon responsible for non-obstructive high trans-prosthetic gradients. Chronicity of high gradients without symptoms and left ventricular hypertrophy is highly suggestive of pressure recovery as the cause. It is common to club intra-valvular pressure

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Fig. 2. (Case #1): Left panel shows wide trans-valvular orifice by color Doppler flow in cross-sectional transesophageal echocardiographic view. Estimated color flow area (panel B) during systole is 1.7 cm². (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 3. (Case #1): Trans-esophageal echocardiographic short axis views showing adequate opening of the aortic tissue valve with irregular orifice shape.
drop independent of flow rate and pressure recovery in the ascending aorta as “total pressure recovery”.8 Pressure recovery usually accounts for <20% of pressure gradients in native stenosed aortic valves and up to 50% of gradients across prosthetic valves.9–11 In biological aortic valves, pressure recovery of 13–35% has been reported.12,13 Although large pressure recovery (about 60%) has been studied in vitro by aortic pulsatile flow model in bioprosthetic valves, accounting for up to 50% under-estimation of Doppler-derived aortic valve area,14 there are hardly any case reports of abnormally high pressure recovery across new design aortic bioprostheses.

Both of our patients had repeated Doppler hemodynamic assessment of their aortic bioprosthetic valves over long periods and were consistently found to have abnormally high trans-prosthetic gradients and reduced effective orifice area falsely suggesting severe prosthetic obstruction. We used geometric area as a substitute for effective orifice area in the modified Gorlin formula and predicted trans-prosthetic mean gradients using cardiac output and ejection time from the Doppler measurements so as to find out trans-prosthetic pressure drop independent of flow rate. It has been reported earlier than there is a close correlation between anatomical or geometric valve orifice area and the effective orifice area in trileaflet native aortic valves.15 As the two bioprostheses were trileaflet with thin sewing ring, we presumed that the anatomical valve area measured by 3D trans-esophageal echocardiographic multi-planar reconstruction would approximate effective orifice area. From predicted trans-prosthetic mean gradients, we estimated that most of the pressure drop was intra-valvular as the pressure recovery measured by energy loss index was 20% and 12% respectively. Abnormal intra-valvular pressure drop (independent of flow rate) was 75–85% of the total pressure loss. Intra-valvular pressure loss of this magnitude has been described (>70% of total pressure recovery) in aortic bioprosthesis but in in vitro studies.14–16 The discrepancy between predicted and Doppler-echocardiographic measurements could be explained by the combination of a non-flat velocity profile inside the tubular structure of these valves, which can cause local low pressure fields that result in true high gradients detected using Doppler, and also pressure recovery.14 It is also possible that some patients after implantation of these bioprostheses could have anti-anatomical orientation of flow resulting into high velocities and turbulence immediately after the flow exits the valve. Effective orifice area of #21 size Perimount and Epic Supra valve in aortic position has been reported to be 1.39 and 1.37 cm² respectively by 4D flow pattern study using cardiac magnetic resonance imaging at a stroke volume of 50 mL and total flow volume of 3.5 L/min.17 Our patients had stroke volume of 80 and 75 mL and flow/minute of 4.32 L and 4.8 L respectively and hence should have provided bigger effective orifice areas (close to that measured by 3D planimetry). Calculated effective orifice areas of 0.72 and 0.8 cm² with normal flow rate are certainly due to intra-valvular flow turbulence as both patients had aortic root size >3 cm. However, it needs to be kept in mind that high flow rates can increase pressure recovery and paradoxically decrease Doppler-estimated area.14

![Fig. 4](image)

**Fig. 4.** (Case #1): 3D-transesophageal views from the left ventricular side. Valve orifice is triangular and measures 1.69 cm².

![Fig. 5](image)

**Fig. 5.** (Case #2): Continuous-Doppler interrogation of the left ventricular outflow tract in apical view and pulsed-wave Doppler spectrum seen in inset. Trans-prosthetic peak velocity averaged 4 m/s and in the left ventricular outflow tract, it was 90 cm/s.
The concept of the pressure recovery phenomenon is based on fluid mechanics theory, showing that static pressure downstream of the stenosis could be increased or recovered because of the reconversion of kinetic energy into potential energy. Therefore, the peak or mean pressure gradient calculated from the maximal Doppler flow velocity could overestimate the true pressure gradient through the stenotic orifice. As blood moves through a prosthetic valve opening, the product of its pressure and velocity must remain the same except for energy lost as heat (i.e. energy loss due to turbulent flow). Different prosthetic valves have different flow patterns. Eccentric flows generate higher velocities and hence greater pressure drop for the same size of orifice. Turbulent flow with vortex formation occurs both in proximity to various types of bioprosthesis and on the ‘ascending aortic’ level. Larger prosthetic sizes lead to decreased flow velocities, but not necessarily to less turbulence. Turbulent flow will decrease pressure recovery and increase the quantum of pressure drop. This report suggests that very large trans-prosthetic gradients can also occur in supra-annular aortic bioprostheses due possibly to local pressure jets as seen in bileaflet mechanical valves.

5. Clinical implication

In patients with aortic bioprosthesis, high trans-prosthetic gradients can be observed despite normal function. Although clinical situation may point toward pressure recovery as the cause

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**Fig. 6.** (Case #2): Trans-esophageal echocardiographic long axis (panel A) and short axis (panel B) views showing 20 mm wide orifice of aortic prosthesis and oblong color flow area of 1.6 cm².

**Fig. 7.** (Case #2): Trans-esophageal echocardiographic valve orifice area measured using cross-sectional 2D (panel A) and by 3D multiplanar reconstructed views (panel C). Panel B shows normally opening leaflets in long axis view. The orifice area averaged 1.6 cm² and was oblong in shape.
of high Doppler gradients, mistakes leading to re-operation can also occur. It has been suggested that in Perimount (Edwards Life Sciences) and Mosaic bioprosthesis (Medtronic, Inc.), one may observe trans-prosthetic Doppler gradients which are at least double of that obtained by invasive studies. Most of this pressure difference occurs within or very close to the prosthesis indicating intra-valvular pressure loss. Hence, presence of normal aortic size does not preclude large pressure recovery.

6. Limitations

We have not performed invasive studies using either Flow Doppler wire or Millar catheter because there are ethical, cost, risk and convenience issues involved in studying completely asymptomatic patients. However, we have deployed robust and validated hemodynamic equations to reach these conclusions.

Conflicts of interest

The authors have none to declare.

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