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Work in progress report - Valves

Influence of orientation of bi-leaflet valve prostheses on coronary perfusion pressure in humans☆

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Abstract

Orientation of a bi-leaflet prosthesis (BLP) might influence coronary perfusion. The aim of this study was to investigate the influence of the orientation on coronary perfusion pressure during hyperemia and adrenergic stimulation. During hyperemia perfusion pressure determines coronary blood flow. Fourteen patients with normal coronary angiogram underwent aortic valve replacement (AVR) by a BLP, and seven received a bio-prosthesis. Patients receiving a BLP were randomized to either orientation A (hinge mechanism perpendicular to a line drawn between the coronary ostia) or B (hinge mechanism parallel to the line between the ostia). Six months after surgery all patients underwent cardiac catheterization. Pressures were measured during resting conditions, during maximum hyperemia, and during maximum adrenergic stimulation with a guiding catheter in the aortic arch (P_{ao}), simultaneously with a sensor tipped guide wire in the coronary artery (P_{cor}) and in the aortic root (P_{root}). P_{ao}-P_{root} described a flow-induced pressure drop in the aortic root (Venturi effect) and the gradient P_{root}-P_{cor} described coronary ostium abnormalities. Only small non-significant differences in myocardial perfusion pressure were found between different orientations of a bi-leaflet prosthesis or between bi-leaflet prostheses and bio-prostheses in P_{ao}-P_{root} and P_{root}-P_{cor}.
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1. Introduction

After aortic valve replacement (AVR) the pressure gradient over the valve decreases significantly with a favorable effect on the relation between intraventricular compressive forces, coronary perfusion pressure, and left ventricular cavity pressure [1], reflected by increase of coronary flow reserve [2, 3].

It has been suggested that different types and orientations of aortic valve prostheses could affect coronary blood flow in a different way [4, 5]. Kleine et al. and Bakhtiary et al. hypothesized that this should be ascribed to a disturbed flow pattern in the proximal part of the aorta distal of the valve [6].

Coronary flow is regulated by a complex interaction of neural and humoral responses, depending on oxygen demand and affecting myocardial resistance. The resistance can be minimized (and, therefore, kept constant) by pharmacological stimuli like adenosine and dobutamine, reflecting maximum exercise in true life. Under such circumstances coronary blood flow has been shown to be directly proportional to coronary perfusion pressure [7–9].

When blood is forced through the orifice of the valve prosthesis, the blood flow velocity increases thereby increasing the kinetic energy at the cost of the hydraulic energy, the pressure. Maximum velocity and, therefore, minimum pressure (Venturi effect) is observed just distal to the prosthetic valve at the position of the coronary ostia [10]. We hypothesized that differences in coronary perfusion pressure caused by a Venturi-like effect, in different orientations of a mechanical bi-leaflet prosthesis (BLP) during hyperemia and adrenergic stimulation, could influence coronary blood flow.

2. Materials and methods

The study was approved by the Medical Ethics Committee of the Catharina Hospital in Eindhoven and written informed consent was obtained from each patient.

2.1. Study population

Twenty-one patients accepted for isolated AVR and a normal coronary angiogram were selected from the total population referred to our hospital. Exclusion criteria were: previous valve surgery in any position; concomitant surgical procedures; left ventricle dilatation; aortic regurgitation ≥grade 2; history of myocardial infarction; preoperative creatine level >150 μmol·l^{-1}; or age over 75 years at time of surgery.

Fourteen patients were selected to receive a BLP (SJM®, St. Jude Medical Inc., St. Paul, MN) and seven patients received a bio-prosthesis (Medtronic Mosiac, Medtronic Inc., Minneapolis, MN). Prior to surgery patients receiving a BLP were randomized to different orientations of the valve, defined as A and B, as in previous studies [5, 6]. In orientation A (orthotopic position) the hinge mechanism was placed perpendicular to a line drawn between the coronary ostia, in orientation B (heterotopic position) the hinging mechanism was placed parallel to a line drawn between the two coronary ostia.

2.2. Surgical procedure

Anesthesia was performed according to routine in our hospital. All patients underwent a sternotomy, followed by arterial cannulation in the ascending aorta and single venous cannulation in the right atrium. Operations were performed under normothermic extra-corporeal circulation and the heart was arrested by antegrade administration of cardioplegia. The native aortic valve was removed and the annulus was decalcified. The valve prosthesis was implanted using running or separate sutures according to the surgeons preference. Mechanical prostheses were implanted with an orientation according to randomization. Most patients were extubated within a few hours and left the ICU the same day.

2.3. Catheterization at follow-up

Follow-up catheterization was performed six months after surgery. Forty-eight hours prior to the procedure, patients were asked to stop beta-blockers in order to avoid inhibition of the maximal adrenergic stimulation by dobutamine. Catheterization was performed by the Judkins approach using 6F guiding catheters with side holes at a distance of 10 cm from the tip, enabling pressure recording at the level of the aortic arch (Zuma, Medtronic Inc., Minneapolis, MN). Through the guiding catheter a high fidelity 0.014 inch pressure guide wire (PressureWire 5, Radi Medical Systems, Uppsala, Sweden; accuracy ± 1 mmHg) was advanced into the proximal coronary artery and pressure measurements were performed as described below under resting circumstances, during maximum coronary hyperemia by intravenous adenosine administration, and during maximum adrenergic stimulation by intra-venous administration of dobutamine. At the end of the procedure, 5 mg of metroprolol was administered to counteract the effect of dobutamine.

2.4. Pressure measurements in the left coronary artery

Pressure was measured in the aortic arch by the fluid filled guiding catheter at the location of the side holes, P_{ao}. All other pressures were compared to this value as a gold standard for arterial pressure. Pressure by the pressure wire was measured at three locations: the location of these side holes called $P_{ao,pw}$; at the level of the ostium of the coronary artery (considered aortic root pressure) called P_{root}; and pressure in the proximal coronary artery called P_{cor} (Fig. 1).
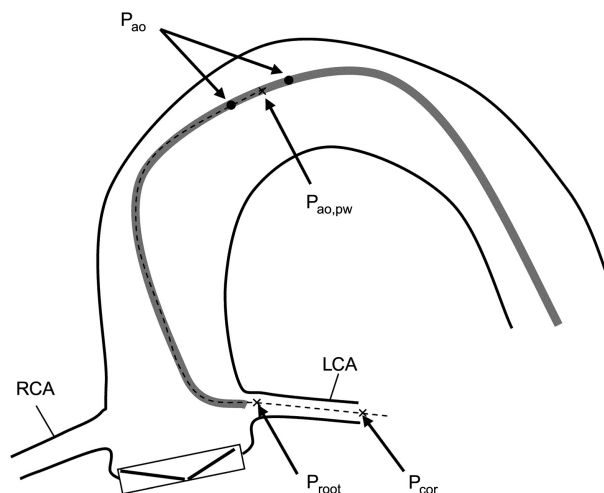

Fig. 1. Schematic representation of the pressure measurements in the aorta. The gray fluid filled catheter is used as a reference pressure and measures pressure at the side holes (P_{ao}). The pressure wire is advanced or pulled back through the guiding catheter and measures pressure at the aortic arch ($P_{ao,pw}$), the aortic root (P_{root}), and the proximal coronary artery (P_{cor}). LCA and RCA represent the left and the right coronary artery, respectively.

At first, pressure measurements were performed under resting conditions. The pressure wire was advanced until the pressure-sensor was at the location of the side holes. At that position equilibration with the fluid-filled catheter was performed ($P_{ao} = P_{ao,pw}$). Thereafter, the two pressure signals were recorded simultaneously throughout the procedure. The wire was advanced into the proximal part of the coronary artery to record P_{root} and further advanced to record P_{cor}. Under normal circumstances all these pressures should be equal [11].

Next, steady state maximum coronary hyperemia was induced by intra-venous infusion of adenosine in a dosage of 140 μg/kg·min as described before [8]. During hyperemia, the pressure wire was slowly pulled back to the aortic root. In the case of a coronary artery ostial stenosis, whether iatrogenic by the preceding AVR or atherosclerotic, a gradient is expected between P_{cor} and P_{root} [7]. Next, the sensor was pulled back to the level of the side holes of the guiding catheter to ensure equal pressures again. After the adenosine administration was stopped, its effect vanishes within a couple of minutes.

Thereafter, the pressure wire was advanced into the coronary artery again and dobutamine i.v. was started at a rate of 10 μg/kg·min and stepwise increased with 10 μg/kg·min every two minutes until the maximum dosage of 40 μg/kg·min was reached. It has been shown previously that dobutamine in this dosage not only stimulates contractility and ejection velocity of blood across the aortic valve, but also induces maximum hyperemia [12].

At maximum adrenergic stimulation, the pressure guide wire was pulled back again in a similar way as during maximum hyperemia by adenosine. The difference between the root and the arch (P_{ao}-P_{root}) indicates presence of a Venturi pressure drop due to artificial valve induced high ejection velocities across the valve.

2.5. Data analysis and statistical analysis

When studying pressure gradients across the coronary ostium it should be kept in mind that this pressure gradient is proportional to aortic pressure during maximal coronary hyperemia. Therefore, gradients were normalized by taking changes in aortic pressure into account. It has been shown that such pressure measurements are highly reproducible [13].

The comparison of the groups was performed by the non-parametric Mann–Whitney test with no Gaussian distribution assumed. Data are expressed as mean with the interquartile range (IQR) and box-and-whisker plots are used for the representation of the perfusion pressure measurements. A *P*-value of 0.05 is considered statistically significant. Baseline patient data are expressed as mean $\pm$ S.D.

3. Results

3.1. Procedural results

Out of our 21 patients, seven patients had a BLP in position A (BLP_A), seven in position B (BLP_B), and seven had a bio-prosthesis (Bio). The preoperative baseline characteristics of these patients are mentioned in Table 1. Average diameter of the prostheses for the different groups was 23.6 mm, 22.9 mm, and 23.9 mm, respectively, for the BLP_A, BLP_B, and Bio.

Two patients refused angiographic follow-up (1 BLP_B and 1 Bio). The six-month follow-up catheterization with hemodynamic measurements could be performed without problems in all the remaining 19 patients.

3.2. Pressure measurements

The values of blood pressure and heart frequency during the catheterization are shown in Table 2. A slight overall decrease in mean aortic pressure was observed for all patients with increasing dosages of dobutamine (101 (23) mmHg–87 (25) mmHg, *P*=0.021). The heart frequency on the other hand increased from 77 (19) to 125 (25) beats per minute (*P*<0.0001) as expected.

The results of the coronary perfusion pressure measurements are presented in Fig. 2. Panels a and b describe the pressure gradients P_{root}-P_{cor} in resting conditions and during adenosine induced hyperemia. No severe proximal coronary or ostial disease was present in any of the groups. Panels c

Table 1
Preoperative patient characteristics[a]

Patients	21
Male/female	13/8
Age, years	63.7 $\pm$ 8.4
Risk factors	
Diabetes	3
Systemic hypertension	10
Smoking	5
Cardiac rhythm	
Sinus	19
Paced	1
Atrial fibrillation	1
Peak gradient, mmHg	90 $\pm$ 21
AVA, cm^2	0.87 $\pm$ 0.25
Medication	
Aspirin	8
Clopidogrel	1
Acenocoumarol	1
Bèta-blockers	9
Statins	8
ACE-inhibitors	7
Diuretics	10

[a]Values are mean $\pm$ S.D.; AVA, aortic valve area.

and d express the Venturi-related pressure drop (P_{ao}-P_{root}) under resting conditions and during sympathetic stimulation by dobutamine infusion. Although a small pressure drop is present at the level of the coronary ostium, no significant differences between the different valve orientations or between the different prostheses were observed.

4. Discussion

In this pilot-study in 21 patients undergoing aortic valve replacement, only a negligible influence of different orientations of the BLP on coronary perfusion pressure was found. Moreover, coronary perfusion pressure was not different between mechanical and biological prostheses.

In our protocol we differentiated between resting conditions, maximal pharmacological coronary hyperemia, and maximal adrenergic stimulation in combination with maximal coronary hyperemia (to mimic maximum exercise in true life). Therefore, we measured pressures in the coronary artery and in the aortic root simultaneously with the pressure in the aortic arch. We are not aware of another way to measure coronary perfusion pressures more accurately.

Recently it has been suggested in acute animal experiments that coronary blood flow is affected by the orienta-

Table 2
Physiologic data during the measurements[a]

	BLP_A		BLP_B		Bio		All	
	P_{ao} [mmHg]	HR	P_{ao} [mmHg]	HR	P_{ao} [mmHg]	HR	P_{ao} [mmHg]	HR
Rest	97 (25)	78 (26)	100 (19)	79 (23)	107 (45)	76 (17)	101 (23)	77 (19)
Adeno	89 (29)	84 (28)	92 (18)	89 (23)	100 (34)	84 (21)	94 (25)	85 (24)
10 dobu	99 (9)	77 (21)	95 (15)	83 (27)	110 (14)	78 (11)	100 (17)	79 (19)
20 dobu	100 (7)	90 (64)	94 (21)	104 (24)	102 (38)	95 (27)	99 (21)	96 (34)
30 dobu	95 (17)	106 (50)	85 (24)	122 (24)	88 (14)	110 (27)	90 (16)	112 (34)
40 dobu	98 (24)	124 (39)	82 (27)	129 (22)	80 (16)	124 (33)	87 (25)	125 (25)

[a]Values are mean (IQR); BLP_A and B, bi-leaflet prosthesis orientation A and B; P_{ao}, aortic pressure; HR, heart rate; adeno, adenosine administration iv; dobu, dobutamine administration iv.
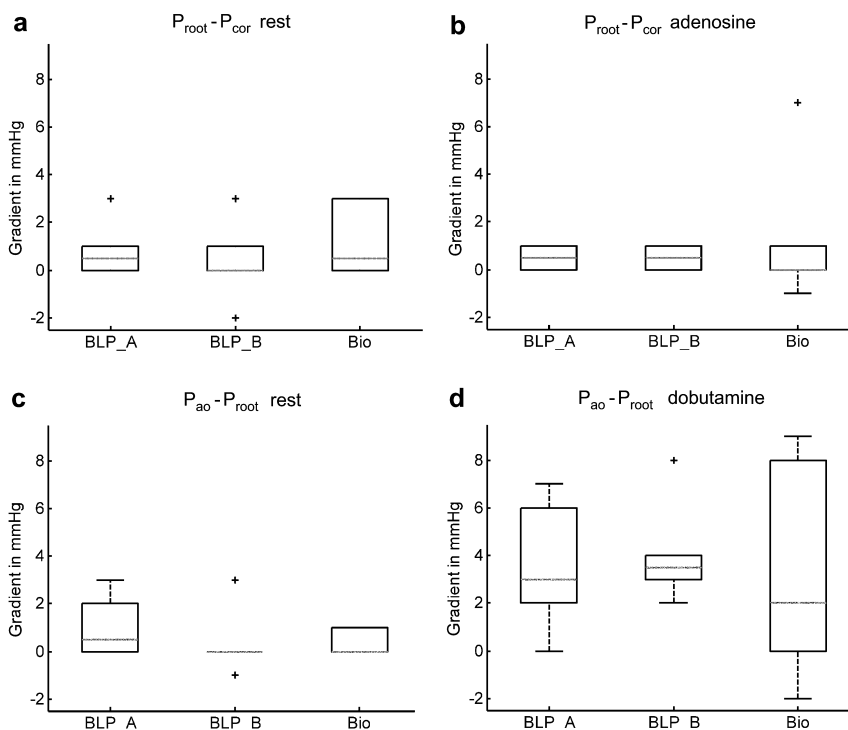
Fig. 2. Box-and-whisker plots for the pressure gradients representing ostial abnormalities (P_{root}-P_{cor}; iatrogenic or atherosclerotic) during resting conditions and during adenosine induced hyperemia (panel a and b). Box-and-whisker plots for the pressure gradients representing the velocity induced Venturi effect (P_{ao}-P_{root}) during resting conditions and during dobutamine induced adrenergic stimulus (panel c and d). BLP_A and BLP_B represent bi-leaflet prosthesis in orientation A and B; Bio represents bio-prosthesis.

tion of a mechanical valve substitute with respect to the origin of the coronary arteries. In these experiments higher coronary flow rates were observed in one orientation of mechanical valves [5]. This specific orientation, comparable with the orthotopic orientation A in our study, was defined as 'optimal' in previous studies of Kleine et al. with respect to hemodynamic parameters measured perioperatively [6, 14, 15]. It was hypothesized from these studies that differences in aortic root turbulence could explain the differences in coronary blood flow.

Coronary blood flow is regulated, depending on oxygen demand and by a complex interaction of neural and humoral responses affecting myocardial resistance. In the perioperative setting this regulatory mechanism is disturbed, among others by the administration of cardioplegia which induces a decrease in coronary artery resistance and blunts autoregulation.

As we performed our measurements six months after successful AVR and not only under resting conditions but also during maximum hyperemia and adrenergic stimulation, we believe that our results are representative for the physiological situation after valve surgery. Autoregulation had been restored at that time and the testing protocol was representative for maximum exercise in true life. We did not find any differences in perfusion pressure for the two orientations of the BLP neither for the bio-prostheses. Additional information on proximal or ostial coronary disease was obtained by the pressure sensor pullback recording during adenosine infusion [7].

Assuming that a Venturi induced pressure drop could influence coronary blood flow, it is expected that these effects would be most pronounced during high cardiac output, i.e. during adrenergic stimulation. During our experiments we administered dobutamine in a high dosage simulating exercise by stimulating contractility and ejection velocity of blood across the aortic valve. Next, a pressure sensor pullback recording was performed and only slight increases in pressure gradients were found between the aortic arch and the aortic root (P_{ao}-P_{root}) compared to resting conditions. These pressure gradients were so small that any influence on coronary perfusion pressure and, therefore, coronary blood flow was clinically irrelevant. In this respect, it should be realized that in normal hearts, maximum perfusion should decrease by at least 25% to result in inducible ischemia [8], a decrease not achieved at all in our patients.

4.1. Limitations

In this study we did not measure transvalvular pressure drop and the accompanying intra-myocardial compressive forces or microvascular resistance. To do so, simultaneous intra-ventricular pressure measurement would also have been mandatory, which for obvious reasons could not be performed. Furthermore, because accurate absolute flow measurement in coronary arteries is not possible in conscious humans neither invasively or non-invasively with MRI, we used coronary perfusion pressure as a surrogate of flow. This is justified because at maximum hyperemia resistance in the coronary circulation is minimal and constant and blood flow is directly proportional to perfusion pressure [7–9].

Finally, the number of patients in our study was small, but since the protocol was extensive we consider the number of patients in this pathophysiologic study sufficient, especially since the pressure differences we observed were small and clinically irrelevant.

5. Conclusion

In this study in 21 patients undergoing aortic valve replacement, only small non-significant differences in myocardial perfusion pressure were found between different orientations of a bi-leaflet prosthesis or between bi-leaflet prostheses and bio-prostheses.

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