Coronary Blood Flow in Patients With Severe Aortic Stenosis Before and After Transcatheter Aortic Valve Implantation

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Patients with severe aortic stenosis and no obstructed coronary arteries are reported to have reduced coronary flow. Doppler evaluation of proximal coronary flow is feasible using transesophageal echocardiography. The present study aimed to assess the change in coronary flow in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation (TAVI). The left main coronary artery was visualized using transesophageal echocardiography in 90 patients undergoing TAVI using the Edwards SAPIEN valve. The peak systolic and diastolic velocities of the coronary flow and the time-velocity integral were obtained before and after TAVI using pulse-wave Doppler. Mean aortic gradients decreased from 47.1 ± 15.7 mm Hg before TAVI to 3.6 ± 2.6 mm Hg after TAVI ($p < 0.001$). The aortic valve area increased from 0.58 ± 0.17 to 1.99 ± 0.35 cm^2 ($p < 0.001$). The cardiac output increased from 3.4 ± 1.1 to 3.8 ± 1.0 L/min ($p < 0.001$). Left ventricular end-diastolic pressure (LVEDP) decreased from 19.8 ± 5.4 to 17.3 ± 4.1 mm Hg ($p < 0.001$). The following coronary flow parameters increased significantly after TAVI: peak systolic velocity 24.2 ± 9.3 to 30.5 ± 14.9 cm/s ($p < 0.001$), peak diastolic velocity 49.8 ± 16.9 to 53.7 ± 22.3 cm/s ($p = 0.04$), total velocity-time integral 26.7 ± 10.5 to 29.7 ± 14.1 cm ($p = 0.002$), and systolic velocity-time integral 6.1 ± 3.7 to 7.7 ± 5.0 cm ($p = 0.001$). Diastolic time-velocity integral increased from 20.6 ± 8.7 to 22.0 ± 10.1 cm ($p = 0.04$). Total velocity-time integral increased >10% in 43 patients (47.2%). Pearson's correlation coefficient revealed the change in LVEDP as the best correlate of change in coronary flow ($R = -0.41$, $p = 0.003$). In conclusion, TAVI resulted in a significant increase in coronary flow. The change in coronary flow was associated mostly with a decrease in LVEDP. **(Am J Cardiol 2014;114:1264−1268)**

Even in the absence of obstructive epicardial coronary artery disease, coronary flow reserve has been found to be impaired in patients with severe aortic stenosis.[1] A number of studies have reported an improvement in this measurement after successful surgical aortic valve replacement. This improvement was detected by a change in coronary blood flow in response to adenosine or dipyridamole administration by means of thermodilution techniques[2] or by transthoracic echocardiography.[3,4] In patients with severe aortic stenosis, coronary blood flow has been shown to improve after aortic valve replacement by means of an intraoperative Doppler probe or by magnetic resonance imaging.[5] Coronary flow can also be assessed during transesophageal echocardiography (TEE), with which Doppler techniques allow detection of flow within proximal coronary arteries.[6,7] Its accuracy in estimating coronary blood flow velocity has been validated with Doppler wire measurement during cardiac catheterization.[8] We recently reported a pilot study in which we demonstrated a significant increase in coronary flow using pulse-wave Doppler during TEE after transcatheter aortic valve implantation (TAVI).[9] In the present report, we seek to confirm these observations in a larger patient cohort and to describe the clinical, echocardiographic, and hemodynamic factors associated with the changes in coronary flow.

Methods

We analyzed 154 consecutive patients with symptomatic severe aortic stenosis who underwent either transapical or transfemoral TAVI using the Edwards SAPIEN valve (Edwards Lifesciences, Irvine, California) from July 2008 to July 2010. Of these, 64 (41.5%) were excluded because of previous coronary artery bypass graft surgery (n = 44), poor image quality (n = 14), procedural failure or the patient was too unstable to obtain coronary flow (n = 4), and failure to obtain a TEE (n = 2). Of the 90 remaining patients, 60 (66.6%) underwent transfemoral TAVI and 30 (33.3%) transapical TAVI using the Edwards SAPIEN valve. Satisfactory imaging of the left main coronary artery was obtained before and after valve implantation.

For transfemoral TAVI, the femoral artery was accessed percutaneously and was closed using 2 Perclose ProGlide vascular suture-mediated closure devices (Abbott Vascular

Division of Cardiology, MedStar Washington Hospital Center, Washington, DC. Manuscript received May 4, 2014; revised manuscript received and accepted July 16, 2014.

See page 1267 for disclosure information.

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0002-9149/14/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2014.07.054

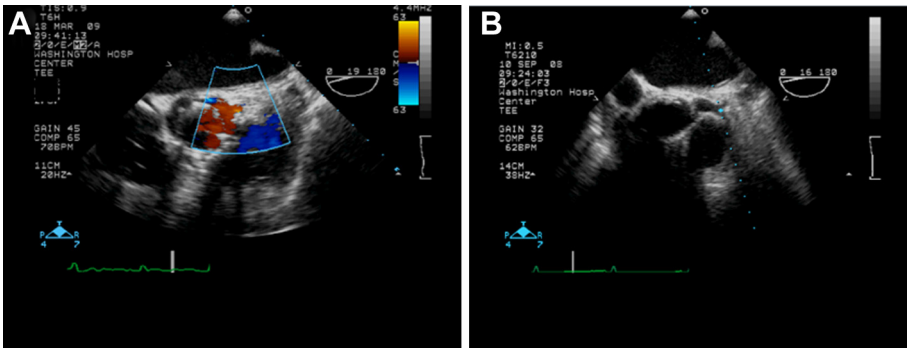

Figure 1. *(A)* Pulse-wave Doppler sample positioned over the portion of the left main coronary artery *(B)*.

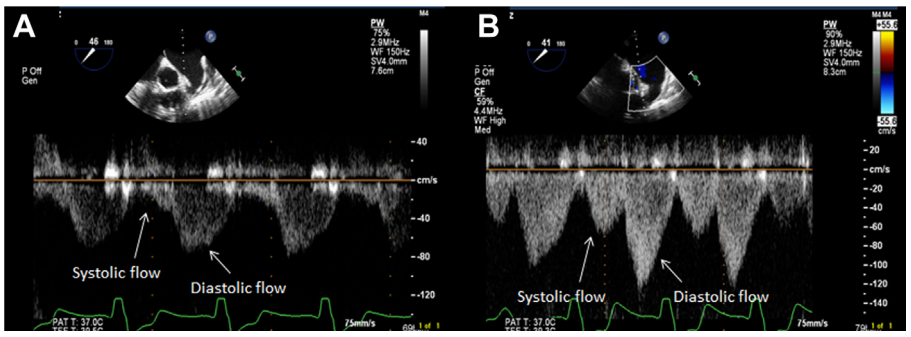

Figure 2. *(A)* Coronary flow before TAVI and *(B)* coronary flow after TAVI.

Devices, Redwood City, California). The access site was enlarged with serial dilators until the appropriate sheath size (22Fr or 24Fr) was reached. For transapical TAVI, a left minithoracotomy was performed, and 2 intramural pledget purse-string apical sutures were placed before apical puncture.

For anticoagulation, heparin was used to maintain an activated clotting time >250 seconds. A Swan-Ganz catheter and temporary pacemaker were placed. Cardiac output was measured by thermodilution technique before valve deployment. In all procedures, aortic valvuloplasty during rapid pacing was performed over an Amplatz Super Stiff guidewire (Boston Scientific, Natick, Massachusetts). Next, the bioprosthetic valve was advanced over the same wire and deployed under rapid pacing with fluoroscopic and TEE guidance.

All patients underwent TEE using a 5-MHz probe (Sonos System 5500 or iE33; Philips, Andover, Massachusetts). The transducer was positioned in the upper esophagus so that a short-axis image of the aortic valve was obtained. Subsequently, the probe was withdrawn cranially until the left main coronary artery was seen along the bifurcation site. The left main coronary artery was localized in the transverse plane with color flow mapping. A "zoomed" image of the area of interest was obtained, and the TEE shaft was rotated to minimize the angle between the Doppler beam and the direction of the coronary blood flow (Figure 1). A pulse-wave Doppler sample volume 5 mm in width was positioned over the portion of the left main coronary artery best aligned with ultrasound beam. The Doppler image was viewed using a 250- or 500-kHz filter, at a gain at which noise began to appear. Care was taken to position the pulse-wave Doppler sample in the same location before and after valve deployment.

Coronary flow was measured at the end of the procedure and after the patient had returned to a steady state so as to reduce, in so far as possible, the effect of reactive hyperemia resulting from any myocardial ischemia entailed by the procedure.

The following Doppler flow parameters were measured: peak systolic velocity (cm/s), peak diastolic velocity (cm/s), systolic velocity-time integral (cm), diastolic velocity-time integral (cm), and total velocity-time integral (cm) (Figure 2). The final values of flow-velocity and time-velocity integrals represent an average of 3 cardiac cycles in patients in sinus rhythm and 5 cycles in patients in atrial fibrillation.

Statistical analysis was performed using SAS, version 9.1 (SAS Institute, Cary, North Carolina). Continuous variables are expressed as mean ± SD or median (twenty-fifth to seventy-fifth interquartile range), as appropriate, according to the variable distribution. Categorical variables are expressed as percentages. The Student *t* test was used to compare continuous variables, and the chi-square test or Fisher's exact test was used to compare categorical variables. Paired data were assessed with the paired Student *t* test or Wilcoxon signed rank test as appropriate. The significance level was set at $p < 0.05$. Correlation between the change in coronary flow and hemodynamic parameter was carried out using Spearman's coefficient.

Results

Hemodynamic measurements at baseline and after valve implantation are listed in Table 1. There were expected hemodynamic changes resulting from the relief of the aortic

Table 1
Hemodynamic and echocardiographic data before and after valve implantation

Variable	Before TAVI (n = 90)	After TAVI (n = 90)	p Value
Systolic blood pressure (mm Hg)	119.6 ± 20.3	134.2 ± 27.1	<0.001
Diastolic blood pressure (mm Hg)	54.7 ± 12.6	55.3 ± 13.1	0.76
Aortic valve area (cm^2)	0.58 ± 0.17	1.99 ± 0.35	<0.001
Mean gradient across aortic valve (mm Hg)	47.1 ± 15.7	3.6 ± 2.6	<0.001
Cardiac output (l/min)	3.4 ± 1.1	3.8 ± 1.0	<0.001
Pulmonary artery systolic pressure (mm Hg)	51.7 ± 16.2	46.4 ± 14.5	<0.001
Left ventricular systolic pressure (mm Hg)	165.0 ± 26.0	138.8 ± 27.5	<0.001
Left ventricular end diastolic pressure (mm Hg)	19.8 ± 5.4	17.3 ± 4.1	<0.001

TAVI = transcatheter aortic valve implantation.

Table 2
Coronary flow parameter before and after valve implantation

Variable	Before TAVI (n = 90)	After TAVI (n = 90)	p Value
Peak systolic velocity (cm/s)	24.2 ± 9.3	30.5 ± 14.9	<0.001
Peak diastolic velocity (cm/s)	49.8 ± 16.9	53.7 ± 22.3	0.04
Total velocity-time integral (cm)	26.7 ± 10.5	29.7 ± 14.1	0.002
Systolic velocity time integral (cm)	6.1 ± 3.7	7.7 ± 5.0	0.001
Diastolic time velocity integral (cm)	20.6 ± 8.7	22.0 ± 10.1	0.04

TAVI = transcatheter aortic valve implantation.

Table 3
Patients' baseline characteristics according to coronary flow

Variable	Coronary Flow Increase ≥10% (n = 43)	Coronary Flow <10% (n = 47)	p Value
Age (years)	84.9 ± 5.0	86.5 ± 5.1	0.14
Men	15 (34.8%)	18 (38.2%)	0.73
Society of Thoracic Surgeons score	11.5 ± 3.1	11.9 ± 3.9	0.58
Logistic EuroSCORE	34.6 ± 22.0	42.1 ± 24.8	0.17
Hypertension	39 (90.7%)	45 (95.7%)	0.60
Diabetes mellitus	19 (44.1%)	14 (29.7%)	0.12
Renal failure	29 (67.4%)	28 (59.5%)	0.38
Atrial fibrillation	7 (16.2%)	21 (44.6%)	0.004
Prior myocardial infarction	6 (13.9%)	7 (14.2%)	0.93
Ejection fraction (%)	55.0 ± 12.0	54.9 ± 13.4	0.98

stenosis. The aortic valve area tripled from 0.58 to 1.99 cm^2 with a decrease in mean aortic systolic gradient, left ventricular end-diastolic pressure (LVEDP), and pulmonary systolic pressure and an increase in the cardiac output.

The following left main Doppler flow measurements increased significantly after TAVI (Table 2): peak systolic velocity 24.2 ± 9.3 to 30.5 ± 14.9 cm/s (p <0.001), peak diastolic velocity 49.8 ± 16.9 to 53.7 ± 22.3 cm/s (p = 0.04), total velocity-time integral 26.7 ± 10.5 to 29.7 ± 14.1 cm (p = 0.002), and systolic velocity-time integral 6.1 ± 3.7 to 7.7 ± 5.0 cm (p = 0.001). Diastolic time-velocity integral increased from 20.6 ± 8.7 to 22.0 ± 10.1 cm (p = 0.04).

Characteristics of the 43 patients (47.7%) in whom the total left main coronary flow velocity-time integral increased by ≥10% are compared in Tables 3 and 4 with those in whom such an increase did not occur. In terms of the baseline characteristics (Table 3), only the frequency of atrial fibrillation was significantly different. It was more frequent (p = 0.004) in those in whom the flow-velocity integral failed to increase. Of the baseline hemodynamic and procedural variables (Table 4), the only significant difference was a higher LVEDP in those whose flow rate increased after TAVI (p = 0.004).

Multivariate adjustment by means of Pearson's correlation coefficient (Table 5) revealed that a lower−LVEDP pulse TAVI was the only variable significantly associated with an increase in coronary flow (R = −0.41, p = 0.003).

Discussion

Our observations indicate that after TAVI, there is a significant increase in coronary flow in the left main coronary artery as measured by increases in peak systolic and diastolic velocities and by total velocity-time integral. Our data are consistent with previous studies that have demonstrated similar results after surgical aortic valve replacement. Bakhtiary et al[5] used magnetic resonance imaging to show a significant increase in coronary flow in both the left and right coronary arteries. Furthermore, Hildick-Smith et al[3] found an increase in peak systolic velocity but not in diastolic velocity after surgical aortic valve replacement using Doppler echocardiography in the left anterior coronary artery.

This increase in coronary flow after aortic valve replacement has not been fully explained. It can be suggested that TAVI immediately improves coronary perfusion pressure and increases coronary flow velocity by at least 2 potential mechanisms: (1) the driving pressure across the coronary bed is increased by an increase in aortic diastolic pressure and/or a decrease in left ventricular diastolic pressure and (2) the high velocity ejection of blood into the proximal aorta is reduced or eliminated reducing any existing Venturi effect on pressures in the proximal coronary arteries. Our study found the first mechanism with the reduction of LVEDP the best associate with the increase in coronary flow. Other studies report that impaired coronary flow in severe aortic stenosis has been related to aortic valve area and peak transvalvular gradients, rather than the degree of left ventricular hypertrophy.[10,11]

In keeping with this notion are the previously reported observations that normalization of coronary artery flow after aortic valve replacement was more pronounced for stentless valves compared with stented valves. It is reasonable that the lower transvalvular gradients and lesser turbulence in the aortic sinuses found in the stentless variety account for this difference.[2]

Improvement in left ventricular performance after aortic valve replacement may also contribute to the acute increase in coronary flow after TAVI. Garcia et al[12] reported that the

Table 4
Patients' hemodynamic and procedural characteristics according to coronary flow

Variable	Coronary Flow Increase ≥10% (n = 43)	Coronary Flow Increase <10% (n = 47)	p Value
Valve size 23 mm vs. 26 mm	31 (72.1%) vs. 12 (27.9%)	28 (59.6%) vs. 19 (40.4%)	0.21
Transfemoral vs. transapical	29 (67.5%) vs. 14 (32.5%)	31 (65.9%) vs. 16 (34.1%)	0.88
Conscious sedation	20 (46.5%)	27 (57.4%)	0.35
Mean gradient before (mm Hg)	44.8 ± 12.5	48.9 ± 17.6	0.21
Aortic valve area before (cm^2)	0.58 ± 0.16	0.57 ± 0.19	0.85
Δ Systolic blood pressure (mm Hg)	15.6 ± 29.5	15.4 ± 31.2	0.98
Δ Diastolic blood pressure (mm Hg)	1.0 ± 18.1	1.3 ± 16.1	0.54
Δ Pulmonary artery systolic pressure (mm Hg)	−4.6 ± 12.4	−5.5 ± 12.1	0.99
Δ Left ventricular systolic pressure (mm Hg)	−23.6 ± 34.6	−30.1 ± 47.4	0.57
Δ Left ventricular end diastolic pressure (mm Hg)	5.2 ± 4.1	1.5 ± 4.2	0.004
Δ Cardiac output (l/min)	0.51 ± 0.89	0.26 ± 1.06	0.23

Δ = after − before.

Table 5
Correlates associated with change in coronary flow

Variable	R	p Value
Δ Pulmonary artery systolic pressure (mm Hg)	0.04	0.68
Δ Pulmonary artery diastolic pressure (mm Hg)	−0.04	0.71
Δ Systolic blood pressure (mm Hg)	0.01	0.90
Δ Diastolic blood pressure (mm Hg)	0.06	0.56
Δ Left ventricular end diastolic pressure (mm Hg)	−0.41	0.003
Δ Cardiac output (l/min)	0.10	0.32

Δ = after − before.

effective orifice area of the aortic valve is one of the main physiological determinates of coronary flow in patients with aortic stenosis. Coronary flow is markedly reduced when aortic stenosis becomes severe (effective orifice area <1 cm^2). Moreover, improved left ventricular performance accompanied by a significant reduction in LVEDP may also enhance coronary flow. It is known that high LVEDP directly impedes myocardial perfusion.[13] In our study, the post-TAVI decrease in LVEDP was an independent determinant of an increase in coronary flow (Table 4).

The acute effects of coronary flow on relief of aortic stenosis by valve replacement are complex. We and others[2–5] have demonstrated an acute improvement in the flow rate presumably by an improvement in left ventricular performance and in flow dynamics in the aortic root. While perfusion pressure is increased, relief of aortic stenosis should also improve left ventricular performance and decrease wall stress, thereby reducing myocardial oxygen demand.[14] Thus, because, under physiologic conditions, coronary flow tracks myocardial oxygen demand closely through modulation of the tone of the coronary resistance vessels, a decrease in coronary flow could be expected. It remains unclear what role the increase in coronary perfusion pressure subsequent to TAVI plays. The "autoregulatory" relation between flow and myocardial oxygen demand is preserved across a broad range of perfusion pressures.

The effect of relief of aortic stenosis on the tone of coronary resistance vessels has been assessed by the measurement of "coronary flow reserve." The difference between coronary flow in the basal state and when the resistance vessels are maximally dilated is referred to as "coronary flow reserve." The reserve is greater if myocardial oxygen demand decreases, and thus, the need for basal flow is diminished. The reserve is smaller when the maximum response to vasodilator drugs is restricted. Thus, in this study, we did not assess coronary reserve and consequently examine the initial impact of TAVI on nutritional coronary flow. Previous studies[2–4] report improvement in coronary flow reserve after surgical aortic valve replacement. The mechanism for improved coronary flow reserve late in the postoperative period may have different pathophysiologic mechanisms from those observed acutely as in our study. Coronary flow reserve is known to be impaired in the presence of left ventricular hypertrophy,[15] and its improvement over the months after relief of severe aortic stenosis correlates with regression in left ventricular mass.[3] Thus, regression in left ventricular mass after successful aortic valve replacement appears to reduce myocardial oxygen demand after valve replacement. The acute increase in flow velocity and flow in our patients and in the studies of others could arguably result from changes in perfusion pressure through the mechanisms cited previously, but this remains unclear. This conclusion is supported by the work of Bakhtiary et al[16] who demonstrated a significant increase in the coronary flow rate after aortic valve replacement, a decrease in coronary perfusion rates at 6 months postoperatively after regression of left ventricular hypertrophy, and a decrease of oxygen consumption. Similarly, Rajappan et al[17] reported significant reduction in myocardial blood flow at rest, 1 year after aortic valve replacement.

There are some limitations to this study. Adequate TEE imaging was not possible in all subjects. Importantly, coronary velocity (and its derivative velocity-time interval) was used in our study as a surrogate for coronary flow. We assumed that the diameter of the left coronary artery would not change after aortic valve replacement. We did not measure coronary flow reserve and do not have follow-up data on coronary flow.

Disclosures

The authors have no conflicts of interest to disclose.

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