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Accuracy of Doppler-echocardiographic parameters for the detection of aortic bileaflet mechanical prosthetic valve dysfunction

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Aims *In vitro* and *in vivo* studies were performed to evaluate the diagnostic accuracy of the different Doppler-echocardiographic parameters proposed in the American Society of Echocardiography guidelines to identify dysfunction of bileaflet mechanical valves (BMV) in the aortic position.

Methods and results Two models of BMV (St Jude HP, MCRI On-X) of different sizes (21;23;25;27 mm) were tested *in vitro* under a wide range of cardiac outputs (3–7 L/min). The motion of one or both leaflets was restricted to induce a mild (25% restriction in total valve orifice area) and moderate-to-severe (50% restriction in total valve area). Doppler-echocardiographic parameters of valve function were also measured in 17 patients with BMV of whom 4 had valve dysfunction confirmed by cinefluoroscopy. The specificity of all the parameters was high (*in vitro*: 83–100%; *in vivo*: 69–100%), but the sensitivity was low (range: 0–83% and 25–100%, respectively). A higher cut-off value for the ratio of peak left ventricular outflow tract velocity to peak aortic velocity or Doppler velocity index (DVI) (<0.35 instead of 0.3 or 0.25) improved the sensitivity ($>90\%$) for the detection of moderate-to-severe dysfunction but remained low for mild dysfunction (50%). Furthermore, a difference of normal reference effective orifice area (EOA) minus measured EOA (EOA-D) >1 standard deviation identified mild and moderate-to-severe dysfunction with sensitivity of 61 and 100%, respectively.

Conclusion The Doppler-echocardiographic parameters and criteria proposed in the guidelines lack sensitivity for the detection of BMV dysfunction. The utilization of a DVI < 0.35 or an EOA-D > 1 SD improved the sensitivity ($>90\%$) for the detection of moderate-to-severe dysfunction, but the sensitivity remained suboptimal ($<65\%$) for detection of mild dysfunction.

Keywords Doppler echocardiography • Prosthetic heart valve • Aortic stenosis

Introduction

Despite the marked improvements in prosthetic valve design and surgical procedures over the past decades, the outcome of patients undergoing valve replacement is often impaired by the occurrence of valve dysfunction. Prosthetic valve stenosis or regurgitation may indeed occur as a result of acute (thrombosis), subacute (endocarditis), or chronic (pannus, calcific degeneration of bioprosthetic leaflets) processes.[1,2] The average rate of prosthetic valve dysfunction ranges between 10 and 30% at 10 years.[3] Early detection of valve dysfunction is thus crucial to successfully manage these complications.[4] Owing to its versatile, non-invasive, radiation-free, and low-cost nature, Doppler-echocardiography is undoubtedly the method of choice to identify and quantitate prosthetic valve dysfunction. In 2009, Zoghbi *et al.*[5] have published the first comprehensive American Society of Echocardiography (ASE) guidelines for Doppler-echocardiographic evaluation of prosthetic valve function. Several parameters and criteria can be used to assess the presence and severity of prosthetic valve dysfunction. Quantitative parameters of prosthetic valve stenosis include transprosthetic

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flow velocity and pressure gradients, valve effective orifice area (EOA), and Doppler velocity index (DVI).

The objective of this study was to evaluate the diagnostic performance of the various parameters and criteria proposed in the ASE guidelines to identify prosthetic valve stenosis. For this purpose, we performed an *in vitro* study and a retrospective clinical study.

Methods

In vitro study

Two models of bileaflet mechanical valves (BMV) of different sizes were tested under a wide range of flow rates and three valve function situations: normal function, mild dysfunction, and moderate-to-severe dysfunction.

Model

Bileaflet mechanical valves were mounted in an *in vitro* mock flow model previously described and validated[6,7] (*Figure 1*). Briefly, the model is mainly made up of a reservoir, a compliant aortic chamber, and a valve resistance. The flow was provided by a computer-controlled DC motor coupled to a gear pump (Vi-CORR, Viking Pump). The left ventricular outflow tract and the aorta were both circular (in cross-section) and rigid and their size was adjusted to be equal to the nominal size of the BMV under evaluation. The compliant chamber was located immediately downstream of the proximal rigid aorta. The fluid was composed of two-third water and one-third of glycerol so that its density (1080 kg/m^3) and viscosity (3.5 cP) were similar to those of blood under high shear rate conditions. The ventricular and aortic pressures were measured with Millar catheters (model MPC 500, accuracy 0.5% full scale) under a sampling frequency of 1000 Hz. For each experiment, 10 cycles were recorded and the average was used to calculate the hemodynamic parameters.

Test protocol

Doppler echocardiographic measurements were performed on seven BMV: four different sizes (21, 23, 25, and 27 mm) of St Jude HP aortic valves and three different sizes (21, 23, and 25 mm) of MCRI On-X aortic valves. The dysfunction of the BMV was induced by restricting the motion of one or both leaflets (*Figure 2*) to represent the most possible prosthetic valve dysfunction scenarios. For the dysfunctional BMVs cases, the normal valve opening area was reduced by 25 and 50% to represent mild and moderate-to-severe valve dysfunction, respectively. These two grades of dysfunction were achieved by restricting the opening angle of one leaflet by 50 and 100%, respectively (*Figure 2*). We also tested additional scenarios with impairment of the opening of both leaflets: (i) 25% restriction in the opening angle of both leaflets (i.e. 25% reduction in valve opening area: mild dysfunction); (ii) 50% restriction in the opening angle of both leaflets (i.e. 50% reduction in valve opening area: moderate-to severe dysfunction).

All BMVs were tested under five different transvalvular flow rates 3–7 L/min, corresponding to stroke volumes of 30–120 mL at a fixed heart rate of 70 bpm [left ventricle (LV) ejection time: 0.3 s]. Aortic systolic and diastolic pressures were maintained under normal conditions: 120 and 80 mmHg, respectively.

Doppler echocardiography

Doppler echocardiographic measurements were performed with a Sonos 5500 (Philips Medical Systems/Agilent Technologies, Andover, MA, USA) ultrasound system and a 2.25 MHz probe using the same principles and methods as in the clinical setting. Peak transprosthetic velocity was obtained by continuous wave Doppler. A particular attention was paid to align the Doppler beam with the jet direction (as it may change with the degree of valve dysfunction).[7,8] The LV outflow tract (LVOT) velocity was measured by pulsed-wave Doppler approximately 0.5 cm upstream from the prosthetic valve. The measurements were performed over three cycles and averaged. Mean transprosthetic gradient was determined with the use of the simplified Bernoulli equation, and the valve EOA with the use of the continuity equation. We also calculated the difference between the normal reference EOA and the measured EOA (EOA-D). The reference EOA values were obtained for the different sizes of SJHP and On-X valves from data published in the literature.[4] The DVI was calculated as the ratio of peak LVOT velocity to peak transprosthetic velocity as recommended

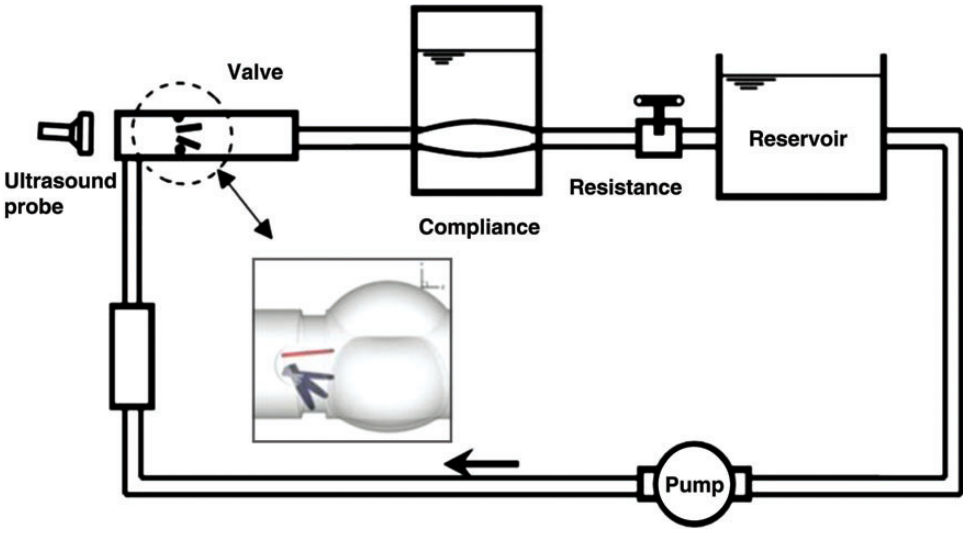

Figure 1 Sketch of the custom-made cardiac simulator.

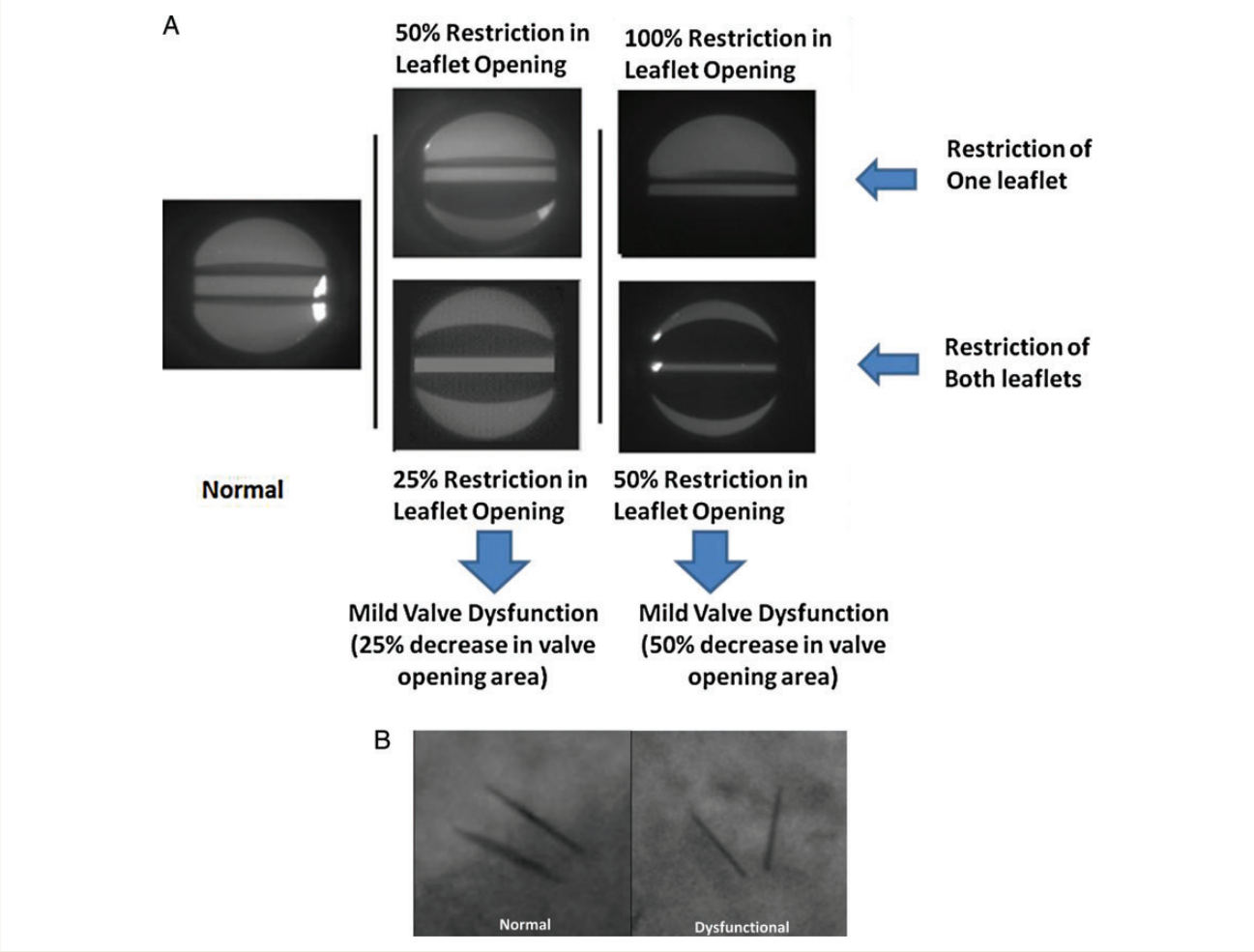

Figure 2 Images of BMV with normal and abnormal functions. This figure shows the maximum opening during ejection for normal and dysfunctional BMV: (*A*) *In vitro* study: high-speed camera images. (*B*) *In vivo* study: cinefluoroscopic images.

in the guidelines. To evaluate the inter-observer variability of the measurement of these parameters, all these measurements were repeated by two blinded observers.

In vivo study

Patient population

From March 2005 to July 2010, 24 patients underwent both a Doppler-echocardiographic exam and a valve cinefluoroscopy within a period of 2 weeks at the Quebec Heart and Lung Institute. These patients were referred to cinefluoroscopy because of suspicion of valve dysfunction at the transthoracic Doppler-echocardiographic exam. Seven patients with normally functioning prosthetic valve at cinefluoroscopy were excluded because Doppler-echocardiographic data were incomplete. The final cohort thus consisted of 17 patients: 13 with normal valve function and 4 with valve dysfunction confirmed by the visualization of abnormal motion of one or two leaflets on cinefluoroscopy. Doppler echocardiographic measurements were performed as recommended in the ASE guidelines.[5] The LVOT diameter was measured just proximal to the insertion of the prosthesis. The LVOT velocity was measured at 0.5–1 cm below the prosthetic valve sewing ring. Multi-window interrogation was used to obtain peak transprosthetic velocity.

Cinefluoroscopy was performed to obtain a tangential view (i.e. X-ray beam parallel to the plane of prosthetic valve ring) of the implanted BMV. For each patient, the maximum leaflet opening and closing angles were determined by averaging the values over three consecutive cardiac cycles.

Statistical analysis

Results are expressed as mean $\pm$ SD. Inter-observer variability was calculated as the absolute difference between the two observations divided by the mean of the observations and expressed as percent. One-way analysis of variance followed by a Tukey's *post hoc* test was used to compare the values of the Doppler-echocardiographic parameters among the three groups: no dysfunction, mild dysfunction, and moderate-to-severe valve dysfunction. The Doppler-echocardiographic parameters were compared between patients with and those without valve dysfunction using the unpaired Student's *t*-test.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

In vitro study

Inter-observer variability for peak LVOT velocity, peak transprosthetic velocity, mean gradient, and EOA was 1.8 ± 1.3, 2.4 ± 1.3, 2.9 ± 2.2, and 5.6 ± 4.4%, respectively.

Bileaflet mechanical valve dysfunction related to restricted motion of only one leaflet has been shown by Montorsi *et al.*[9] to be the most difficult to detect in clinical practice. We thus focused primarily on the presentation and analysis of the results obtained with this scenario. *Table 1* and *Figure 3* show the data of peak transprosthetic velocity, mean transprosthetic gradient,

Table 1 Results of the *in vitro* study: Doppler-echocardiographic parameters as a function of the degree of valve dysfunction caused by restriction of the motion of one valve leaflet

Parameter	Normal	Mild dysfunction	Moderate-to-severe dysfunction	*P*-value
Peak aortic jet velocity (m/s)	2.33 ± 0.58 (1.19–3.80)	2.72 ± 0.67 (1.73–4.06)	4.0 ± 0.93*§ (2.21–6.00)	<0.001
Mean pressure gradient (mmHg)	11 ± 5 (3–27)	16 ± 7 (6–34)	34 ± 16*§ (11–74)	<0.001
Doppler velocity index	0.52 ± 0.03 (0.45–0.60)	0.43 ± 0.03* (0.37–0.47)	0.29 ± 0.03*§ (0.24–0.34)	<0.001
Effective orifice area (cm^2)	2.23 ± 0.44 (1.51–3.11)	1.87 ± 0.34* (1.19–2.55)	1.33 ± 0.29*§ (0.77–1.90)	<0.001

Values represent the mean ± SD and ranges between parentheses.
*$P < 0.001$ vs. normal.
§$P < 0.001$ vs. mild dysfunction.

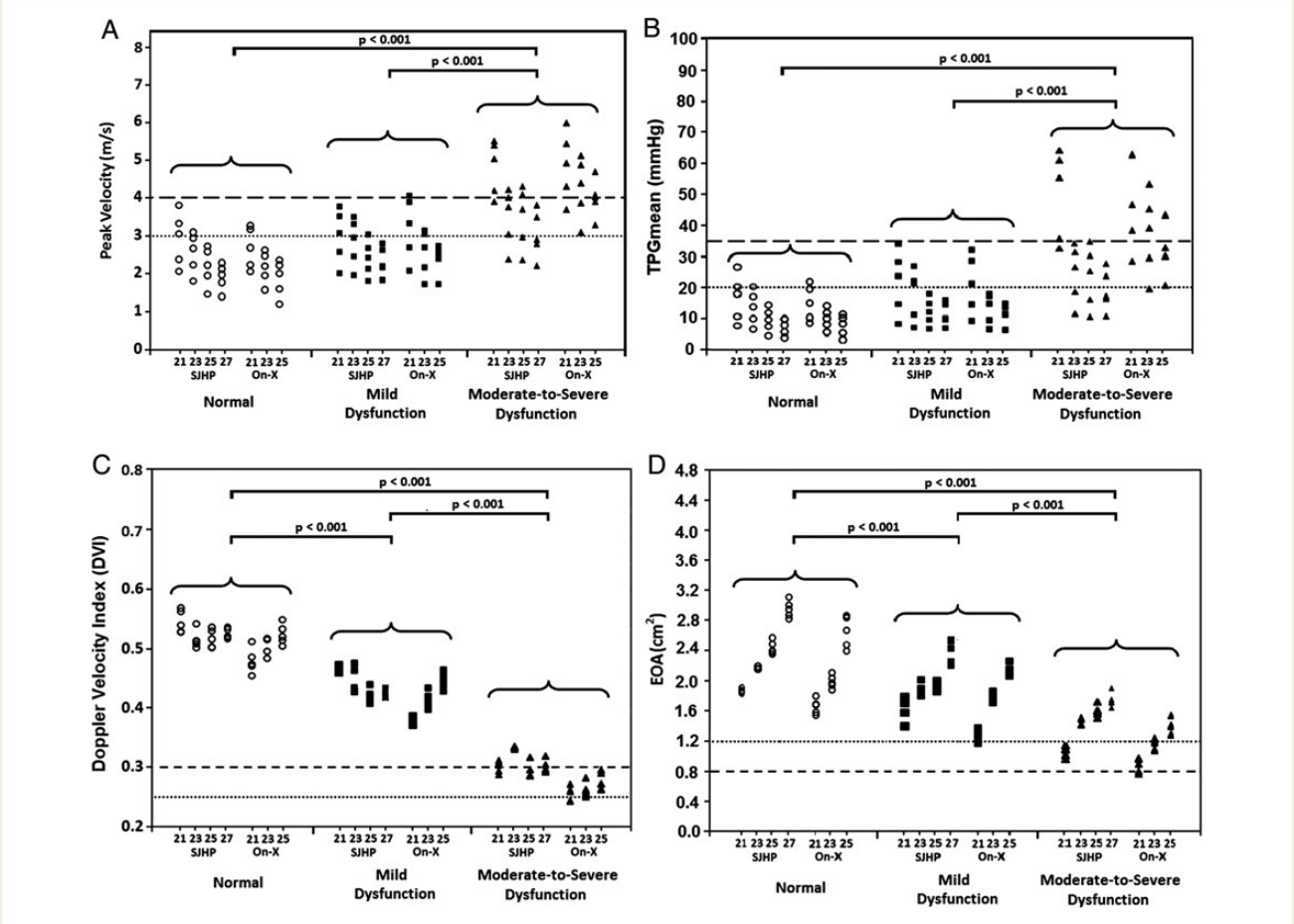

Figure 3 *In vitro* data of the Doppler-echocardiographic parameters according to the presence and severity of prosthetic valve dysfunction caused by restriction of the motion of one leaflet. This figure shows the distribution of the *in vitro* data of the Doppler-echocardiographic parameters as a function of the models and sizes of tested bileaflet mechanical valves and the degree (0, 50, 100%) of valve dysfunction induced by restricting the motion of only one valve leaflet. (*A*) Peak transprosthetic velocity; (*B*) mean transvalvular pressure gradient; (*C*) Doppler velocity index (DVI); and (*D*) effective orifice area (EOA). The dashed and dotted lines represent the cut-off values proposed in the ASE guidelines[5] and suggesting possible and significant stenosis, respectively. SJHP: St-Jude Hemodynamic Plus bileaflet valve; On-X: MCRI On-X bileaflet valve.

valve EOA, and DVI as a function of type and size of prosthetic valve and degree of dysfunction: 0, 50, and 100% restriction of the opening of one leaflet, corresponding to no, mild (25% restriction in total valve area), and moderate-to-severe valve (50% restriction in total valve area) dysfunction, respectively. The average values were significantly different between 100 vs. 50% and 0% dysfunction as well as between 50 vs. 0% for all these Doppler-echocardiographic parameters except for peak transprosthetic velocity and mean gradient (*Table 1* and *Figure 3*). However, as shown in *Figure 3*, there was a considerable overlap between the 0, 50, and 100% leaflet dysfunction categories for the peak transprosthetic velocity, mean gradient, and valve EOA (*Figure 3*). Less overlap was, however, observed for DVI. The ASE guidelines developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee have proposed cut-off values for each of these parameters to identify valve dysfunction. For example, according to these guidelines, a DVI ≤ 0.3 suggests possible stenosis, whereas values <0.25 suggest significant stenosis. Pibarot and Dumesnil[4] have proposed to use a higher value of DVI (<0.35) to identify valve stenosis. For this purpose, they also suggested comparing the measured EOA with the normal reference value of EOA for the type and size of implanted prosthesis; an EOA-D $>$ 1 standard deviation (SD), suggesting possible stenosis. The mean and SD values of normal EOAs were obtained from the data published in the literature.[4] *Table 2* shows the results of sensitivity and specificity of these different parameters and criteria for the detection of valve dysfunction. The specificity for the detection of 25% restriction in total valve area (i.e. mild valve dysfunction) was good in all cases ranging between 83 and 100%. However, the sensitivity was low, ranging between 3 and 61%. For the detection of 50% restriction in total valve area (i.e. moderate-to-severe valve dysfunction), the sensitivity and specificity were $>$80% for the three following criteria: peak transprosthetic velocity $\geq$3 m/s, DVI ≤ 0.35, and EOA-D $>$ 1 SD.

The experiments with restriction of opening of both leaflets provided similar results, in terms of performance of the different Doppler-echo parameters and sensitivity and specificity analysis, to those with restriction of only one leaflet. The data of these experiments (*Figure 4* and *Table 2*) suggest that a 25% restriction applied on each leaflet (i.e. 25%/25%) is equivalent, from a haemodynamic standpoint, to a 50% restriction of only one leaflet (i.e. 50%/0%); both situations indeed lead to a 25% reduction in total valve opening area (i.e. mild dysfunction). Likewise, a 50% restriction of both leaflets is equivalent to a 100% restriction of one leaflet (50% reduction in valve area: moderate-to-severe dysfunction).

In vivo study

Consistent with the results of the *in vitro* study, peak transprosthetic velocity was significantly higher and EOA and DVI were significantly lower in patients with dysfunctional valves compared with those with normally functioning valves (*Table 3*). There was no significant difference for TPG_{mean}, *in vivo*. However, some overlap was observed between normal vs. dysfunctional valves for all Doppler-echocardiographic parameters (*Figure 5*). As the *in vitro* study, the DVI appears to have the least overlap between the dysfunctional vs. normal valves.

Table 4 shows the results of sensitivity and specificity for the different Doppler-echocardiographic parameters and criteria. The specificity of these criteria ranged between 69 and 100%, whereas the sensitivity ranged between 25 and 100%. The sensitivity and specificity were $>$90% for the two following criteria: DVI $\leq$ 0.35 and EOA-D $>$ 1 SD.

Discussion

The main findings of this study are that: (i) the Doppler-echocardiographic parameters and criteria proposed in the ASE

Table 2 Results of the *in vitro* study: sensitivity and specificity of the different Doppler-echocardiographic parameters and criteria to detect valve dysfunction

Parameter	Diagnosis criteria for dysfunction	Detection of ≥mild dysfunction		Detection of moderate-to-severe dysfunction[a]	
		Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Peak aortic jet velocity	≥4 m/s	29 (23)	100	51 (46)	100
	≥3 m/s	57 (57)	83	83 (80)	83
Mean transprosthetic gradient	≥35 mmHg	19 (16)	100	31 (31)	100
	≥20 mmHg	49 (47)	89	77 (71)	89
Doppler velocity index	≤0.35	50 (50)	100	100 (100)	100
	≤0.3	34 (36)	100	71 (71)	100
	≤0.25	7 (0.0)	100	14 (0.0)	100
Effective orifice area	≤1.2 cm^2	21 (16)	100	43 (29)	100
	≤0.8 cm^2	3 (0.0)	100	6 (0.0)	100
EOA-D	>1SD	61 (61)	100	100 (100)	100

The table shows the results of sensitivity and specificity of the Doppler-echocardiographic parameters for the detection of prosthetic valve dysfunction induced by restriction of the motion of one leaflet. The values between brackets correspond to the values of sensitivity for the detection of valve dysfunction induced by restricting the motion of both valve leaflets. The results of specificity were identical in both types of dysfunction.
EOA-D, difference between normal EOA and measured EOA.
[a]Mild dysfunction excluded from this analysis.

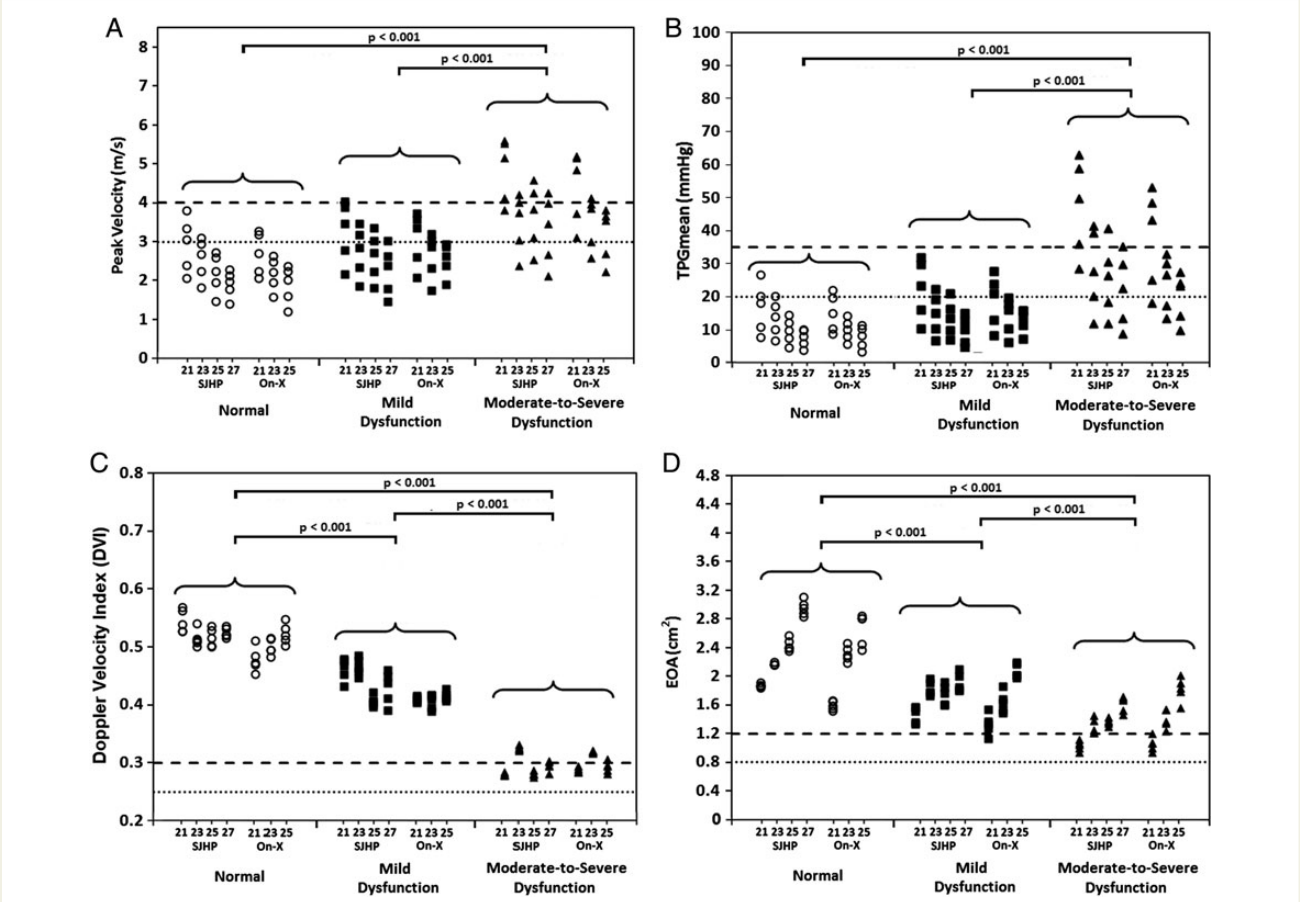

Figure 4 *In vitro* data of the Doppler-echocardiographic parameters according to the presence and severity of prosthetic valve dysfunction caused by restriction of the motion of both leaflets. This figure shows the distribution of the *in vitro* data of the Doppler-echocardiographic parameters as a function of the models and sizes of tested bileaflet mechanical valves and the degree (0, 50, 100%) of valve dysfunction induced by restricting the motion of both valve leaflets. (*A*) Peak transprosthetic velocity; (*B*) mean transvalvular pressure gradient; (*C*) Doppler velocity index (DVI); and (*D*) effective orifice area (EOA). The dashed and dotted lines represent the cut-off values proposed in the ASE guidelines[5] and suggesting possible and significant stenosis, respectively. SJHP: St-Jude Hemodynamic Plus bileaflet valve; On-X: MCRI On-X bileaflet valve.

guidelines[5] lack sensitivity for the detection of BMV dysfunction. (ii) The cut-off values (<0.25 or 0.3) proposed in the guidelines may be too low to identify valve dysfunction; a value <0.35 provides better sensitivity (>90%) for the detection of moderate-to-severe dysfunction but remains low (50%) for the detection of mild dysfunction. (iii) A difference between the normal reference EOA and the measured EOA >1 SD provides >95% sensitivity and specificity for the detection of moderate-to-severe BMV dysfunction but sensitivity for detection of mild dysfunction is 61%.

Transprosthetic velocity and gradient

The data of peak aortic jet velocity and mean gradient obtained *in vitro* and *in vivo* revealed an important overlap between the normal vs. abnormal valve function groups. These results are consistent with those of Aoyagi *et al.*[1] First, in some cases (*in vitro*: 21 and 23 mm valves at higher flow rates, *Figure 4*; *in vivo*: patients #2, 6, 7, 8, 10, *Table 3*), the peak velocity or gradient was abnormally high (according to the ASE guidelines) despite normal valve function. These false positive cases are most likely related to prosthesis-patient mismatch. This problem indeed occurs when the EOA of a normally functioning prosthesis is too small in relation to the patient's body size (and thus cardiac output requirements), resulting in abnormally high postoperative velocities and gradients.[4] Vice versa, in other cases, the peak jet velocity and mean gradient were within normal ranges despite presence of valve dysfunction (*in vitro*: several cases, *Figure 4*; *in vivo*: patient#16; *Table 3*). These false negative cases are likely related to the presence of low transvalvular flow rate. The velocity and gradient may thus be relatively low (i.e. they are 'pseudo-normalized') despite the presence of prosthetic valve dysfunction. Hence, the absence of a high transprosthetic velocity or gradient does not necessarily imply the absence of prosthesis dysfunction and vice versa the presence of high velocity or gradient does not necessarily imply the presence of prosthesis dysfunction. Furthermore, Baumgartner *et al.*[10] have reported, in a study on a Carbomedics 19 mm BMV, that such discrepancies between Doppler and

Table 3 Results of the *in vivo* study: individual Doppler-echocardiographic data for the 17 patients with bileaflet mechanical valve (BMV) included in this study

Patient no.	Valve type	Valve size (mm)	Stenosis degree	LVOT (mm)	SV (mL)	V_{peak} (m/s)	TPG_{mean} (mmHg)	(DVI)	EOA (cm^2)	EOA_{normal}–$EOA_{measured}$ > 1 SD
	Normal BMV									
1	SJM	21	Normal	21	69	2.41	15.4	0.41	1.28	No
2		25	Normal	22	88	3.1	25	0.44	1.60	No
3		25	Normal	24	68	2.04	9.0	0.44	2.13	No
4		25	Normal	26	76	2.14	9.3	0.43	2.06	No
5		25	Normal	23	79	2.15	9.0	0.40	1.88	No
6	CMTH[a]	21	Normal	21	87	3.51	27	0.34	1.23	No
7		23	Normal	23	113	3.45	25	0.38	1.77	No
8		23	Normal	22	114	3.75	30	0.40	1.90	No
9		23	Normal	22	69	1.81	7.0	0.45	1.76	No
10		25	Normal	24	107	2.89	24	0.36	1.78	No
11	Advantage	21	Normal	19	77	2.8	13	0.44	1.39	Yes
12	On-X	19	Normal	19	77	2.49	13	0.44	1.39	No
13		23	Normal	23	84	1.87	7.4	0.62	2.2	No
Mean value				22	85	2.65	16	0.43	1.72	
Standard deviation				1.89	15.61	0.63	8.12	0.07	0.31	
	Dysfunctional BMV									
14	SJM	23	35°–10°	22	61	3.26	20	0.22	0.97	Yes
15		25	56°–56°	19	47	4.3	42	0.18	0.52	Yes
16	SJHP	27	35°–35°	23	100	3.29	17	0.35	1.56	Yes
17	CMTH	27	22°–32°	21	94	4.08	41	0.29	1.14	Yes
Mean value				21	76	3.73*	30	0.26*	1.05*	
Standard deviation				1.48	22.16	0.46	11.56	0.07	0.37	

LVOT, left ventricle outflow tract; SV, stroke volume; V_{peak}, peak aortic jet velocity; TPG_{mean}, mean transprosthetic gradient; DVI, Doppler velocity index; SJM, St Jude Medical Standard; SJHP, St Jude Hemodynamic Plus; CMTH, carbomedics top hat.
[a]Reference EOA values are taken from the ASE guidelines.[5]
*$P < 0.05$ vs. normally functioning BMV.

catheter TPGs are reduced in the presence of BMV dysfunction. These findings have been further confirmed by a previous numerical study from our laboratory.[8] This phenomenon can be explained by the fact that: (i) less pressure is recovered downstream of a dysfunctional BMV; (ii) a very severe dysfunctional BMV generally display a configuration with a single orifice thus minimizing the discrepancies between Doppler and Catheter due to localized high pressure gradients within the central valve orifice. It should also be noted that the pressure recovery downstream of a normal or dysfunctional BMV also depends on the aorta size.[11]

Doppler velocity index

The Doppler velocity index has been originally proposed by Chafizadeh and Zoghbi[12] to screen for valve obstruction, when the cross-sectional area of the LVOT cannot be measured. In this study, the DVI was, among the traditional parameters of valve function (i.e. peak velocity, mean gradient, EOA), the one that provided the best accuracy to separate normal from dysfunctional valves. However, there was nonetheless some substantial overlap between valves with normal function vs. those with mild dysfunction (*Figures 3 and 4* and *Table 3*). Furthermore, both the *in vivo* and *vitro* data obtained in this study suggest that the cut-point values of 0.25 or 0.30 proposed in the ASE guidelines[5] lack sensitivity to detect valve dysfunction (*Tables 2* and *4*). The cut-point value of <0.35 seems more appropriate to identify moderate-to-severe valve dysfunction but still remains suboptimal for the detection of mild dysfunction. Similar results and conclusions were obtained when the ratio of VTIs was used instead of the ratio of peak velocities. Increasing the cut-point of DVI may increase the risk of over-diagnosing. However, in the context of BMV, even a mild dysfunction could rapidly become severe and life-threatening. Hence, it is probably preferable to use more sensitive thresholds and refer patients with suspicion of dysfunction to cinefluoroscopy for confirmation of diagnosis.

Valve effective orifice area

There was an important overlap between normal vs. dysfunctional valves with regards to valve EOA and the cut-point values of <0.8 or 1.2 cm^2 proposed in the ASE guidelines provided low sensitivity to detect valve dysfunction both *in vitro* (*Table 2*) and *in vivo* (*Table 4*). These cut-point values to identify prosthetic valve dysfunction, however, have important limitation given that they

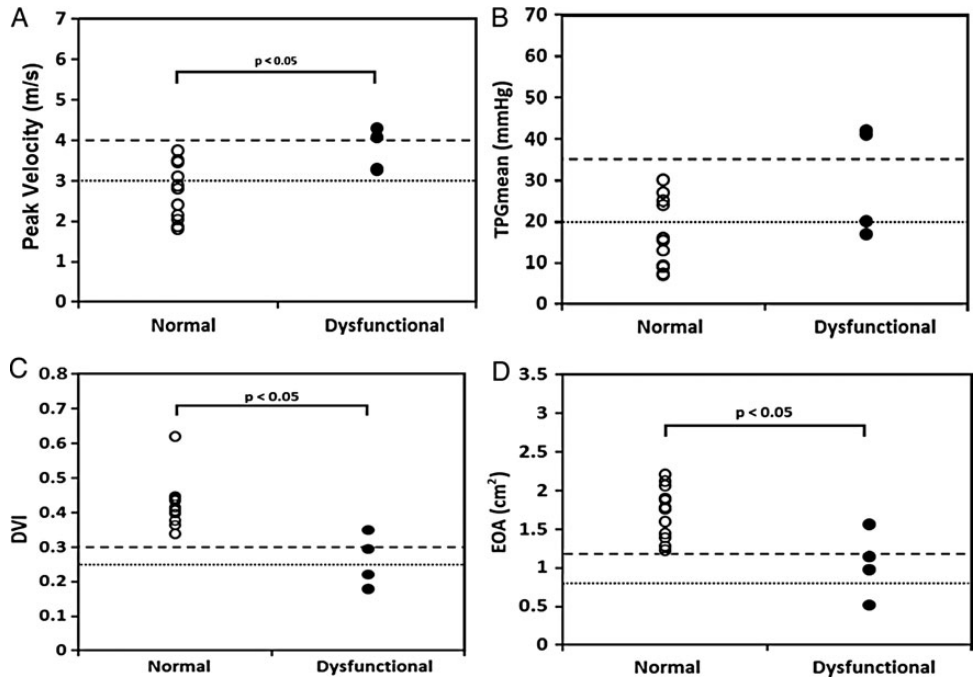

Figure 5 *In vivo* data of the Doppler-echocardiographic parameters according to presence or absence of prosthetic valve dysfunction. Distribution of the *in vivo* data of the Doppler-echocardiographic parameters as a function of the presence or absence of valve dysfunction as confirmed by cinefluoroscopy. (*A*) Peak transprosthetic velocity; (*B*) mean transvalvular pressure gradient (TPG_{mean}); (*C*) Doppler velocity index (DVI); and (*D*) effective orifice area (EOA). The dashed and dotted lines represent the cut-off values proposed in the ASE guidelines (Zoghbi *et al.*[5]) and suggesting possible and significant stenosis, respectively. The white and black circles represent the normal and dysfunctional valves, respectively.

Table 4 Results of the *in vivo* study: sensitivity and specificity of the different Doppler-echocardiographic parameters and criteria to detect valve dysfunction

Parameter	Diagnosis criteria for dysfunction	Sensitivity (%)	Specificity (%)
Peak aortic jet velocity	≥4 m/s	50	100
	≥3 m/s	100	69
Mean transprosthetic gradient	≥35 mmHg	50	100
	≥20 mmHg	100	69
Doppler velocity index	≤0.35	100	92
	≤0.3	75	100
	≤0.25	50	100
Effective orifice area	≤1.2 cm^2	75	100
	≤0.8 cm^2	25	100
EOA-D	>1SD	100	92

EOA-D, difference between normal EOA and measured EOA.

overlap substantially with the normal reference values of EOA of several prostheses models. The results of this study reveal that recognition of prosthetic valve stenosis is better achieved by comparing the measured EOA to the normal reference value of EOA for the model and size of prosthesis implanted in the patient rather than applying fixed cut-off values to all patients regardless of the characteristics of their prosthesis. Indeed, all standard Doppler-echocardiographic parameters (i.e. TPGs, EOA, DVI) are dependent on the specific model and size of prosthetic valve and what is normal for a given type and size of valve may be abnormal for another one. The EOA-D may help overcome, at least in part, this limitation and the criteria of an EOA-D > 1 SD provided the best accuracy to identify valve dysfunction both *in vitro* (*Table 2*) and *in vivo* (*Table 4*). These findings underline the point that the EOA measured in the patient should be interpreted in reference to the normal EOA for the model and size of the implanted prosthesis. The mean ± SD values of the normal reference EOAs for the most frequently used prosthetic valves are available in the literature.[4] There are, however, two caveats with this method: (i) the calculation of the EOA requires the inclusion of several measures and this parameter is therefore more prone to measurement errors; (ii) this method requires reliable sources for normal reference values of EOAs for the different models and sizes of prosthetic valves used in practice.

Localized high velocity within the central valve orifice

An abnormally high gradient corresponding to a localized high velocity may be recorded by continuous-wave Doppler interrogation

through the smaller central orifice of BMV.[4,13] The magnitude of the localized high velocity and thus of the overestimation by Doppler depends on the size and the specific design of the valve.[13–15] This phenomenon may lead to an overestimation of peak velocity and gradient, an underestimation of DVI and EOA, and an abnormal EOA-D (i.e. >1 SD). These findings may thus yield to a false suspicion of prosthesis dysfunction. Hence, the recording of central localized high velocity may have been responsible for some false positive cases in our study.

The very high specificity (>90%) obtained with DVI and EOA-D suggests that the magnitude of central localized gradient was low in this study. This may be related to the limited number of valve models and sizes and of flow conditions tested in this study. Also, there is some controversy in the literature whether the phenomenon of central localized high gradient occurs systematically in all patients with BMV or sporadically in some very specific valve/flow conditions and whether the magnitude of localized high gradient is clinically relevant.[11,3,16] In the clinical study of Aljassim *et al.*,[16] Doppler overestimated catheter TPGs. However, the magnitude of this overestimation was similar in bioprosthetic valves vs. mechanical valves and the discrepancy between Doppler and catheter was totally explained by the pressure recovery in the aorta. The authors thus concluded that localized high gradient (i.e. 'within prosthesis pressure recovery') likely had little contribution to the Doppler overestimation of TPG in their series.

Angle-independent parameters

The ASE guidelines also proposed to use the parameters of ejection dynamics measured on the continuous-wave Doppler recording of transprosthetic flow to identify prosthesis obstruction.[5] In this regard, a recent study by Ben Zekry *et al.*[17] reported that a cut-off value of acceleration time of 100 ms had sensitivity and specificity of 86% for identifying prosthetic valve stenosis and an acceleration time/LV ejection time ratio of 0.37 had sensitivity of 96% and a specificity of 82%. The ejection dynamic parameters were not measured in the present study. These parameters offer the advantage of being angle-independent but, on the other hand, their accuracy may be affected by LV chronotropy and function as well as by arterial haemodynamics. Also, these parameters and criteria have not been validated for the detection of mild prosthesis dysfunction.

Complementarity between Doppler echocardiography and cinefluoroscopy

Cinefluoroscopy is probably the best method to confirm the status of BMV function in case of uncertainties at the Doppler-echocardiographic exam. However, cinefluoroscopy is associated with radiation exposure, which limits its utilization for routine follow-up, especially in the younger population. It is thus important to optimize the Doppler-echo parameters and criteria for the detection of prosthetic valve dysfunction in order to ensure optimal screening process and rationale utilization of cinefluoroscopy. The findings of the present study may help refine the identification of valve dysfunction on Doppler echocardiography and thus to better select the patients who should be assessed by cinefluoroscopy.

Study limitations

The *in vitro* models like the one used in this study cannot precisely replicate all the characteristics of the complex flow dynamics occurring in patients with aortic BMVs. In particular, the dimension, geometry, and biomechanical properties of the aorta were the same for all *in vitro* experiments, which limit our ability to assess the effect of proximal aorta size and compliance on flow dynamics and pressure recovery downstream of the valve. However, it has been shown that these factors have no direct effect on the Doppler-echocardiographic measures of valve gradient, EOA, and DVI, which are the parameters generally used to identify prosthetic valve stenosis.[18,19] Another limitation is that in the *in vitro* study, only dysfunctions due to incomplete valve opening were considered (no or minimal central regurgitant jet during diastole). Further studies evaluating the correlation between valve dysfunction due to incomplete closure of the leaflets and the resulting central regurgitant jet will be interesting. Finally, although there was a strong coherence between the results of the *in vitro* study and that of the *in vivo* study, the latter was a retrospective study and included a small number of patients with prosthetic valve dysfunction. Further prospective studies including a larger number of patients with valve dysfunction, confirmed by cinefluoroscopy are needed to corroborate and extend the results of the present study.

Conclusion

The Doppler-echocardiographic parameters and criteria proposed in the ASE guidelines lack sensitivity for the detection of aortic BMV dysfunction. The utilization of a DVI < 0.35 or an EOA-D > 1 SD improved the sensitivity (>90%) for the detection of moderate-to-severe dysfunction, but the sensitivity remained suboptimal (<65%) for detection of mild dysfunction. Bileaflet mechanical valve dysfunction may progress rapidly from mild to severe dysfunction and may thus become life-threatening within a short period of time. This situation is more likely to occur when thrombosis is the underlying cause of the valve dysfunction. Hence, detection of valve dysfunction at an early stage of the pathologic process is essential to rapidly initiate treatment (thrombolysis or surgery) before patient's haemodynamic condition deteriorates. However, given that all Doppler-echocardiographic parameters of valve function have important limitations and may be subject to measurement errors, it is preferable to use a comprehensive, multi-parametric approach as recommended in the ASE guidelines. Furthermore, since all these parameters have suboptimal sensitivity for the detection of mild BMV dysfunction, it is helpful to assess valve leaflet mobility, preferably by cinefluoroscopy, when there is a suspicion of valve dysfunction at clinical or echocardiographic exam.

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