Feasibility and Diagnostic Accuracy of Quantitative Assessment of Mechanical Prostheses Leaflet Motion by Transthoracic and Transesophageal Echocardiography in Suspected Prosthetic Valve Dysfunction

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Transthoracic (TTE) and transesophageal echocardiography (TEE) are the standard techniques for the evaluation of prosthetic valve function. However, quantitative evaluation of leaflet(s) motion is not routinally carried out, although leaflet(s) opening and closing angle measurements are important information to recognize prosthetic dysfunction. For this purpose, cinefluoroscopy is considered the "gold standard" technique. The aim of this study was the evaluate the diagnostic accuracy of TTE and TEE in the quantitative assessment of leaflet motion in patients with mechanical protheses. One hundred-eleven patients with mitral (single disk 18; bileaflet 48) and aortic (single disk 22; bileaflet 23) prostheses, were referred to TTE, TEE, and cinefluoroscopy for electrical cardioversion of atrial fibrillation (n = 40) or suspected prosthesis dysfunction (n = 71). Echocardiographic evaluation included leaflet(s) opening and closing angle measurements; results were compared with cinefluoroscopy. For mitral prostheses, opening and closing angles were correctly identified by TTE in 85% and by TEE in 100% of patients, regardless of prosthetic valve type, with a good concordance with cinefluoroscopy. For aortic prostheses, opening angles were correctly identified by TTE and TEE, respectively, in 40% and 77% of patients with single-disk and in 13% and 35% of patients with bileaflet prostheses. Both TTE and TEE were rarely able to identify closing angles. In conclusion, quantitative evaluation of mitral leaflet(s) motion may be accurately achieved with TTE and TEE, leading to increased diagnostic efficacy of prosthetic valve dysfunction. In the aortic position, TTE and TEE allow a quantitative evaluation of leaflet(s) dynamics only in a minority of patients and cinefluoroscopy still remains the first-choice technique. **(Am J Cardiol 2006;97:94–100)**

The aim of this study was to examine the roles of transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) in the quantitative assessment of leaflet motion in patients with either normally functioning mechanical valve prostheses or clinically suspected prosthetic valve thrombosis (PVT). The results were compared with those obtained with cinefluoroscopy, the "gold standard" technique for the evaluation of prosthetic leaflet motion.

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From June 2001 to January 2004, 111 consecutive patients (mean age 61 ± 12 years; 65 women) with mitral (n = 66; single-disk 18; bileaflet 48) and aortic (n = 45; single-disk 22; bileaflet 23) prostheses were enrolled into the study. Patients underwent TTE, TEE, and cinefluoroscopy as part of a specific diagnostic workup before the electrical cardioversion of atrial fibrillation (n = 40) or for suspected PVT (n = 71). Patients' characteristics are reported in Table 1.

Table 1
Patient characteristics (n = 111)

Characteristic	Value
Age (yrs)	61±12
Men/women	46/65
Prosthesis type	
Bileaflet	71 (64%)
Mitral	48 (67%)
Aortic	23 (33%)
Single-disk	40 (36%)
Mitral	18 (45%)
Aortic	22 (55%)
Atrial fibrillation	40 (36%)
Suspected prosthesis dysfunction	71 (64%)
Heart failure	44 (62%)
Aortic Doppler mean gradient >30 mm Hg	14 (20%)
Embolic events	4 (5%)
Infective-like disease	9 (13%)

Each patient underwent TTE, cinefluoroscopy, and TEE on the same day. TTE was usually carried out first. The local ethics committee approved the study protocol, and written informed consent was obtained from each patient.

Two-dimensional and Doppler echocardiographic studies (TTE) were performed using a Hewlett-Packard (Palo

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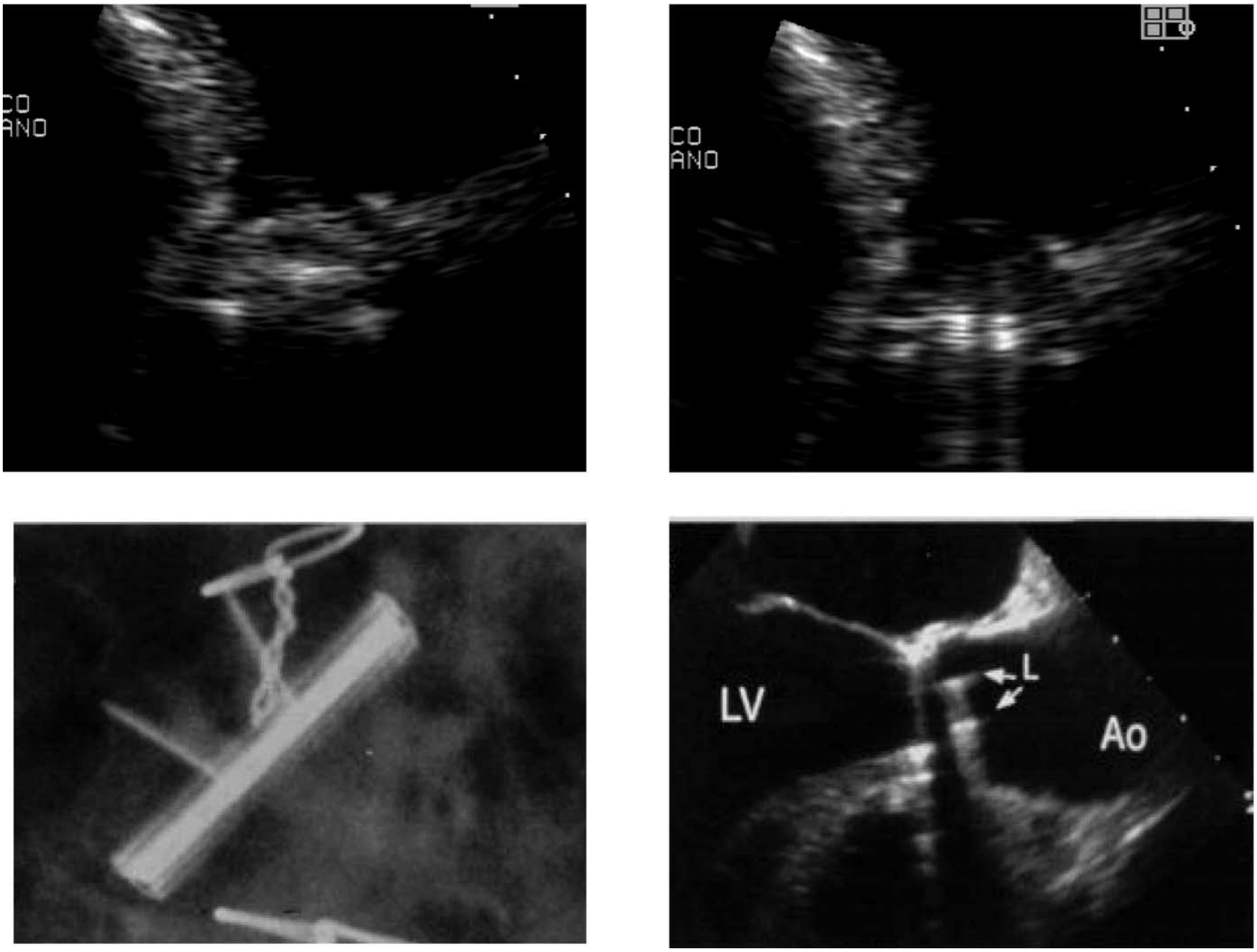

Figure 1. Normally functioning aortic bileaflet prosthesis. Closing angle and opening angle in apical 5-chamber transthoracic view *(top panels)*, opening angle by cinefluoroscopy *(bottom left panel)* and by TEE long-axis view at 127° *(bottom right panel)*. Ao = aorta; LV = left ventricle.

Alto, California) ultrasound unit (Sonos 5500, M2424A); the system has 2.5- and 3.5-MHz transducers (2-dimensional echocardiography) and 2.0-, 2.5-, and 1.9-MHz transducers for pulsed, continuous steerable, and stand-alone continuous Doppler, respectively. A complete 2-dimensional echocardiographic evaluation was performed to visualize leaflet prosthetic motion in multiple cross-sectional views. The continuous-wave mode was used to study flow across the prosthetic valves. Mean pressure gradients were obtained by planimetry of the Doppler velocity envelope with the software package of the ultrasound unit. Effective orifice mitral area was calculated with the pressure halftime method, and effective orifice area for aortic prostheses was calculated by the continuity equation: $A2 = A1 \times VT1/VT2$, where A1 is the subaortic cross-sectional area, VT1 is the subaortic velocity integral, and VT2 is the transaortic velocity integral.

TEE was performed with 5-MHz or 5- to 6.2-MHz multiplane probes inserted into the esophagus and connected to the echocardiographic system. TEE was performed with the patient in the left lateral position; aerosolized lidocaine for local anesthesia of the oropharynx and intravenous midazolam were administered before the introduction of the probe. A complete examination of prostheses included lower and upper esophageal and transgastric views. The entire sewing ring and the leaflets of the prostheses were scanned in the upper esophagus for aortic prostheses and in the lower esophagus for mitral prostheses, through the electronic rotation of the transducer (0° to 180°). The criteria for mitral or aortic PVT were evidence of thrombus or pannus with or without altered mobility of the leaflets and abnormal washing jets through the prostheses. Thrombus was defined as a distinct mass of abnormal echoes attached to the prostheses and clearly seen throughout the cardiac cycle, and distinction between thrombus and pannus was identified by clinical characteristics (the duration of symptoms, anticoagulation status), by echocardiographic parameters (thrombi are in general larger than panni), and by qualitative and quantitative ultrasound intensity.[1]

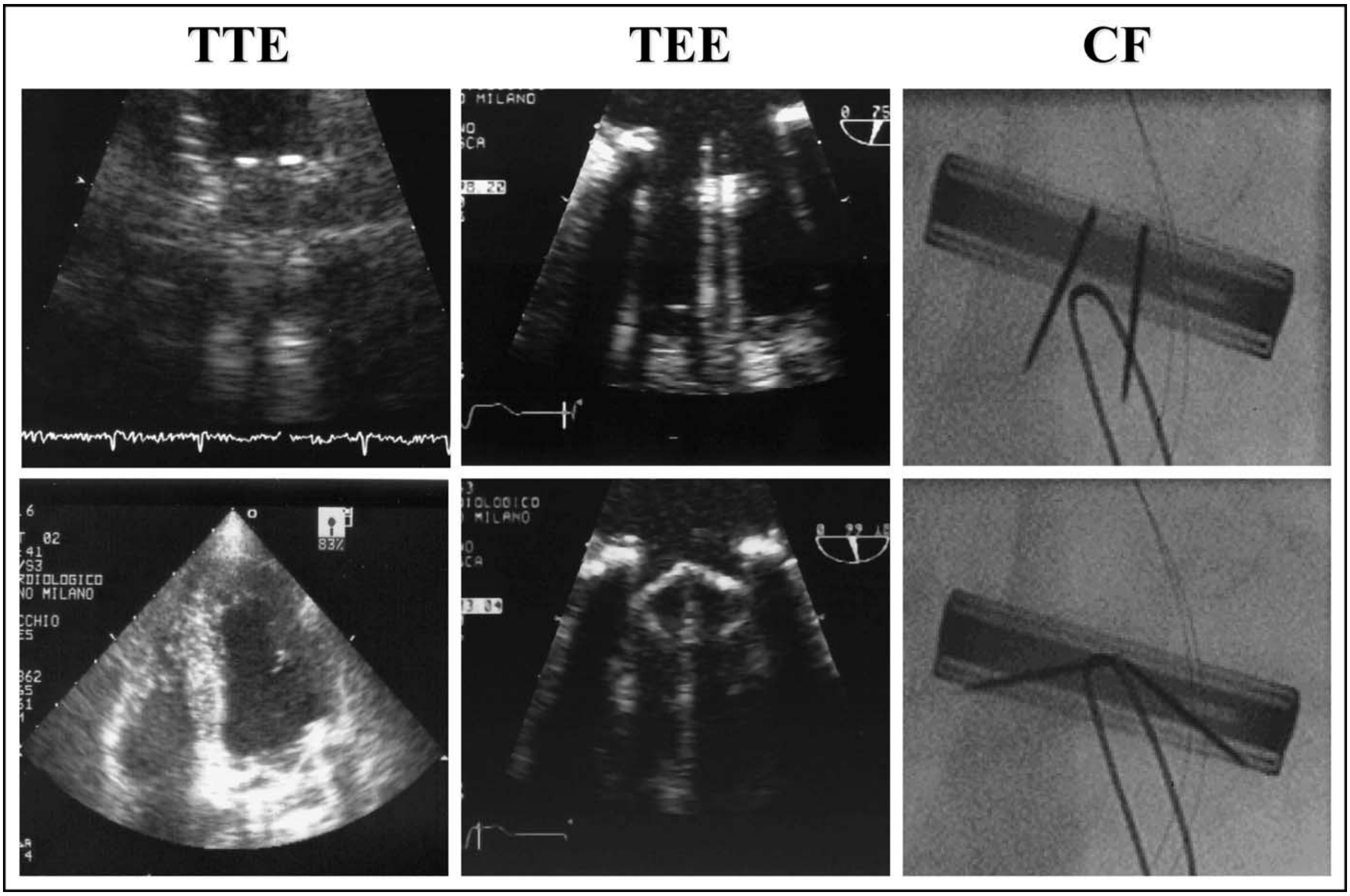

Figure 2. Normal functioning mitral bileaflet prosthesis: opening (*top panels*) and closing (*bottom panels*) angles in transthoracic apical 4-chamber view *(left)*, TEE view *(middle)*, and cinefluoroscopy (CF) *(right)*.

Cinefluoroscopy was performed with Toshiba CAS10 equipment (Toshiba Medical Systems Corporation, Tokyo, Japan), as previously described.[2,3] The evaluation was considered appropriate when the prosthetic tilting disk projection (i.e., with the x-ray beam parallel to the valve ring plane and the tilting axis of the disks) was obtained. This view allows the proper visualization of prosthetic leaflet motion so that opening and closing angles can be calculated. When the tilting disk projection was obtained, a short cinefluoroscopic film (usually 3 to 10 cardiac cycles) at 50 frames/s was recorded. Frames of interest were selected, magnified, and printed with a Polaroid camera (Polaroid Corporation, Waltham, Massachusetts) connected to the video analyzer.

Opening and closing angles were defined as the distance between the valve housing and the disk at its full opening and closing in single-disk valves and as the distance between leaflets in the fully open and closed positions for bileaflet valves (Figures 1 and 2). Values of opening and closing angles were calculated as the mean of 3 (during sinus rhythm) or 5 (during atrial fibrillation) consecutive cardiac cycles measurements.

A test was considered feasible when opening and closing angles were detectable. A test was considered accurate when measurements were similar to those obtained by cinefluoroscopy, the reference technique. The fluoroscopic criterion for prosthetic valve obstruction was the persistent restriction of leaflet motion with a calculated opening angle greater than the mean (+2 SDs) values obtained in a reference group of patients with normally functioning valves of the same type and size.[3]

Variables are presented as mean ± 2 SD. All analyses were performed using SAS statistical software (SAS Institute Inc., Cary, North Carolina). Chi-square analysis was used for nominal data. The Bland-Altman test was used to compare opening and closing angles obtained with TTE, TEE, and cinefluoroscopy. A p value <0.05 was considered statistically significant.

Normal and abnormal prosthetic function (cinefluoroscopy) was found in 71 and 40 patients, respectively. Overall, the feasibility of leaflet motion assessment was greater with TEE than with TTE, for mitral compared with aortic prostheses and for single-disk compared with bileaflet valves (Figure 3). When feasible, results were well comparable with those obtained with cinefluoroscopy (Figure 4 and Table 2), and diagnostic accuracy was increased by adding leaflet motion evaluation to the initial Doppler study (Table 3).

Leaflet movement identification and opening angle calculations were made by TTE in 85% of mitral prostheses

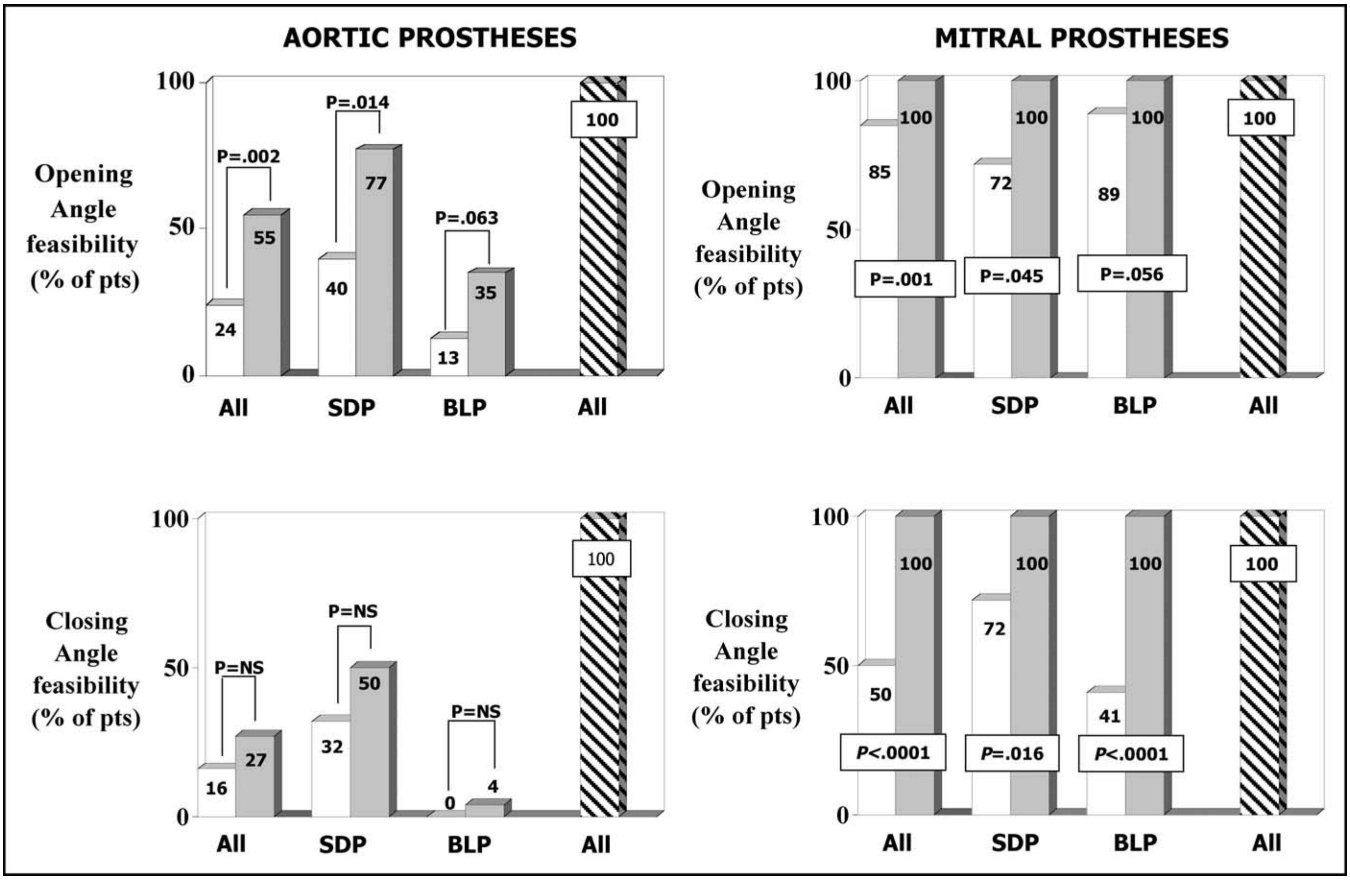

Figure 3. Feasibility of opening angle and closing angle measurements of TTE *(white bars)*, TEE *(gray bars)*, and cinefluoroscopy *(dashed gray bars)* in aortic and mitral prostheses. BLP = bileaflet prosthesis; SDP = single-disk prosthesis.

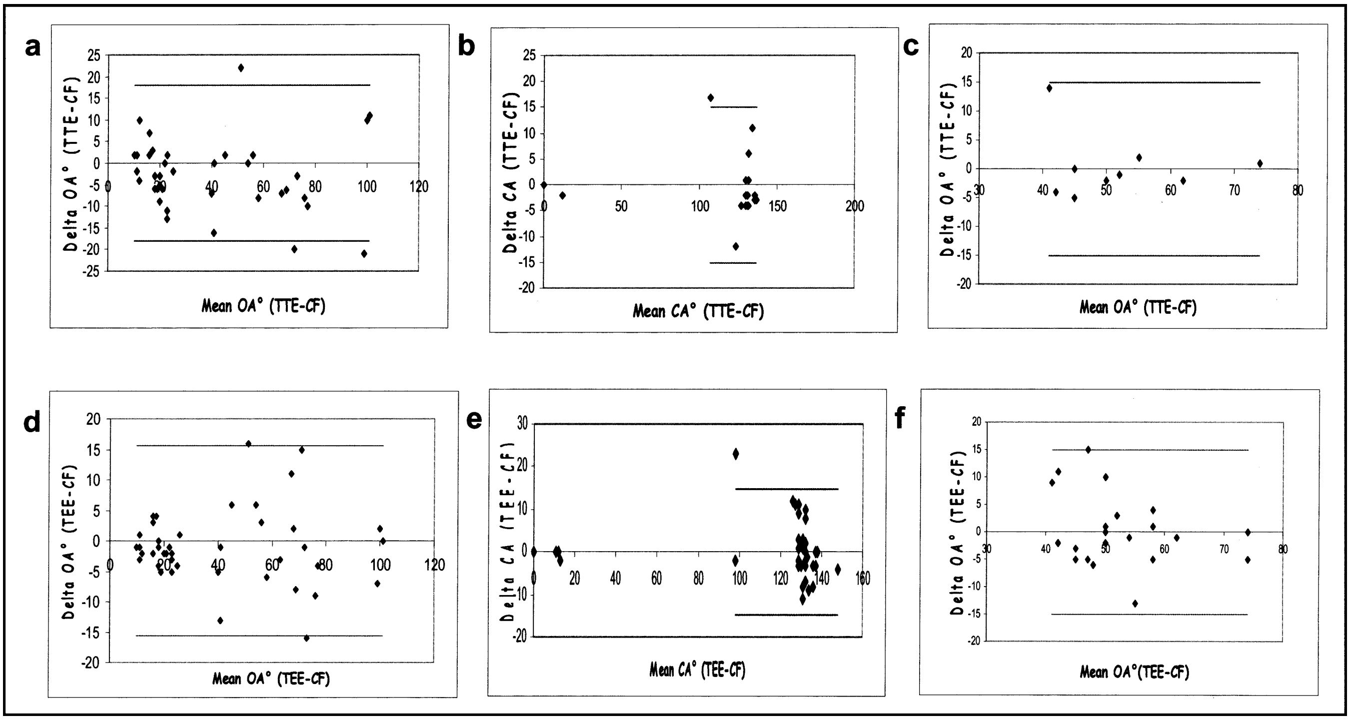

Figure 4. Comparison of opening angle (OA) and closing angle (CA) with TTE *(A, B, C)* and TEE *(D, E, F)* for mitral prostheses *(left, middle)* and aortic prostheses *(right)*. CF = cinefluoroscopy.

Table 2
Sensitivity, specificity, and negative and positive predictive values of TTE and TEE

Variable	TTE Doppler Study	TTE Disk Motion	TEE
Sensitivity			
Aortic prostheses	64%	64%	85%
Mitral prostheses	71%	82%	100%
Specificity			
Aortic prostheses	77%	93%	100%
Mitral prostheses	100%	100%	100%
Negative predictive value			
Aortic prostheses	83%	85%	94%
Mitral prostheses	83%	88%	100%
Positive predictive value			
Aortic prostheses	56%	81%	100%
Mitral prostheses	100%	100%	100%

(72% of single-disk prostheses and 89% of bileaflet prostheses). Conversely, closing angles were obtained by TTE in 50% of cases (72% of single-disk prostheses and 41% of bileaflet prostheses). TEE correctly identified opening and closing angles in all patients, regardless of prosthetic type (Figure 3).

Calculated opening and closing angle values showed good correlation with values obtained with cinefluoroscopy in normal and abnormal prostheses. The Bland-Altman analysis showed low variability between opening and closing angle values calculated by TTE or TEE and by cinefluoroscopy. Mean errors of underassessment of $-2.8 \pm 8.3°$ with TTE ($p = 0.03$) and $-1 \pm 5.6°$ with TEE ($p = 0.1$) were found.

Leaflet movement identification and opening angle calculations were made by TTE in 24% of aortic prostheses (40% of single-disk prostheses and 13% of bileaflet prostheses), whereas closing angles were obtained in only 16% of cases. Opening angles were identified by TEE in 55% of aortic valves (77% and 35% of single-disk and bileaflet valves, respectively), and closing angles were obtained in 27% of cases (50% of single-disk prostheses and only 4% of bileaflet prostheses) (Figure 3).

In 2 cases (9%) with bileaflet prostheses and normal pressure gradients in whom echocardiographic evaluations were unsuccessful, cinefluoroscopy identified significant reduction of the opening angle of 1 disk. One patient underwent reoperation for concomitant coronary artery disease and was found to have subvalvular pannus ingrowth as the cause of disk motion alteration. The second patient refused reintervention and was discharged on medical treatment.

Calculated opening and closing angle values showed good correlation with values obtained with cinefluoroscopy in normal and abnormal prostheses. Bland-Altman analysis showed a low variability of the differences between opening angles calculated by TTE and TEE and by cinefluoroscopy, with mean errors of underassessment of $-2.4 \pm 9.8°$ with TTE ($p = 0.4$) and $0.2 \pm 6.4°$ with TEE ($p = 0.8$).

Of the 40 patients with proved prosthetic dysfunction, 2 underwent thrombolysis with success (indirect confirmation of thrombus), and 38 underwent reoperation. In each case, intraoperative findings confirmed the diagnosis of PVT.

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The aim of this study was threefold: to investigate feasibility (i.e., the percentage of patients in whom leaflet excursion could be identified and calculated); to evaluate the accuracy of leaflet motion assessment by TTE and TEE (i.e., a comparison of values obtained by this technique with those obtained by cinefluoroscopy); and to explore the additional role of this information on test diagnostic accuracy (i.e., the effects of leaflet motion assessment on the sensitivity, specificity, and negative and positive predictive values of ultrasound workup for suspected PVT).

Overall, the quantitative assessment of leaflet motion by ultrasound was feasible and accurate and improved diagnostic accuracy for PVT. However, when results were evaluated according to the type of ultrasound technique used (TTE vs TEE), the site (aortic vs mitral), and the type of implanted prostheses (single disk vs bileaflet), significant differences were found.

In mitral prostheses, leaflet motion analysis was feasible by TTE and TEE in most patients. However, TEE had a higher rate of success than TTE for single-disk and bileaflet prostheses (Figure 3). When feasible, a fairly good concordance of opening and closing angle values with those obtained by cinefluoroscopy was detected by Bland-Altman analysis. This suggests that TTE and TEE are valid alternative methods to cinefluoroscopy to assess leaflet motion in patients with artificial valves in the mitral position.[4,5] After the initial Doppler evaluation, sensitivity and specificity for PVT were 71% and 100%, respectively. When 2-dimensional leaflet motion analysis was added, sensitivity increased to 82%. This was the result of the identification of reduced leaflet motion in patients believed to have normally functioning prostheses according to normal Doppler pressure gradient. This led to the reclassification of these cases as "true-positive" results, with an increase in negative predictive value to 88%. This specific condition, called "Doppler-silent PVT," has been detected by cinefluoroscopy in up to 35% of patients with PVT and mitral bileaflet prostheses.[6,7] A potential explanation is the favorable design of bileaflet prostheses, which allows the maintenance of near-normal transprosthesis blood flow (and related pressure gradient), even in the case of severe hypomobility or a block of 1 disk. Thus, initial echocardiographic evaluation should systematically include Doppler and 2-dimensional leaflet motion assessment.

Analysis of leaflet motion by TEE confirmed the results obtained with TTE. The additional improvement in test sensitivity by TEE was entirely due to the identification of "nonobstructive" PVT cases (normal pressure gradient, normal leaflet motion), as reported by Gueret et al.[8] This

Table 3
Opening angle (OA) and closing angle (CA) values by cinefuoroscopy (CF), TTE, TEE and Doppler gradients

Site, Type of Prosthesis, and Leaflet Motion	Patients (n)	OA TTE (°)	OA TEE (°)	OA CF (°)	CA TTE (°)	CA TEE (°)	CA CF (°)	Mean Gradient (mm Hg)
Mitral, single-disk, normal	11	61 ± 9	61 ± 11	61 ± 10	0	0	0	4 ± 2
Mitral, single-disk, abnormal	7	37 ± 6	37 ± 4	41 ± 1	0	0	0	8 ± 1
Mitral, bileaflet, normal	27	16 ± 5	16 ± 5	19 ± 6	126 ± 14	129 ± 11	129 ± 9	6 ± 2
Mitral, bileaflet, abnormal	21	80 ± 22	83 ± 16	87 ± 14	123 ± 10	136 ± 6	133 ± 8	12 ± 5
Aortic, single-disk, normal	18	55 ± 11	56 ± 9	54 ± 8	0	0	0	24 ± 14
Aortic, single-disk, abnormal	4	43 ± 4	41 ± 1	45 ± 0	0	0	0	34 ± 6
Aortic, bileaflet, normal	15	—	13 ± 5	17 ± 5	—	—	131 ± 5	23 ± 12
Aortic, bileaflet, abnormal	8	—	20 (n = 1)	25 (n = 1)	—	—	78 (n = 1)	68 ± 12

Data are expressed as mean ± SD.

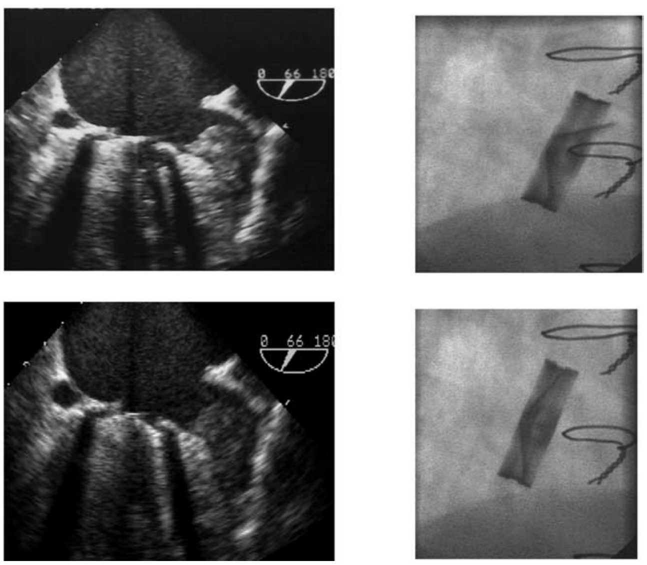

Figure 5. Patient with bileaflet mitral prosthetic thrombosis: opening angle and closing angle by TEE *(left)* and opening angle and closing angle by cinefluoroscopy *(right)*. Thrombus in left atrial appendage is demonstrated by TEE.

confirms that the primary role of TEE in the diagnostic workup of patients with suspected mitral PVT is the direct identification and characterization of thrombus type, size, and location to appropriately guide treatment strategy [9–13] (Figure 5). The positive predictive value of combined TTE and TEE was maximal at each step of the diagnostic workup, indicating that an abnormal Doppler result (either obstruction or regurgitation) is always the result of a thrombotic process .

In aortic prostheses, the overall feasibility of leaflet motion analysis was significantly less than in mitral valves for TTE (24% vs 85%) and TEE (55% vs 100%). This was particularly true for patients with bileaflet valves, the most implanted prosthesis worldwide, in whom opening angle analysis was successfully carried out with TTE and TEE in only 13% and 35% of cases, respectively. Anatomic and technical reasons make the alignment of the TEE ultrasound transducer with the moving parts of single or bileaflet prostheses difficult,[14] especially if implanted with antianatomic orientation (i.e., leaflets perpendicular to the septum). This is the recommended orientation if a hypertrophic septum is present to avoid interference with the leaflet opening. Similar observation has been previously reported by Shapira et al.[15] Thus, leaflet mobility assessment is not feasible in a consistent proportion of patients with aortic prostheses by TTE and TEE. Cinefluoroscopy should always be part of the diagnostic workup in these cases.[16] As for mitral prostheses, a fairly good concordance of values between ultrasound and cinefluoroscopy was detected.

After the initial Doppler evaluation, sensitivity and specificity for PVT were 64% and 77%, respectively. In contrast to mitral valves, 2-dimensional leaflet motion analysis improved specificity to 93%. This was the result of the identification of normal leaflet excursion in patients with large Doppler pressure gradients that led to a reclassification as "true-negative" results, with an increase of positive predictive value to 81%. Hemodynamic (such as large stroke volume) and prosthesis-related (small size, patient-prosthesis mismatch, pressure recovery phenomenon) factors have been reported to cause large transvalvular velocities in normally functioning prostheses.[4,17,18] When in doubt, the repetition of echocardiography or comparison with previous tests (if available) may help differentiate functional from organic changes. We found that the addition of 2-dimensional leaflet evaluation is a useful, complementary test to exclude or prove PVT. TEE further improved sensitivity and specificity through the direct visualization of the thrombotic process (Figure 6). Interestingly, in 2 patients with completely normal TTE and TEE evaluations, cinefluoroscopy detected initial opening angle reductions that were due to subvalvular pannus encroaching on the sewing ring in 1 patient.

Two previous studies have been published examining 2-dimensional leaflet motion assessment in bileaflet mechanical prostheses. As in our study, successful analysis was reported in all cases with mitral prostheses. In contrast, a high rate (77%) of successful leaflet imaging was reported for aortic prostheses by Shapira et al.[15] The lack of a quantitative analysis of disk motion and a comparison with cinefluoroscopic results hamper comparison with our study.

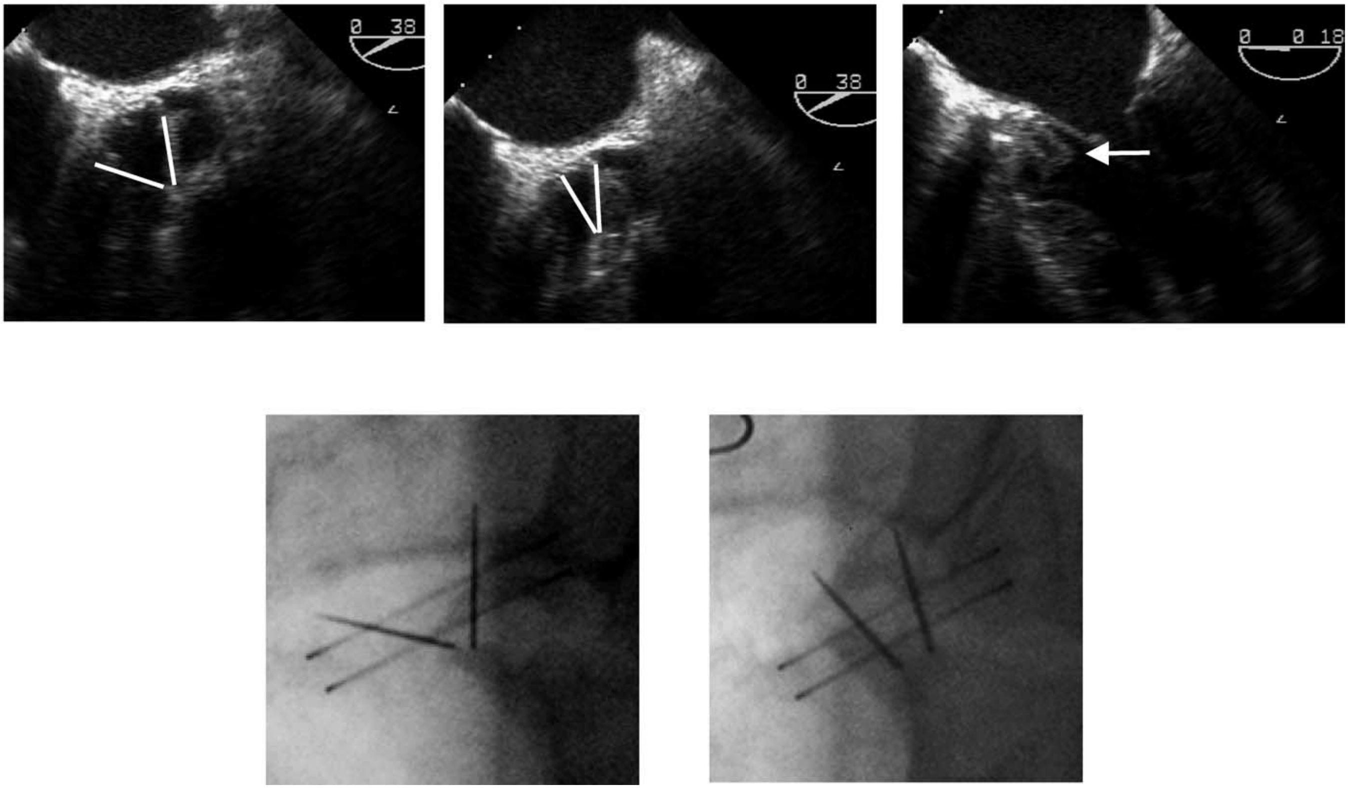

Figure 6. Patient with bileaflet aortic prosthetic thrombosis: closing angle and opening angle on TTE short-axis view at 38° *(top left, top middle)* and on cinefluoroscopy *(bottom)*. *Upper right panel* shows thrombus *(arrow)*.

1. Barbetseas J, Nagueh SF, Pitsavos C, Toutouzas PK, Quinones MA, Zoghbi WAL. Differentiating thrombus from pannus formation in obstructed mechanical prosthetic valves: an evaluation of clinical, trans-thoracic and trans-esophageal echocardiographic parameters. *J Am Coll Cardiol* 1998;32:1410–1417.
2. Montorsi P, Cavoretto D, Repossini A, Bartorelli LA, Guazzi MD. Valve design characteristics and cine-fluoroscopic appearance of five currently available bileaflet prosthetic valves. *Am J Cardiol Imaging* 1996;10:29–41.
3. Montorsi P, Repossini A, Bartorelli LA. Cinefluoroscopic identification of Bjork-Shiley prosthetic heart valves. *Eur Heart J* 1993;14: 1514–1518.
4. Keser N, Nanda N, Miller A, Voros S, Soydas C, Agrawal G, Liguori C, Naftel D, Pacifico AD, Kirklin J, et al. Hemodynamic evaluation of normally functioning Sulzer Carbomedics prosthetic valves. *Ultrasound Med Biol* 2003;29:649–657.
5. Khandheria B, Seward J, Oh J, Freeman WK, Nichols BA, Sinak LJ, Miller FA Jr, Tajik AJ. Value and limitations of trans-esophageal echocardiography in assessment of mitral valve prostheses. *Circulation* 1991;83:1956–1968.
6. Montorsi P, Cavoretto D, Parolari A, Muratori M, Alimento M, Pepi M. Diagnosing prosthetic mitral valve thrombosis and the effect of the type of prostheses. *Am J Cardiol* 2002;90:73–76.
7. Montorsi P, Cavoretto D, Alimento M, Muratori M, Pepi M. Prosthetic mitral valve thrombosis: can fluoroscopy predict the efficacy of thrombolytic treatment? *Circulation* 2003;108(suppl):II-79–II-84.
8. Gueret P, Vignon P, Fourinier P, Chabernaoud JM, Gomez M, LaCroix P, Bensaid J. Trans-esophageal echocardiography for the diagnosis and management of non-obstructive thrombosis of mechanical valve prostheses. *Circulation* 1995;91:103–110.
9. Habib G, Cornen A, Mesana T, Monties JR, Djiane P, Luccioni R. Diagnosis of prosthetic heart valve thrombosis: the respective values of trans-thoracic and trans-esophageal Doppler echocardiography. *Eur Heart J* 1993;14:447–455.
10. Om A, Sperry R, Paulsen W. Trans-esophageal echocardiography for the evaluation of thrombosed mitral valve prostheses during thrombolytic therapy. *Am Heart J* 1992;124:781–783.
11. Roudaut R, Labbe T, Lorient-Roudaut MF, Gosse P, Baudet E, Fontan F, Besse P, Dallaocchio M. Mechanical cardiac valve thrombosis: is fibrinolysis justified? *Circulation* 1992;86(suppl):8–15.
12. Lengyel M, Fuster V, Keltai M, Roudaut R, Schulte H, Seward J, Chesebro J, Turpie A. Guidelines for management of left-sided prosthetic valves thrombosis: a role for thrombolytic therapy. *J Am Coll Cardiol* 1997;30:1521–1526.
13. Lengyel M, Vandor L. The role of thrombolysis in management of left-sided prosthetic valve thrombosis: a study of 85 cases diagnosed by trans-esophageal echocardiography. *J Heart Valve Dis* 2001;10:636–649.
14. Mohr-Kahaly S, Kupferwasser I, Erbel R, Wittlich N, Iversen S, Oelert H, Meyer J. Value and limitations of trans-esophageal echocardiography in the evaluation of aortic prostheses. *J Am Soc Echocardiogr* 1993;6:12–20.
15. Shapira Y, Mordehay V, Perlmuter M, Sagie A. Feasibility of two-dimensional bileaflet valve imaging: a prospective trans-thoracic echocardiographic study. *J Heart Valve Dis* 2002;11:576–582.
16. Montorsi P, De Bernardi F, Muratori M, Cavoretto D, Pepi M. Role of cine-fluoroscopy, trans-thoracic and trans-esophageal echocardiography in patients with suspected prosthetic heart valve thrombosis. *Am J Cardiol* 2000;85:58–64.
17. Baumgartner H, Khan S, DeRobertis M, Czer L, Maurer G. Discrepancies between Doppler and catheter gradients in aortic prosthetic valves in vitro: a manifestation of localized gradients and pressure recovery. *Circulation* 1990;82:1467–1475.
18. Baumgartner H, Schima H, Tulzer G, Kuhn P. Effect of stenosis geometry on the Doppler-catheter gradient relation in vitro: a manifestation of pressure recovery. *J Am Coll Cardiol* 1993;21:1018–1025.