Detection of Non-obstructive Prosthetic Valve Thrombosis: Clinical Significance and Associations

Hussein Ali Bassiri MD, Najmeh Reshadati MD, Anita Sadeghpour MD, FASE, Majid Kiavar MD and Jafar Hashemi MD

Abstract

Background- The purpose of this study was to determine how frequently prosthetic valve non-obstructive thrombosis is associated with prosthetic mitral and aortic valves and to assess their correlation with the anticoagulant status and symptoms of patients.

Methods- From January 2006 to April 2007, all the patients with prosthetic heart valves who were referred for clinically-indicated transesophageal echocardiography (TEE) were evaluated for the presence of non-obstructive thrombosis. Clinical information was collected through patient interviews. Non-obstructive thrombosis was defined as a distinct mass (more than 1 mm in width and 2 - 15 mm in length) with abnormal echoes attached to the normally functioning prosthesis and clearly seen throughout the cardiac cycle via two-dimensional, Doppler, and cinefluoroscopy studies. Masses were classified according to their size as small (<5 mm), moderate (5-10 mm), and large (>10 mm).

Results- The study recruited 102 consecutive patients (64 female) with a mean age of 51 ±11.4 years with non-obstructive thrombosis. There were 132 prosthetic valves (PVs), of which 94 were prosthetic mitral valves (PMVs) and 38 were prosthetic aortic valves (PAVs). The mean time between surgery and TEE examination (age of the prosthesis) was 12 ± 7 years. INR value was less than 1.5 in 50 (49%) cases, between 1.5 – 2.5 in 42 (41.2%) patients, and more than 2.5 in 10 (9.8%). Additionally, 34 (33.3%) patients had recent systemic emboli, 32 (31.9%) had exacerbation of dyspnea, and 14 (13.7%) were asymptomatic.

Conclusions- Sub-therapeutic anticoagulation (INR values < 2.5), systemic emboli, and dyspnea are the key factors for the detection of non-obstructive thrombosis. Moreover, TEE is particularly useful when the thrombus is not visualized by TTE ***(Iranian Heart Journal 2009; 10 (2):20-24).***

Key words: heart valve prosthesis ■ echocardiography ■ thrombosis

Abbreviations list: transesophageal echocardiography (TEE), transthoracic echocardiography (TTE) , left ventricle (LV), atrial fibrillation (AF), ejection fraction (EF), international normalized ratio (INR), prothrombin time (PT), prosthetic mitral valves (PMVs), prosthetic aortic valves (PAVs)

Evaluation of mechanical heart valve prostheses is currently done with transthoracic Doppler echocardiography and occasionally with fluoroscopy.

Identifying non-obstructive thrombosis may be difficult, especially in the presence of a normally functioning prosthesis on clinical examination and on transthoracic echocardiography.

Received Dec. 12, 2008; Accepted for publication May 22, 2009.

From the Department of Cardiovascular Medicine, Shaheed Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran.

Corresponding author: Hossein Ali Bassiri, MD, Associate Professor of Cardiology, Department of Cardiovascular Medicine, Shaheed Rajaie Cardiovascular Medical and Research Center, Tehran, Iran.
Email: www.rhc.ac.ir Tel: +98-21-23922144 Fax: +98-21-22042026

The mechanical heart valve creates artifacts that are projected into the left atrium, yielding an examination of poor sensitivity for the detection of prosthetic thrombi, especially when the clot does not impede leaflet motion and Doppler parameters are within normal limits.

However, non-obstructive prosthetic valve thrombosis is frequently detected by transesophageal echocardiography (TEE), which is the method of choice for detecting the thrombosis of prosthetic valves. [1-7] The frequency, clinical significance, and outcome of this event are not clear, which makes treatment difficult.[8] The aim of this study was to assess how frequently non-obstructive prosthetic valve thrombosis is associated with prosthetic mitral and aortic valves and to assess its correlation with the anticoagulant status and symptoms of the patients.

Methods

Patient population

From January 2006 to April 2007, all the patients with prosthetic heart valves who were referred for clinically-indicated TEE were prospectively studied for the presence of non-obstructive thrombosis. Clinical information was collected at the time of TEE evaluation through patient interviews and in-patient chart examination. The study protocol was reviewed and approved by our institutional human subjects review board, and all the patients gave written informed consent.

Echocardiographic study

The echocardiographic study was standardized and in all the patients, and complete transthoracic and transesophageal echocardiographic examinations were carried out by two experienced echocardiologists. Patients with absolute contraindications for TEE, prosthetic valve malfunction, and infective endocarditis were excluded. Multiplane TEE was performed according to the standard technique using a Vivid 3 (GE Vingmed, Horten, Norway) imaging system and a 5-MHz multiplane transducer. Non-obstructive thrombosis was defined as a distinct mass of abnormal echoes attached to the prosthesis and clearly seen throughout the cardiac cycle,[9] with a normally functioning valve prosthesis by two-dimensional, Doppler, and cinefluoroscopy studies. These masses were more than 1 mm in width in all the cases and from 2 to 15 mm in length (<5 mm designated as small thrombi, 5-10 mm moderate, and >10 mm considered as large thrombi).

Statistical analysis

The interval data are presented as mean or median ± standard deviation (SD). The categorical data were classified and presented as count (percent). The means of the interval data were compared between the two groups using Student's t-test (or its non-parametric equivalent, Mann Whitney U-test) and between more than two groups, using one-way analysis of variance (ANOVA) (or its non-parametric equivalent, Kruskal – Wallis test). Comparisons of the ordinal data between the two groups were also performed using Mann Whitney U or Kruskal – Wallis tests. The nominal data were compared between the two groups using chi-square or Fisher's exact test. A P-value < 0.05 was considered statistically significant.

The adjusted associations were investigated using different regression models, including ordinal and binary logistic regression models and Pearson regression models.

Statistical analysis was performed using SPSS® 15 for Windows® (SPSS Inc, Chicago, Illinois).

Results

Baseline data

One hundred two patients (64 female; mean age 51±11.4 years, range 21 to 77 years) participated, with a total of 132 prosthetic valves (PVs), of which 94 were prosthetic mitral valves (PMVs) and 38 were prosthetic aortic valves (PAVs). Sixty-four patients

(62.7%) had only PMVs, 8 (7.8%) had only PAVs, and 30 (29.5%) had both PMVs and PAVs. All but 2 PVs were mechanical. The mean time between surgery and TEE examination (age of the prosthesis) was 12±7 years (range 1 to 32 years). All of the PVs were functioning normally.

INR levels less than 1.5 were detected in 50 (49%) patients, while INR levels between 1.5 to 2.5 were found in 42 (41.2%) and INR > 2.5 in 10 (9.8%) patients. Fifty-three (52%) patients were taking a daily dose of aspirin (ASA).

Size and number of clots

No relationship was found between the size and number of clots (P-value=0.31). Associations between the size of the thrombi and other predisposing factors, including sex, age, age of the PV, INR level, and treatment with ASA, were investigated by using appropriate statistical tests and the results are presented in Table I.

Table I. Size of the clots and its relationships with other factors

	Size of the Thrombus (mm)			P-value
	< 5 (n=7)	**5 – 10 (n=87)**	**> 10 (n=8)**	
Sex Female (n=64)	4 (57.1%)	58 (66.7%)	2 (25%)	0.16
Male (n=38)	3 (42.9%)	29 (33.3%)	6 (75%)	
Age *years*	50 (±12.0)	51 (±11.0)	49 (±16.6)	0.89
Age of the Prosthesis *years*	12 (±1.8)	12 (±6.8)	7 (±6.0)	0.11
MPV (n=64)	4 (57.1%)	55 (63.20%)	5 (62.5%)	0.58
APV (n=8)	0	7 (8.1%)	1 (12.5%)	
Both MPV and APV (n=30)	3 (42.9%)	25 (28.7%)	2 (25%)	
INR level INR > 1.5 (n=52)	2 (28.6%)	46 (52.9%)	4 (50%)	0.45
INR < 1.5 (n=50)	5 (71.4%)	41 (47.1%)	4 (50%)	
INR > 2.5 (n=10)	1 (14.3%)	6 (6.9%)	3 (37.5%)	0.10
INR < 2.5 (n=92)	6 (85.7%)	81 (93.1%)	5 (62.5%)	
Daily Aspirin Intake Yes (n=53)	6 (85.7%)	42 (48.3%)	5 (62.5%)	0.44
No (n=49)	1 (14.3%)	45 (51.7%)	3 (37.5%)	

Table II. Patients' clinical presentations

	Clinical Presentation						
	Asymptomatic (n=14)	**TIA (n=34)**	**DOE (n=32)**	**Chest Pain (n=6)**	**Palpitation (n=5)**	**Others (n=11)**	**P value**
Sex Female (n=64)	11 (78.6%)	20 (58.8%)	19 (59.4%)	2 (33.3%)	2 (40%)	10 (90.9%)	0.10
Male (n=38)	3 (21.4%)	14 (41.2%)	13 (40.6%)	4 (66.7%)	3 (60%)	1 (9.1%)	
Age *years*	47 ±10.1	48 ±11.4	55 ±12	52 ±11.6	51 ±11.7	51 ±9.0	0.16
Age of the Prosthesis *years*	8 ±5.4	16 ±5.7	15 ±7.7	13 ±7.9	12 ±3.3	10 ±5.0	0.007
MPV (n=64)	10 (71.4%)	25 (73.5%)	18 (56.3%)	3 (50%)	1 (20%)	7 (63.6%)	0.37
APV (n=8)	0	3 (8.8%)	3 (9.4%)	0	1 (20%)	1 (9.1%)	
Both MPV and APV (n=30)	4 (28.6%)	6 (17.6%)	11 (34.4%)	3 (50%)	3 (60%)	3 (27.3%)	
INR level INR > 1.5 (n=52)	6 (42.9%)	20 (58.8%)	16 (50%)	3 (50%)	2 (40%)	5 (45.5%)	0.90
INR < 1.5 (n=50)	8 (57.1%)	14 (41.2%)	16 (50%)	3 (50%)	3 (60%)	6 (54.5%)	
INR > 2.5 (n=10)	0	2 (5.9%)	6 (18.8%)	2 (33.3%)	0	0	0.09
INR < 2.5 (n=92)	14 (100%)	32 (94.1%)	26 (81.3%)	4 (66.7%)	5 (100%)	(100%)	
Daily Aspirin Intake No(n=49)	8 (57.1%)	18 (52.9%)	12 (37.5%)	1 (16.7%)	2 (40%)	8 (72.7%)	0.19
Yes (n=53)	6 (42.9%)	16 (47.1%)	20 (62.5%)	5 (83.3%)	3 (60%)	3 (27.3%)	

INR levels were considered with 2 different cut-points: 1.5 and 2.5. No statistically significant associations were observed between the size and the above-mentioned factors in these bivariate analyses.

The adjusted associations between the size and the other variables were found using ordinal logistic regression (OLR) models. Different categorizations of INR levels were included in the different OLR models. Also, the location of PVs was broken into two dummy variables, determined by the existence of MVP or AVP. There was an

adjusted negative association between the size of clots and INR level with the cut–point of 2.5 (β = -1.84 ± 0.91, P-value = 0.045; odds ratio = 0.16 [CI95%: 0.03 – 0.96]). This means that INR levels less than 2.5 were associated with greater sizes of non-obstructing thrombi on the PVs.

Patients' clinical presentations

The frequencies of symptoms and signs among the patients were systemic emboli in 34 (33.3%), dyspnea exacerbation in 32 (31.9%), chest pain in 6 (5.9%), and palpitation in 5 (10.8%) patients. Fourteen (13.7%) patients were asymptomatic and 11 (10.8%) had other presentations. In Table II, the relationships of these presentations and other determinants are shown. Statistically significant associations were found between the type of presentations and age of the prosthesis (P-value = 0.007). After using the Bonferroni post-hoc test, it was clear that the age of the PVs in the patients with systemic emboli (16±5.7 years) and dyspnea (15±7.7 years) was significantly greater than that in the asymptomatic patients (8±5.4 years).

Discussion

In patients with mechanical heart valve prostheses, TEE has been demonstrated to be superior to TTE for studying prosthetic valve dysfunction. TEE is particularly useful in detecting a thrombus not visualized by TTE due to interfering echo artifacts produced by the prosthesis or because of the small size of the clot.[9]

The superiority of TEE over TTE for detecting non-obstructive thrombosis in our study is evident. In our series of 102 patients with a mechanical prosthesis and non-obstructive thrombosis, TTE and fluoroscopy did not detect any abnormality in all the patients except for mildly increased pressure half time in some patients.

INR levels less than 2.5 were associated with greater sizes of non-obstructive thrombi on the PVs. We found INR values less than 2.5 in about 90% of our patients, which could be suggestive of the significance of anticoagulant status in these patients. TEE has shown a high incidence of non-obstructive thrombosis after valve replacement with a mechanical prosthesis. Finding non-obstructive thrombosis is a dilemma insofar as outcome, management, and the period during which the complication arises is unpredictable.[13] The most common size for non-obstructive thrombus in our study was 5-10 mm, which is the overlap size between moderate and large thrombi in different studies and the optimal management for these thrombi is controversial.[8,10-,13]

Systemic emboli and shortness of breath were the most common symptom and sign in our patients (in about 65% of patients). Pascal et al. suggested that recent history of a systemic embolic event was highly associated with the presence of a thrombus, and it is now generally recommended that patients with a systemic embolic event be examined by TEE.[2,9]

We found more thromboses on mitral prostheses compared to aortic prostheses, but we could not find any associations between the size of the thrombi and the other predisposing factors such as sex, age, age of the PV, and treatment with aspirin. We concluded that non-obstructive thrombosis is not uncommon, especially in patients with INR values less than 2.5 and in patients with mechanical prostheses suffering from systemic emboli or shortness of breath.

Study limitations

Our study cannot establish a direct cause-and-effect relation for non-obstructive prosthetic thrombosis and cerebral embolism. The natural history and treatment of patients with non-obstructive prosthetic valve thrombosis is not clear, which needs more studies.

Conclusion

The present study demonstrates that TEE is a highly reliable method to detect thrombi on a

mechanical valve prosthesis, particularly when TTE Doppler examination appears to be normal and the patient has an INR value less than 2.5 or complains of recent systemic emboli or shortness of breath.

References

1. Laplace G, Lafitte S, Labèque JN, Perron JM, Baudet E, Deville C, Roques X, Roudaut R. Clinical significance of early thrombosis after prosthetic mitral valve replacement: a postoperative monocentric study of 680 patients. J Am Coll Cardiol 2004 Apr 7; 43(7): 1283-90.

2. Alton ME, Pasierski TJ, Orsinelli DA, Eaton GM, Pearson AC. Comparison of transthoracic and transesophageal echocardiography in evaluation of 47 Starr-Edwards prosthetic valves. J Am Coll Cardiol 1992; 20: 1503-1511.

3. Om A, Sperry R, Paulsen W. Transesophageal echocardiography for evaluation of thrombosed mitral valve prosthesis during thrombolytic therapy. Am Heart J 1992; 124: 781-783.

4. Van den Brink R, Visser CA, Basart DCG, Duren D, de Jong AP, Dunning AJ. Comparison of transthoracic and transesophageal color Doppler flow imaging in patients with mechanical prosthesis in the mitral valve position. Am J Cardiol 1989; 63: 1471-1474.

5. Alam M, Serwin JB, Rosman MS, Sheth M, Sun I, Silverman NA, Godstein S. Transesophageal color flow Doppler and echocardiographic features of normal and regurgitant St Jude medical prosthesis in the mitral valve position. Am J Cardiol 1990; 66: 871-873.

6. Mohr-Kahaly S, Kupferwasser I, Erbel R, Oelert H, Meyer J. Regurgitant flow in apparently normal valve prosthesis: improved detection and semi-quantitative analysis by transesophageal two-dimensional color-coded Doppler echocardiography. J Am Soc Echocardiogr 1990; 3: 187-195.

7. Lange HW, Olson JD, Pedersen WR, Kane MA, Daniel JA, Mooney MR, Goldenberg IF. Transesophageal color Doppler echocardiography of the normal St Jude medical valve prosthesis. Am Heart J 1991; 122: 489-494.

8. Vahanian A, Baumgartner H, Bax J, Butchart E, Dion R, Filippatos G, Flachskampf F, Hall R, Iung B. Guidelines on the management of valvular heart disease. January 26, 2007 European Heart Journal, doi:10.1093/eurheartj/ehl428.

9. Gueret P, Vignon P, Fournier P, Chabernaud JM, Gomez M, LaCroix P, Bensaid J. Transesophageal echocardiography for the diagnosis and management of nonobstructive thrombosis of mechanical mitral valve prosthesis. Circulation 1995; 91: 103-110.

10. Roudaut R, Labbe T, Lorient-Roudaut MF, Gosse P, Baudet E, Fontan F, Besse P, Dallochio M. Mechanical cardiac valve thrombosis: is fibrinolysis justified? Circulation 1992; 86 (suppl II): II8-II15.

11. McKay CR. Prosthetic heart valve thrombosis: what can be done with regard to treatment? Circulation 1993; 87: 294-296.

12. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. ACC/AHA 2006 Guidelines for the Management of Patients with Valvular Heart Disease. J Am Coll Cardiol 2006; 48: 1-148.

13. Laurent M, Lelong B, Lenormand C, De Place C, Matali P, Leurent G, Verhoye JP, Almange C, Leguerrier A. Early non-obstructive thrombosis of mechanical mitral valve prostheses. Arch Mal Coeur Vaiss 2005 Dec; 98 (12): 1192-8.