Frequency and Associations of Prosthetic Valve Fibrin Strands

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Abstract

- Background- Filamentous fibrin strands (FSs) attached to valve prostheses have been well described in patients undergoing transesophageal echocardiography (TEE), but the frequency and clinical significance of these strands remain poorly defined. We aimed to determine the frequency of prosthetic valve strands and to assess their association with anticoagulant status, location, type, and number of prosthetic heart valves.
- Methods- In total, 300 consecutive patients with prosthetic heart valves, who were referred for clinically indicated TEE, were evaluated for the presence of FSs (defined as highly mobile, fine, filamentous masses with less than 1 mm thickness).
- **Results-** FSs were found in 141 (47%) patients. Significant associations were observed between the presence of FSs and anticoagulant status (P-value < 0.001). The location and number of the prosthetic valves had no statistically significant associations with the strands. The FSs were found more frequently on mechanical than on bioprosthetic values (P-value = 0.004). A logistic regression model showed that greater values of international normalized ratio, bioprosthetic values, and daily intake of ASA, had negative associations with the strands.
- *Conclusions* There were significant associations between FSs and patients' anticoagulation status; we would, therefore, suggest intense anticoagulation and close follow-up for these patients (Iranian Heart Journal 2008; 9 (4):23-31).

Key words: echocardiography fibrin strands heart valves bioprosthesis mechanical

Abbreviations list:

Transesophageal echocardiography (TEE); fibrin strands (FSs); transthoracic echocardiography (TTE); left ventricle (LV); atrial fibrillation (AF); ejection fraction (EF); international normalized ratio (INR); prothrombin time (PT)

Trosthetic valve strands are frequently detected bv transesophageal echocardiography (TEE). They are usually located at the inflow side of the prosthetic valve (i.e. the atrial side of a mitral prosthesis or the ventricular side of an aortic prosthesis).

There is a significant difference in the prevalence of strands between studies.

The finding of prosthetic valve-associated strands represents a clinical dilemma because the cause and management of this finding is not clear.

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Received Sept. 21, 2007; Accepted for publication April 5, 2008.

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They are more commonly detected in patients being evaluated for a suspected cardioembolic event and thus represent a potential cardiac source of embolism.¹⁻³

Valvular fibrin strands (FSs) are defined as highly mobile, fine filamentous structures less than 1 mm thick and more than 2 mm in length. The length may vary up to 30 mm.^{4,5} Histopathology shows that strands are composed of elastic collagen fibers and connective tissue, and are covered by endothelium. It has also been suggested that the histopathology of this structure is similar between native and prosthetic valves.^{6,7} Prosthetic valve strands have been observed as early as 2 hours after valve replacement operations and in this setting, reports have suggested a fibrin composition.⁸⁻¹⁰

The purpose of the present study was to determine the prevalence of FSs in patients undergoing TEE examinations and to determine how frequently prosthetic valve strands are associated with prosthetic mitral and aortic valves, anticoagulant status, aspirin therapy, atrial fibrillation rhythm, and age of the prostheses.

Methods

Patient population

In total, 300 consecutive patients (from March 2004 to January 2006) with prosthetic heart valves, who were referred with clinical indications to our echocardiography lab for TEE, were prospectively studied. Clinical information was collected at the time of TEE evaluation through patient interviews and inpatient 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 complete transthoracic echocardiography (TTE) and TEE 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. Strands were mobile. linear defined as echo-dense structures less than 1 mm wide and several mm long attached to the prostheses, which were visible in different cardiac cycles. Structures of different shapes, of limited mobility, wider than 1 mm, or with a widebased attachment to the valve prosthesis were not appreciated as strands.

Statistical analysis

The interval data were presented as mean or median \pm standard deviation (SD). The categorical data were classified and presented as frequency (%). To compare the means of the interval data between the two groups, Student's t-test or its non-parametric equivalent, the Mann Whitney U test, was used. Comparisons of the ordinal data between the two groups were also performed using the Mann Whitney U test. The nominal data were compared between the two groups using the chi-square or Fisher exact test. The odds ratio (OR) and its 95% confidence interval (CI 95%) were calculated to measure the strength of the association between the study outcomes and other factors.

Logistic regression models were fitted to determine the adjusted associations between the study outcomes and other determinants. The independent factors were selected according to their importance in biological relationships and statistical significance in the bivariate analysis.

Inter- and intra-observer variability

All the echocardiographic examinations were performed by two board-certificated echocardiologists. For measuring intraobserver reliability, 30 records were randomly selected; and the echocardiologists, who were blinded to the name and diagnosis of the patient, re-evaluated the films for finding the FSs. Kappa statistics were calculated for this purpose. Eleven records were evaluated as positive and 16 evaluated as negative for the FSs in both examinations. Kappa statistic \pm SE was 0.79 \pm 0.18; thus the agreement between the two evaluations could be considered good to excellent.

Results

The present study recruited 300 consecutive patients with a mean age of 50 ± 12.4 years (range 17 to 79 years). The study population included 188 (62.7%) women. There were 132 (44%) prosthetic mitral valves, 50 (16.7%) prosthetic aortic valves, 102 (34%) combined mitral and aortic valve prostheses, 11 (3.7%) mitral and tricuspid valve prostheses, and 4 (1.3%) multiple valve prostheses.

The valve prosthesis was mechanical in 284 patients and bioprosthetic in 16 patients. Atrial fibrillation was present in 157 of the patients.

The mean age of the prosthetic valves was 8 ± 7.5 years (median 6 years). The mean ejection fraction (EF) was 45% ($\pm9\%$), and the mean left ventricular (LV) end-diastolic dimension was 50 (±7) mm.

FSs were found in 141 (47%) patients. The strands were identified in 118 (out of 249) mitral and 29 (out of 156) aortic prosthetic valves.

The mean international normalized ratio (INR) during the month before the examination was 2.4 ± 0.51 .

Fibrin strands on prosthetic valves and their associations with other factors

The relationships between the presence of FSs (FS+) and other determinants are shown in Table I.

No significant difference was observed between the age, sex, and LVEF between the two groups.

The mean time between surgery and TEE examination (age of the prosthesis) was 9.4±7.6 months in FS+ and 7.1±7 months in FS- patients (P- value=0.001). Significant associations were observed between the presence of FSs and prothrombin time (PT) and INR test results in the patients. The mean PT was 18±3 sec in the FS+ and 21 ± 3 sec in the FS- groups (P-value < 0.001). Also, INR before examination and the average INR through the month before TEE, had means of 2.13±0.54 and 2.21±0.49 in the FS+ and 2.63±0.55 and 2.55±0.47 in the FSgroups, respectively. No association was found between the strands and partial thromboplastin time (PTT) of the patients. The location and number of the prosthetic statistically valves had no significant with associations the strands. The bioprosthetic valves decreased the risk of strands in comparison with the mechanical valves (P-value = 0.004; OR = 0.15 [CI95%: 0.03- 0.67]). Daily use of aspirin showed a negative association with the detection of FSs (P-value = 0.001; OR = 0.45 [0.29-0.73]).Patients with a history of atrial fibrillation (AF) had a greater possibility for strands (Pvalue = 0.001; OR = 2.16 [CI95%: 1.36 -3.44]). Smoke pattern in the left atrium (LA) was observed in 85 (28.3%) patients. This finding had a significant association with the presence of FSs (P-value = 0.002; OR = 2.23[CI95%: 1.33 - 3.75]). No association was found between FSs and detecting clots on the prosthetic valves or in the LA (Table I).

A logistic regression model was used to determine the adjusted association between each of the above-mentioned factors and the presence of FSs. After adjustment, it was clear that greater values of INR, bioprosthetic valves, and daily intake of ASA had negative associations with the presence of strands. Also, AF could be considered a predictor of strands, but no statistically significant relationship was found (Table II).

Table I. Associations between presence of fibrin strands on prosthetic cardiac valves and other determinants.

	Fibrin Strands Present Absent		р	OR [95%
			P	
	(n = 141)	(n = 159)	value	CIJ
	()	()		
Age vears	49 ± 11.6	50 ± 13.1	0.33	_
Age years	49 ± 11.0	50±15.1	0.55	1.04.[0.65
Sex			0.87	1.04 [0.05
$M_{ala}(n - 112)$	52 (26 00/)	60(27.70)		- 1.00]
Male $(n = 112)$	52 (36.9%)	60(37.7%)		
Female $(n = 188)$	89 (63.1%)	99 (62.3%)		
Age of the	9.4 ± 7.6	7.1 ± 7	0.001	
Prosthesis years	<i>y = 1</i> .0	, = <i>i</i>	0.001	
Cardiac Rhythm			0.001	2.16 [1.36
Cinus Dhythm				- 5.44]
Sinus Knythm $(n - 142)$	53 (37.6%)	90 (56.6%)		
(11 = 145)	45.2 + 0.5	44.9 + 6.6	0.21	
LVEF %	45.2 ± 9.5	44.8 ± 0.0	0.31	-
Number of			0.16	-
Prosthetic Valves				
1 (n = 183)	80 (56.8%)	103 (64.8%)		
2(n-113)	59 (41.8%)	54 (34 0%)		
2(n - 115)	2(1.0%)	2(1.20%)		
J (II - 4) Tune of Presthest-	2 (1.470)	2(1.270)		0.15 10.02
Type of Prostnesis			0.004	- 0.67]
Mechanical	139	145		
(n = 284)	(98.6%)	(91.2%)		
Mitral Prosthesis	(, , , , , , , , , , , , , , , , , , ,			1.10 [0.60
			0.87	- 2.001
Ves(n - 249)	118	131]
$1 \cos(11 - 247)$	(83.7%)	(82.4%)		
$N_0(n-51)$	23 (16 3%)	28 (17.6%)		
$\mathbf{NO}\left(\mathbf{H}=\mathbf{J1}\right)$	23 (10.370)	20(17.070)		1.04.10.66
Aortic Prostnesis			0.88	- 1.63]
Yes (n = 156)	74 (52.5%)	82 (51.6%)		
$N_0 (n - 1/4)$	67 (17 5%)	77 (48 4%)		
Tot	07 (47.570)	//(40.470)		0.09 [0.25
Tricuspia			0.98	0.98 [0.33
Prostnesis	7 (50()	0 (50()		- 2.79]
Yes(n = 15)	/ (5%)	8(5%)		
No $(n = 285)$	134 (95%)	151 (95%)		
Average INR the	221 ± 0.49	255 ± 0.47	< 0.001	_
month before	2.21 ± 0.49	2.55 ± 0.47	< 0.001	-
examination				
INK	2.13 ± 0.54	2.63 ± 0.55	< 0.001	-
PT seconds	18 ± 3	21 ± 3	< 0.001	-
PTT seconds	45 ± 9.5	48 ± 8.6	0.40	-
ASA Prophylaxis			0.001	0.45 [0.29
			0.001	- 0.73]
Yes $(n = 165)$	62 (A1 70)	102		
	63 (44.7%)	(64.2%)		
No $(n = 135)$	78 (55.3%)	57 (35.8%)		
Smoke Pattern in	(2. (20.070)		2 23 [1 33
LA			0.002	- 3.75]
Yes (n = 85)	52 (36.9%)	33 (20.8%)		
No (n = 215)	80 (62 10/)	126		
	89 (03.1%)	(79.2%)		
Clots on Prosthesis			0.42	1.21 [0.77
		B.C. (15 000)		- 1.90]
Yes (n = 150)	74 (52.5%)	76 (47.8%)		
No (n = 150)	67 (47.5%)	83 (52.2%)		
Clots in LA			0.28	1.85 [0.59
Vec(n-13)	8 (5 7%)	5 (3 1%)		5.60]
$N_0 (n - 207)$	122	154		
1NO(n = 287)	155	154		
1	(94.5%)	(90.9%)	1	

LVEF: left ventricular ejection fraction; LA: left atrium; PT: prothrombin time; INR: international normalized ratio; PTT: partial thromboplastin time Table II. Multivariate analysis for determining the adjusted associations between the presence of fibrin strands and other variables.

	Coefficient $(\beta) \pm SE$	P Value	OR [CI95%]
Age of the Prosthesis	0.02 ± 0.02	0.19	1.03 [0.99 - 1.06]
AF Rhythm	0.51 ± 0.30	0.09	1.67 [0.93 - 3.00]
Smoke Pattern in LA	0.19 ± 0.32	0.55	1.21 [0.65 - 2.26]
ASA Prophylaxis	-0.62 ± 0.28	0.03	0.54 [0.31 - 0.93]
Average INR	-1.60 ± 0.28	< 0.001	0.20 [0.12 - 0.35]
Bioprosthetic Valves	-2.23 ± 0.87	0.009	0.10 [0.02 – 0.56]

LA: left atrium; INR: international normalized ratio

Fibrin strands on mitral prosthetic valves

Of the 300 patients, 249 had prosthetic mitral valves. Strands were observed on 118 (47.3%) prostheses. The mean age was 48 ± 11.8 years in the FS+ and 51 ± 11.7 years in the FS- groups (P< 0.04).

No difference was observed in the female/male ratio between the groups. The mean LVEF between the two groups did not have an important difference. A borderline relationship was observed between cardiac rhythm and strands (OR for AF = 1.67, [CI 95%: 1-2.8]; P-value = 0.05).

Age of the prostheses was 8.7 ± 6.8 years in the FS+ and 6.7 ± 6.1 years in the FS- patients (P< 0.007).

The mechanical prosthesis could be considered a risk factor for the presence of strands (OR = 4.28, [CI 95%: 0.90 - 20]; P-value= 0.05).

A negative association existed between the hypo-coagulation state and the presence of strands.

PT, INR before examination, and the average INR through the month before TEE had means equal to 18 ± 3.1 , 2.15 ± 0.56 , and 2.22 ± 0.51 in the FS+ and 21 ± 3.2 , 2.64 ± 0.58 , and 2.55 ± 0.46 in the FS- groups, respectively (all P-values < 0.001).

In addition, we divided the participants into two groups, according to their INR values (INR ≤ 2.5 and INR > 2.5).

In this regard, the odds ratio for the relationship between INR (> 2.5) and the strands was 0.12 [CI 95%: 0.07 - 0.22] (Table III).

Daily ASA prophylaxis showed a preventive effect on the presence of the strands (OR = 0.41, [CI 95%: 0.25 - 0.68]; P-value = 0.001). The presence of smoke pattern in echocardiography and clots on the prosthetic valves had positive associations with the FSs (OR was 1.82 and 4.25, respectively), but clots in the left atrium did not show any important relationship (Table III).

A multivariate analysis was performed to investigate the adjusted associations between the above variables.

All the variables which showed significant associations in the bivariate analysis were selected.

Because of autocorrelations, only the "average INR in the month before the examination" (as a categorical data) was entered into the model and PT and the last INR were not considered.

Fitting a logistic regression model revealed that only "average INR" and "observing clots on the prosthesis" had significant associations with FSs, adjusted for other determinants.

(For INR > 2.5, β = -2.12, P-value < 0.001; OR=0.12 [CI95%: 0.05 - 0.30]; for presence of clots, β = 1.26, P-value = 0.02; OR= 3.53 [CI95%: 1.19 - 10.50]).

Patient's age and daily ASA showed borderline associations, but it seems that the relationships were not clinically important (Table IV).

Fibrin strands on aortic prosthetic valves

Out of the 300 patients, 156 had a prosthesis at the aortic valve location, and FSs were observed in 74 (47.4%) of them. No significant difference was found between the mean age and male/female ratio between the FS+ and FS-groups.

	Fibrin Strands			OD [050/	
	Present	Absent	P value	OK [95%	
	(n = 118)	(n = 131)		CIJ	
Age vears	48 ± 11.8	51 ± 11.7	0.04	-	
Sov	40 ± 11.0	51 = 11.7	0.69	1 12 [0.65	
JEX			0.08	1.12 [0.05 -	
N 1 (77)	25	40		1.91]	
Male $(n = 77)$	35	42			
	(29.7%)	(32.1%)			
Female $(n = 172)$	83	89			
	(70.3%)	(67.9%)			
Age of the	8.7 ± 6.8	6.7 ± 6.1	0.007		
Prosthesis vears					
Cardiac Rhythm			0.05	1.67[1.00-	
Carulac Kilytiini			0.05	2 801	
Atrial Fibrillation	80	73		2.00]	
Anial Fibilitation $(n - 152)$	(67.80/)	(55 70/)			
(II = 133)	(07.8%)	(33.7%)			
Sinus Rhythm (n =	38	58			
96)	(32.2%)	(44.3%)			
LVEF %	45 ± 9.1	44 ± 8.3	0.09	-	
Average INR in	2.22 ±	2.55 ±	< 0.001	-	
the month before	0.51	0.46			
examination					
Average INR			< 0.001	0 19 [0 11 -	
(cotegorized)			< 0.001	0.331	
(categorizeu)	20	0.4		0.55]	
> 2.5 (n = 114)	30	84			
	(25.4%)	(64.1%)			
$\pounds 2.5 (n = 135)$	88	47			
	(74.6%)	(35.9%)			
INR	$2.15 \pm$	$2.64 \pm$	< 0.001	-	
	0.56	0.58			
INR (categorized)			< 0.001	0.12 [0.07 -	
				0.221	
> 25 (n - 115)	25	90		•·]	
2.0 (II = 115)	(21.2%)	(68 7%)			
6 6 <i>F</i> ((21.270)	(00.770)			
$f_{2.5}(n = 10^{-10})$	93	41			
134)	(78.8%)	(31.3%)			
PT seconds	18 ± 3.1	21 ± 3.2	< 0.001	-	
PTT seconds	48 ± 20.0	44 ± 12.7	0.34	-	
ASA Prophylaxis			0.001	0.41 [0.25 -	
1 0				0.68]	
Yes $(n = 130)$	48	82			
100 (ii 100)	(40.7%)	(62.6%)			
$N_0 (n - 110)$	70	(02:070)			
100(n - 119)	(50,20/)	(27,40/)			
G D // ·	(39.5%)	(37.4%)	0.02	1.02.01.07	
Smoke Pattern in			0.03	1.82 [1.06 -	
LA			ļ	5.12]	
Yes (n = 80)	46 (39%)	34 (26%)			
No (n = 169)	72 (61%)	97(74%)			
Clots on the			0.001	4.25 [1.81 -	
Prosthesis			1	9.97]	
Yes $(n = 91)$	51 (85%)	40	1	1	
		(27.1%)			
$N_0 (n - 30)$	0(15%)	30			
100(n - 39)	9(1370)	(42.00/)			
Clata in L t		(42.9%)	0.20	1 92 [0 59	
Clots in LA			0.29	1.83 [0.58 -	
			ļ	5.77]	
Yes $(n = 13)$	8 (6.8%)	5 (3.8%)			
No (n = 236)	110	126			
	(93.2%)	(96.2%)	1		
Type of the			0.05	4.28 [0.90-	
Prosthesis				20.001	
Mechanical	116	122	1	201001	
(n - 229)	(08 20/)	(03.104)	1		
(II = 236)	(90.3%)	(93.1%)			
Bioprosthetic	2(1.7%)	9 (6.9%)	1		
(n = 11)	1	1	1	1	

LVEF: left ventricular ejection fraction; LA: left atrium; PT: prothrombin time; INR: international normalized ratio; PTT: partial thromboplastin time

Table III .Fibrin strands on prosthetic mitral valves and their associations with other determinants.

	Coefficient	Р	OR [CI95%]
	$(\beta) \pm SE$	Value	
Age	-0.04 ± 0.21	0.07	0.96 [0.929 - 1.00]
AF Rhythm	1.04 ± 0.52	0.94	1.04 [0.38 - 2.79]
Smoke Pattern	0.67 ± 0.47	0.15	1.96 [0.79 - 4.90]
in LA			
ASA	-0.83 ± 0.47	0.08	0.43 [0.17 - 1.09]
Prophylaxis			
Average INR	-2.12 ± 0.48	< 0.001	0.12 [0.05 - 0.30]
(> 2.5)			
Bioprosthetic	-0.08 ± 1.35	0.95	0.92 [0.07 - 13.00]
Valves			
Age of the	-0.35 ± 0.30	0.25	0.70 [0.39 - 1.27]
Prosthesis			
Clots on	1.26 ± 0.56	0.02	3.53 [1.19 - 10.50]
Mitral Valves			

Table IV. Multivariate analysis for determining the adjusted associations between the fibrin strands on mitral prosthetic valves and other variables.

LA: left atrium; INR: international normalized ratio

The mean age of the prostheses was greater in the patients with FSs (10.5 \pm 8.4 years, compared to 8 \pm 7.0 years; P-value=0.05). As was expected, anticoagulant state had a positive association with the presence of FSs. PT, the last INR test result, and the average INR through the month before TEE had means of 18 \pm 2.8 sec., 2.22 \pm 0.51, and 2.28 \pm 0.53 in the FS+ and 20 \pm 2.9 sec., 2.70 \pm 0.5, and 2.63 \pm 0.43 in the FS- groups, respectively (all Pvalues < 0.001). Average INR < 2 and the strands had a crude association with an odds ratio of 4.94 [CI95%: 2.14–1.34]. Daily intake of ASA showed no association with strand presence.

AF had a significant relationship with the presence of FSs (P-value < 0.001; OR = 3.98 [CI95%: 2.04–7.74]). LVEF was without statistical difference in the two groups. No evidence of clots was found on the prosthetic valves. Also, no relationship was found between clots in the left atrium and FSs on the aortic prosthetic valves; nonetheless, there was a significant association between observing the smoke pattern in the left atrium and the strands (P-value=0.001; OR=3.31 [CI95%: 1.58 -6.94]). No important relationship was found between the type of prosthetic valves and FSs (Table V).

	Fibrin Strands			
	Present (n = 74)	Absent (n = 82)	P value	OR [95% CI]
Age years	51 ± 10.9	49 ± 13.5	0.42	-
Sex			0.93	0.97 [0.52 - 1.83]
Male (n = 68)	32 (43.2%)	36 (43.9%)		
Female (n =88)	42 (56.8%)	46 (56.1%)		
Age of the	10.5 ±	8 ± 7.0	0.05	
Prosthesis years	8.4			
Cardiac Rhythm			< 0.001	3.98 [2.04 - 7.74]
Atrial Fibrillation (n =74)	48 (64.9%)	26 (31.7%)		
Sinus Rhythm (n =82)	26 (35.1%)	56 (68.3%)		
LVEF %	44 ± 10.1	45 ± 8.9	0.73	-
Average INR in the month before examination	2.28 ± 0.53	2.63 ± 0.43	< 0.001	-
Average INR			< 0.001	4.94 [2.14-1.34]
(categorized)				
$\leq 2 \ (n = 37)$	28 (37.8%)	9 (11.0%)		
> 2 (n = 119)	46 (62.2%)	73 (89.0%)		
INR	2.22 ± 0.51	2.70 ± 0.51	< 0.001	-
INR (categorized)			< 0.001	6.46 [2.89–14.43]
$\leq 2 (n = 45)$	35 (47.3%)	10(12.2%)		
> 2 (n = 111)	39 (52.7%)	72 (87.8%)		
PT seconds	18 ± 2.8	20 ± 2.9	< 0.001	-
PTT seconds	39 ± 17.4	44 ± 15.8	0.29	-
ASA Prophylaxis			0.31	0.72 [0.38 - 1.37]
Yes (n = 95)	42 (56.8%)	53 (64.6%)		
No (n = 61)	32 (43.2%)	29 (35.4%)		
Smoke Pattern in LA			0.001	3.31 [1.58 - 6.94]
Yes (n = 44)	30 (40.5%)	14 (17.1%)		
No (n = 112)	44 (59.5%)	68 (82.9%)		
Clots in LA			0.11	5.87 [0.69-51.46]
Yes (n = 6)	5 (6.8%)	1 (6.8%)		
No (n = 150)	69 (93.2%)	81 (93.2%)	0.51	
Type of the Prosthesis			0.21	4.74 [0.54–41.55]
Mechanical (n = 150)	73 (98.6%)	77 (93.9%)		
Bioprosthetic $(n - 6)$	1 (1.4%)	5 (6.1%)		

Table V. Fibrin strands on prosthetic aortic valves and their associations with other determinants

LVEF: left ventricular ejection fraction; LA: left atrium; PT: prothrombin time; INR: international normalized ratio; PTT: partial thromboplastin time

A logistic regression model was fitted for the multivariate analysis. Only the factors which showed significant results in the bivariate analysis were considered in the model. Among the variables presenting the coagulation state, only the average INR (as a categorical data) was entered into the model. Average INR > 2 had a significant negative association ($\beta = -1.44$, P-value = 0.001; OR=0.24 [CI95%: 0.10 - 0.58]), and AF had a significant positive association ($\beta = 1.11$, Pvalue = 0.003; OR= 3.05 [CI95%: 1.47 -6.31]) with the presence of FSs, adjusted for the age of the prostheses and smoke pattern.

Discussion

FSs were found in 141 (47%) patients, 118 (out of 249) were detected on mitral prostheses. The literature review on the rate of strands found a wide variation from 32% ^{8,14} by Orsinelli, 6% to 45% by Renee,¹ 54% by Zakarkaite and even 73% by Stoddard et al. in patients with the St. Jude Medical type MVP.¹⁴

This variation can be explained by the different methods and patient selection (Orsinelli's study was a retrospective study and some of the studies evaluated FSs only in patients with a history of embolic events, not in patients with prosthetic heart valves).

Our study demonstrated that there was a significant association between anticoagulant status and presence of FSs (PT and INR before TEE examination), where INR before examination and the average INR through the month before TEE had means of 2.13±0.54 and 2.21±0.49 in patients with FSs and 2.63 ± 0.55 and 2.55 ± 0.47 in patients without FSs (P-value < 0.001). Although Robert et al. suggested no significant relationships between anticoagulant status and presence of strands, their study was retrospective and only with patients mitral prostheses were included.15

After adjustment by logistic regression model, we found that greater values of INR,

bioprosthetic valves, and daily intake of ASA had negative associations with the strands.

The mean time between surgery and TEE examination (age of the prosthesis) was 9.4 ± 7.6 months in the FS+ and 7.1 ± 7 months in the FS- patients, which clinically is non-significant; and the other authors have also suggested that the age of mitral prostheses does not influence the rate of strands.⁵

The mechanical prosthesis, smoke pattern in the left atrium, and clots on the prosthetic valves had positive associations with FSs and taking aspirin showed a preventive effect. Fitting a logistic regression model revealed that only "average INR" (INR > 2.5, P-value < 0.001) and "observing clots on the prosthesis" had significant associations with FSs.

Out of the 300 patients, 156 had aortic prostheses, and FSs were observed on 74 (47.4%) of them. The average INR < 2 had a crude association with strands, with an odds ratio of 4.94. Daily intake of ASA showed no association with FSs on the aortic prostheses. AF had a significant relationship with the presence of FSs (P-value < 0.001). The logistic regression model after adjustment for the age of the prostheses and smoke pattern showed a significant negative association (Pvalue = 0.001) for average INR > 2 and significant positive association for AF (Pvalue=0.003) with the presence of FSs. The literature data on the rate of aortic prostheses with FSs are limited, but our major finding for the presence of FSs on all prostheses was hypocoagulant status (INR <2 for aortic prostheses and INR<2.5 for mitral prostheses).

We suggest intense anticoagulation and close follow-up for these patients and follow -up with TEE if there is a history of cardioembolic events, although future research will need to clarify the natural history of patients with prosthetic valve strands and to define optimal therapeutic interventions.

Conclusions

Prosthetic valve strands are frequently detected by TEE. There is a significant association between the presence of strands and patients' anticoagulant status; as a result, we suggest intense anticoagulation and close follow-up for these patients.

Study Limitations

Our study cannot establish a cause-and-effect relation for prosthetic strands and cerebral embolism or elimination of strands by intense anticoagulation. The natural history of patients with prosthetic valve strands is not clear and needs more studies.

Conflict of Interest

No conflicts of interest have been claimed by the authors.

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