INCIDENCE OF LEFT ATRIAL AND PROSTHETIC VALVE THROMBOSIS AFTER MITRAL VALVE SURGERY AND THE ROLE OF EARLY HEPARINIZATION FOR PREVENTION

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Although cumulative incidence of thromboembolic events following prosthetic valve replacement has increased in the recent years, it has been documented that the episode happens mostly in postoparative first month, especially within first ten days. By means of transesophageal echocardiography, non-symptomatic and suspected left atrial and prosthetic valve thrombosis were investigated during early postoperative period following mitral valve surgery, and an effective anticoagulation treatment was emphasized.

Currently, although different anticoagulation regimens are available, there are no comperative studies. In the present study, 141 consequtive patients who underwent mitral valve surgical intervention were evaluated by transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) within early postoperative period. Patients were divided into three groups: Group I (early heparinized), Group II (early fraxiparinized), Group III (not heparinized or fraxiparinized). Postoperative left atrial thrombosis incidence was 16.1% in group I, 0% in group II, and 29.5% in group III. Postoperative prosthetic valve thrombosis incidence was 9.6% in group I, 15.3% in group II, and 5.6% in group III. Atrial fibrillation, left atrial thrombectomy and left atrial SEC were found to be the causative factors in left atrial thrombosis formation in both univariant and multivariant analyses.

Left atrial and prosthetic valve thrombosis formation after mitral valve surgical interventions were higher than we expected. Heparinization during early postoperative period seemed to decrease this incidence.

Although there are no studies available concerning the use of low molecular weight heparins (LMWHs) in patients with prosthetic valves, in the present study we suggest that fraxiparine is more effective, easily useable and has less advers effects compared to standard heparin.

Key words: thromboembolism, prosthetic valve thrombosis, anticoagulation, mitral valve surgery

Thromboembolic events remain as one of the most important determinants of morbidity and mortality in patients with native valvulary heart disease and in patients who undergo prosthetic valve replacements (1). Although cumulative incidence of thromboembolic events following prosthetic valve replacement has increased in the recent years, it was documented that the episode happens mostly at the postoparative first month, especially within first ten days (2). By means of transesophageal echocardiography, non-symptomatic and suspected left atrial and prosthetic valve thrombosis were ruled out during early postoperative period following mitral valve surgery , and an effective anticoagulation was emphasized(3-5). Currently, there are different anticoagulation regimens used in different centers. While oral anticoagulation is started in postoperative first day without preceeding heparinization in some clinics, only heparine is used for anticoagulation during early postoperative period in the others (1).

Although most of the authors suggest heparinization during early postoperative period (1,2), there are no comperative studies on the issue. Moreover, there is not any experience in low molecular weight heparin use following mitral valve replacement (MVR).

In the present study, the aim was to investigate incidence and effective factors in left atrial and prosthetic valve thrombosis formation and to compare non-fractionalized standard heparin with low molecular weigth heparin by means of transthoracic and transesophageal echocardiography.

PATIENTS AND METHODS

In Koşuyolu Heart and Research Hospital, between September 1995 and May 1997, 141 consequtive patients who underwent mitral valve surgical intervention were evaluated by TTE and TEE within postoperative 15±7th day. Warfarin sodium and acetilsalisilic acid 150 mg per day were administered to all patients on postoperative first day. Patients were followed-up with partial tromboplastin time (PTT) and international normalized ratio (INR) values. INR value was within 2.0-2.5. In addition to oral anticoagulation, 31 patients were given 20.000 IU/day of heparin in 4 divided bolus intravenous doses, 3 to 12 hours after operation, according to drainage amount and controlled by activated clotting time (ACT) (Group I). ACT values were within 1.5-2 times of normal values. Heparin was administreted for 3 days. In 39 patients 15.000 AXa ICU/day of subcutaneous nadroparin sodyum (fraksiparin) was given in divided 2 doses for two days (Group II). 71 patients were given only warfarin sodyum (Group III). Preoperative, perioperative and postoperative parameters in these three groups were compared with each other by chi-squared, Student's t and Mann Whithney U tests. Chi-squared, Student's t, linear correlation and multiple regression tests were used in order to investigate the factors that affect left atrial and prosthetic valve thrombosis formation. Patient characteristics and preoperative echocardiographic features are shown in Table 1. Among the 141 patients, while 124 underwent MVR, mitral valve reconstruction was performed in 17 patients. Surgical interventions performed are shown in Table 2, while prosthetic mitral valves chosen are shown in Table 3.

Table 1. Patient characteristics and preoperative echocardiographic findings.

	Group I (n=31)	Group II (n=39)	Group III (n=71)
Mean Age	37.6	40.3	35.8
Sex			
Male	65.6%	52.6%	60.6%
Female	34.4%	47.4%	39.4%
Preop CVA	3.1%	5.3%	5.6%
AF	62.5%	57.9%	56.3%
Mean LA dia.(cm)	5.91	5.8	5.61
LA Throm.	16.1%	10.2%	9.8%
LA SEC	28.1%	34.2%	21.1%
LAA Throm	6.4%	5.1%	7%
Preop MVA (cm2)	1.36	1.33	1.19
Preop MR (3 and +)	53.2%	52.6%	67.6%
Pure MS	16.1%	15.3%	22.5%
Preop EF	63.9%	60.9%	62.09%

Table 2. Surgical interventions performed

Procedures	Group I (n=31)	Group II (n=39)	Group III (n=71)
MVR	28	35	61
MitralValve Recons.	3	4	10
Additional procedures			
LAA Lig.	7	8	5
LA Plication	0	1	0
LA Resection	5	0	0
LA thrombus	5	4	9
Tric. Recons.	6	8	21
AVR	7	8	15
Aort Recons.	1	2	1
CABG	1	1	0
ASD closure	1	1	0

Table 3. Prosthetic mitral valves used in MVR.

Prosthetic Valves	Group I (n=31)	Group II (n=39)	Group III (n=71)
SUude	3	4	8
Ultracor	4	5	10
Medtronic	11	15	12
Duramedics(BL)*	-	-	1
Sorin (BL)*	4	6	15
Sorin (TD)**	6	5	13
Carbomedics	-	-	1
Biocor	-	-	1

*BL:Bileaflet, **TD:Tilting disk

RESULTS

During postoperative period, transthoracic and transesophageal echocardiography were performed to 141 patients. Left atrial and prosthetic valve thrombosis were found in 26 (18.4%) and 13 (9.2%) patients, respectively. Localizations of left atrial thrombosis is shown in Table 4.

Table 4. Localization of left atrial thrombosis.

Localization	n	%
Left Atrium	14	53.8
Left atrial app.	2	7.6
Left atrium + left atrial app.	6	23.3
Left atrium+ prosthetic valve	4	15.3
Total	26	100

Of the 24 thrombosis cases in the left atrium, 11 was on the posterior wall, 7 was on the septal wall, 4 was on the lateral wall and 2 was just next to right upper pulmonary vein. It was found that, within different determinants, atrial fibrillation, left atrial spontaneous echo contrast (SEC) and left atrial trombectomy increased left atrial thrombus formation postoperatively (Table 5).

Table 5. Factors that affect left atrial thrombosis formation

	Left atrial Throm.(+) (n=26)	Left atrial Throm. (-) (n=115)	p
Atrial fibrillation	24(%92)	58(%50)	0.0013
Mean LA diameter(cm)	6.13	5.71	0.087
EF(%)	63.3	63.4	0.951
LVESD(cm)	3.8	3.7	0.816
LVEDD(cm)	5.6	5.5	0.800
Left atrial max. grad.	12.3	11.7	0.184
MVA(cm2)	2.68	2.81	0.112
Postop SEC	17	34	0.0006
LA thrombectomy	10(%38.4)	6(%4.2)	0.0001
Age(mean)	39.1	37.9	0.534
LA resection	0(%0)	5(%4.3)	0.3875
PTT (before TEE) (sec)	19.7	20.4	0.87
MY ≥ 3°	14	71	0.140
MY ≤ 2°	12	44	0.104

In addition, linear correlation test showed that while atrial fibrillation, left atrial thrombectomy, left atrial enlargement and SEC increased left atrial thrombosis, fraxiparine administration decreased its formation.

Atrial fibrillation, SEC and left atrial thrombectomy were also found to be independent predictors in multiple regression test.

On the other hand, prosthetic valve thrombosis formation was not associated with any of the determinants according to chi- squared, Student's t (Table 6), lineer correlation and multiple regression tests.

Table 6. Some of the factors that effect prosthetic valve thrombosis formation.

	Pr. valve thr.(+) (n=13)	Pr.valve thr.(-) (n=128)	p
Age(mean)	36.0	38.3	0.673
Atrial fibrillation	8	77	0.9526
Mean LA diam.(cm)	5.70	5.79	0.661
Postop. MVA (cm2)	2.71	2.79	0.789
Postop. max.mit.gr.	12.9	11.8	0.121
Postop. SEK	3	48	0.5363
LA thrombectomy .	2	14	0.6058
Postop. EF(mean %)	61.7	63.4	0.397
PTT (bef.TEE)(sec.)	19.8	20.3	0.901

As it was shown in table 7, there was not any difference between prosthetic valves in terms of prosthetic valve thrombosis formation.

Table 7. Types of prosthetic valves in relation to thrombosis.

	Throm.(+) (n=13)	Throm.(-) (n=111)	Total
St Jude	2(%12.5)	14	16
Sorin BL	2(%7.4)	25	27
Sorin ML	3(%12)	22	25
Ultracor	2(%9.5)	19	21
Medtronic	4(%12.5)	28	32
Carbomedics	0	1	1
Duramedics	0	1	1
Biocor	0	1	1
Total	13	111	124

Comparison of three groups with each other according to left atrial and prosthetic valve thrombosis formation are shown in Tables 8-9 and 10.

While there was not any statistically significant difference within three groups in prosthetic valve thrombosis formation, left atrial thrombosis formation in group I and especially in group II were significantly lower than group III.

Tablo 8. Determinants of thrombus formation in Group I and Group II.

	Grup I (n=31)	Grup II (n=39)	p
Postop. LA throm.	5(%16.1)	–%0	0.03
Postop prost.valve throm.	3(%9.6)	6(%15.3)	0.915
Postop. LA dia.(cm2)	5.15	5.1	0.786
Postop. AF	19	20	0.746
Postop. LA SEC	11	11	0.819
PTT (before TEE (sec)	20.1	2.05	0.80
Postop. EF (%)	63.6	62.9	0.603
Postop. CVA	1(%3.1)	–%0	0.931

Table 9. Determinants of thrombus formation in Group I and Group III

	Group I (n=31)	Group III (=71)	p
Postop. LA throm.	5	21	0.3245
Postop. prost.valve throm.	3	4	0.4555
Postop.LA dia.(cm2)	5.15	5.16	0.931
Postop. AF	19	39	0.866
Postop. SEC	11	29	0.6854
PTT (before TEE (sec)	20.1	19.2	0.6
Postop EF (%)	69.6	62.8	0.651
Postop CVA	1(%3.1)	7(%9.9)	0.4331

DISCUSSION

Although there is a consensus on the use of anticoagulation following mechanical valve replacement, and clinicians try to select the most appropriate one, most of these applications depend on traditional and arbitrary decisions (1). On literature, different kinds of early postoperative period anticoagulation regimens have been reported. These can be summarized as:

1. Oral anticoagulation administration on postoperative first and second days, without heparin (6-9).
2. In addition to oral anticoagulation administration on postoperative first day, intravenous continuous heparinization (20.000 U/day) during postoperative first hours (10,11).
3. Subcutanous heparine administration in addition to oral anticoagulation on postoperative first day (12).
4. Intravenous continuous heparinization (100-200 U/kg/day) for the first three days postoperatively,then, subcutaneous heparin for four days. Oral anticoagulation administration in the postoperative first week (3).
5. Intravenous continuous heparinization (200 U/kg/day) for postoperative first week, then oral anticoagulation administration (13).
6. Intravenous continuous heparinization on postoperative first day, subcutaneous heparin till postoperative seventh day, and oral anticoagulation after then (14).
7. Subcutanous heparin for postoperative ten days, then oral anticoagulation (15).
8. Oral anticoagulation on postoperative first day and dextran solution of 500 cc on early postoperative hours (16).

Tablo 10. Determinants of thrombus formation in Group II and Group III.

	Grup II (n=39)	Grup III (=71)	p
Postop LA throm.	–	21	0.001
Postop prost.valve throm.	6(%15.3)	4(%5.6)	0.3979
Postop. LAdia. (cm2)	5.1	5.1	0.931
Postop. AF	20	39	0.9779
Postop. SEC	11	29	0.3079
PTT (before TEE (sec)	20.5	19.2	0.7
Postop. EF(%)	62.9	62.8	0.651
Postop. CVA	–%0	7(%9.9)	0.1116

Altough there was not any comperative studies about which anticoagulation regimen is the perfect one to be used, most authors suggest that heparinization is necessary during early postoperative period since thromboembolism is highest during this period and oral anticoagulant agents take a few days for achieving therapeutic levels (1,2,17-19). In recent years, by means of TEE, early postoperative anticoagulation administration gained more importance. TEE remains to be the main method in left atrial and prosthetic valve thrombosis evaluation (5,20,21). In a group of studies performed in postoperative second week by TEE, thrombosis, fibrillary strands and SEC in the left atrium and trombosis and fibrillary strands on the prosthetic valve were revealed (3,5). In a study of 129 cases performed in postoperative second week by TEE, Dadez reported that there was prosthetic valve thrombosis and fibrillary strands in 8.5% and 43%, respectively. Dadez also suggested that left atrial SEC was an independent predictor (3). Malerque found 15% thrombosis in left atrium in postoperative 10th day by TEE (5). Both of them used intravenous heparin in postoperative first 3 days, and then subcutaneous heparin for 15 days. They

administered oral anticoagulation after 7th day. Bonnefoy found thrombosis in 11.7% of patients that underwent prostetic valve replacement within postoperative 24 hours and advised to use early heparin administration, in spite of its complications (4). In the present study, we found that left atrial thrombosis formation was 29.5% in non-heparinized and non-fraxiparinized group, while it was 16.1% in heparinized group and 0% in fraxiparinized group. We concluded that heparin or fraxiparine administration decreased left atrial thrombosis formation.

Although there are no studies available concerning the use of LMWHs in patients with prosthetic valves and such a use is not recommended at present (1), we found that fraxiparine was even more successful in decreasing left atrial thrombosis formation compared to heparine.

CONCLUSION

Atrial fibrillation, left atrial thrombectoy, left atrial SEC are the main determinants in early postoperative left atrial thrombosis formation after mitral valve surgical interventions. Heparin or fraxiparine administration during early postoperative period decreases thrombosis formation. Although there were no prior studies on the use of LMWHs, we found that fraxiparine was even more effective in decreasing early left atrial thrombosis formation compared to heparin.

Unlike left atrial thrombosis formation, prosthetic valve thrombosis formation did not seem to decrease by early postoperative heparin or fraxiparine administration.

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