Can Embolic Events Be Predicted by the Properties of Vegetation in Infective Endocarditis? A Single Center Experience

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ABSTRACT

Objective: We aimed to investigate the predisposing factors of embolic events and the role of vegetation properties on the embolic complications for infective endocarditis (IE).
Patients and Methods: The archive records of 119 patients with a definite diagnosis of IE between January 1997 and November 2004 were reviewed for clinical, echocardiographic, microbiologic properties and embolic events.
Results: Major arterial embolization was observed in 28 (23.5%) of 119 study patients on admission. These patients were included in the embolization group. Parameters such as culture positivity (p=0.017, 95% confidence interval (CI)=1.1-24.6) ejection fraction (EF) (p=0.003, 95% CI=1.1-1.4), presence of vegetation (p=0.013, 95% CI=1.1-1.13), size of vegetation (p=0.002, 95% CI= 1.1-2.1), vegetation mobility (p=0.01, 95% CI=2.1-24.5), and chordal rupture (p=0.041, 95% CI=1.07-7.14) were identified as significant predictors of embolization.
Conclusion: In patients with infective endocarditis, culture positivity, EF, presence of vegetation, vegetation mobility, size of vegetation, and the presence of chordal rupture are the variables with predictive value for embolization. Further prospective controlled trials are required in order to identify the predictive value of the presented data and other variables.
Key Words: Infective endocarditis; embolic events; vegetation

Enfektif Endokarditte Embolik Olaylar Vejetasyon Özellikleri ile Predikte Edilebilir mi? Tek Merkez Deneyimi

ÖZET

Amaç: Kurumumuzda modifiye Duke kriterlerine göre enfektif endokardit tanısı konularak takip ve tedavi edilen 119 enfektif endokardit hastasında embolik olaylar açısından predispozan faktörlerin ve vejetasyon özelliklerinin embolik komplikasyon üzerine olan etkilerinin araştırılmasıdır.
Hastalar ve Yöntem: Kurumumuz hastane kayıtları incelenerek, Ocak 1997-Kasım 2004 tarihleri arasında başvuran ve enfektif endokardit tanısı konan 119 hasta klinik, ekokardiyografik ve mikrobiyolojik açıdan değerlendirildi.
Bulgular: Başvuru anında 119 hastanın 28 (%23.5)'inde majör arteriyel emboli gözlemlendi. Bu hastalar emboli grubunu oluşturdu. Kültür pozitifliği (p=0.017, %95 güven aralığı (GA)=1.1-24.6), ejeksiyon fraksiyonu (EF) (p=0.003, %95 GA=1.1-1.4), vejetasyon varlığı (p=0.013, %95 GA=1.1-1.13), vejetasyon büyüklüğü (p=0.002, %95 GA=1.1-2.1), vejetasyon mobilitesi (p=0.01, %95 GA=2.1-24.5), ve korda rüptürü (p=0.041, %95 GA=1.07-7.14) gibi parametrelerin emboli açısından anlamlı prediktörler olduğu tespit edildi.
Sonuç: Endokardit tanılı hastalarda kültür pozitifliği, EF, vejetasyon varlığı mobilitesi ve büyüklüğü ile korda rüptürü varlığı emboli açısından prediktif değere sahip değişkenlerdir. Bu prediktif değişkenlerin ve daha başka değişkenlerin değerinin anlaşılması için daha fazla prospektif kontrollü çalışmaya ihtiyaç vardır.
Anahtar Kelimeler: Enfektif endokardit; embolik olaylar; vejetasyon

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INTRODUCTION

Infective endocarditis (IE) is the microbial involvement of the endothelial surface of the heart. The characteristic lesion of IE, vegetations are commonly present on the heart valves, also can be present in any area of the endocardium. Vegetations are responsible from embolic events which might cause fatal complications[1]. In recent years, morphologic features of the vegetations are visualized better with the widespread application of transesophageal echocardiography (TEE) in addition to transthoracic echocardiography (TTE)[2,3]. Hence, contrary to the results of some studies[3,4] vegetation size and mobility are shown to be important predictors of embolic events in recent researches[5-7]. So we aimed to investigate the predisposing factors of embolic events and the role of vegetation properties on the embolic complications in IE patients.

PATIENTS and METHODS

Design

The study population consisted of 119 consecutive patients who admitted to our center between January 1997 and November 2004 with a definite IE diagnosis based on modified Duke criteria. The patients with suspected IE were excluded. The patients were retrospectively evaluated using archive records.

Patient Evaluation

All patients were evaluated with routine physical examination, postero-anterior chest X-ray, electrocardiography, routine biochemistry, full blood count, blood cultures, transthoracic and transeusophageal echocardiography. Data were collected onthe following: age, sex, underlying heart disease, predisposing conditions for bacteremia, complications, echocardiographic and microbiological findings.

Microbiologic Evaluation

Three sets of 10 cc blood samples were obtained on admission from each patient for blood cultures under sterile conditions. The sampling procedures were performed every 60 minutes from seperate veins. conventional manual systems (BacT/ALERT3D, BioMérieux, Durham, NC, USA) were used withat least three aerobic and anaerobic bottles inoculated with blood for at least 14 days. The Wright seroagglutination test was used for brucella microorganisms

Echocardiography

All patients were evaluated with TTE and 67 (56%) of the patients underwent TEE. All procedures were performed by Vingmed CFM 800 (Horten, Norway) and Vivid 5 (GE, Horten, Norway) echocardiograhic devices using 3.25 MHz multifrequency transthoracic and 5 MHz multiplane transesophageal transducers. Echocardiographic data were classified by using the Duke echocardiographic criteria. Major echocardiographic findings included vegetation, abscess, new partial dehiscence of the prosthetic valve and valvular perforation. Vegetation was defined as a fixed or oscillating mass adherent to a leaflet or other cardiac structure with a distinct echogenic structure and independent motion. The lesion had to be visible in multiple views and detectable during the complete cycle. The measurements of vegetations were obtained in various planes, and the maximal length was used. In the presence of multiple vegetations, the largest value was used for analysis. The mobility of the vegetation was evaluated using a four-point scale.

Statistical Analysis

The variables are expressed as frequency or mean±standart deviation. Cathegorical variables are compared by Chi-square or Fisher's exact test and continuous variables are compared by Student's t test or Mann-Whitney U test, whichever is appropriate.

The parameters which remained significant in the univariate analysis were included in the multivariate analysis model and evaluated by stepwise logistic regression analysis. A p value <0.05 was accepted as statistically significant in all analysis.

RESULTS

Major arterial embolization was the reason of admission in 28 (23.5%) of 119 study patients. These patients were labeled as embolization group (Group 1) and the remaining patients were labeled as non-embolization group (Group 2). Distribution of the localization of embolization was cerebral (n=13), pulmonary (n=8), peripheral (n=4), renal (n=1), both renal and cerebral (n=2) (Graphic 1).

Vegetation was present in all patients who admitted with embolization in TTE or TEE examination (Group 1). Vegetation was not observed in 18 patients of Group 2. The major endocarditis criteria was the presence of abscess in 14 patients and new paravalvular prosthetic valve regurgitation in 4 patients.

When the echocardiographic parameters of the 2 groups are compared, pulmonary artery systolic pressures, left ventricular end diastolic diameters and left atrial sizes were similar. End systolic diameters of group 1 were significantly lower (3.4±0.6 cm vs 3.7±0.6 cm, p=0.027, z=-2.215). The ejection fractions of the patients in embolization group were significantly higher (%64±5.4 vs %58.5±9.1, p=0.001, z=-1.315).

Table 1. Complications of infective endocarditis with respect to presence of embolization

	Embolus +	Embolus -	p value
Periannular abssess	3 (10.7%)	11 (12.1%)	0.844
Chordal rupture	6 (21.4%)	7 (7.7%)	0.042
Perforation of cusp or leaflet	6 (21.4%)	21 (23.1%)	0.895
Progression of CHF	12 (42.9%)	52 (57.1%)	0.185
Pericardial effusion	2 (7.1%)	3 (3.3%)	0.336
Renal failure	6 (21.4%)	14 (15.4%)	0.563

CHF: Congestive heart failure

The embolization group patients were significantly younger (34.2±15.3 years vs 41.4±16.1 years, p=0.037).

Chordal rupture was more common in the embolization group (21.4% vs 7.7%, p=0.042). The frequency of other IE complications, such as periannular abscess, leaflet or cuspal perforation, development of congestive heart failure, renal complications and pericardial effusion were similar in two groups (Table 1).

Table 2. Comparison of culture positivity and causative pathogen with respect to presence of embolization

	Embolus +	Embolus -	p value
Culture positivity	18 (64.3%)	31 (34.8%)	0.006
Str.Viridans	2 (11.1%)	8 (25.8%)	0.196
MSSA	8 (44.4%)	5 (16.1%)	0.035
MRSA	2 (11.1%)	11 (38.7%)	0.059
Other	6 (11.6%)	6 (7.6%)	0.062

MSSA: Methicilline sensitive Staphylococcus aureus; MRSA: Methicilline resistant Staphylococcus aureus

Table 3. Localization of vegetation with respect to presence of embolization

	Embolus +	Embolus -	p value
Aortic valve	8 (28.6%)	35 (38.5%)	0.341
Mitral valve	10 (35.7%)	26 (28.6%)	0.472
Aortic + mitral valve	2 (7.1%)	21 (23.1%)	0.048
Tricuspid valve	3 (10.7%)	4 (4.4%)	0.353

Table 4. Univariate and multivariate analysis

	Univariate analysis	Multivariate analysis	
	p value	p value	%95 CI
Presence of vegetation	0.007	0.013	1.1-1.13
Vegetation size	0.002	0.002	1.1-2.1
Vegetation mobility	0.001	0.01	2.1-24.5
Vegetation number	NS		
Mitral valve	NS		
Aortic + mitral valve	0.048	NS	
Aortic valve	NS		
Tricuspid valve	NS		
Culture positivity	0.006	0.017	1.1-24.6
MSSA	0.035	NS	
EF %	0.001	0.003	1.1-1.4
LV ESD	0.027	NS	
Chordal rupture	0.042	0.041	1.07-7.14
Tachycardia	0.029	NS	
Age	0.037	NS	
Duration of symptoms	0.001	NS	
Leucocytosis	0.023	NS	

NS: Not Significant, EF: Ejection Fraction; MSSA: Methicilline sensitive staphylococcus aureus; LV ESD: Left Ventricule End Systolic Diameter; CI: Confidence Interval

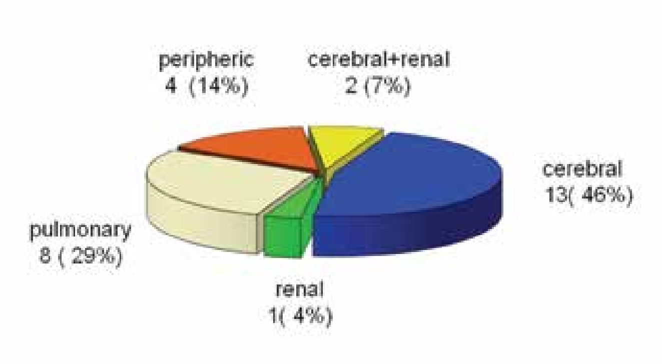
Culture positivity, particularly methicilline sensitive Staphylococcus aureus (MSSA), methicilline resistant Staphylococcus aureus (MRSA) was more frequent in the embolization group (culture positivity; 64.3% vs 34.8%, p=0.006, MSSA; 44.4% vs 16.1%, p=0.035 and MRSA; 11.1% vs 38.7%, p=0.059) (Table 2).

When localization of vegetation is concerned, combined aortic and mitral valve involvement was more common in the embolization group (7.1% vs 23.1%, p=0.048) (Table 3).

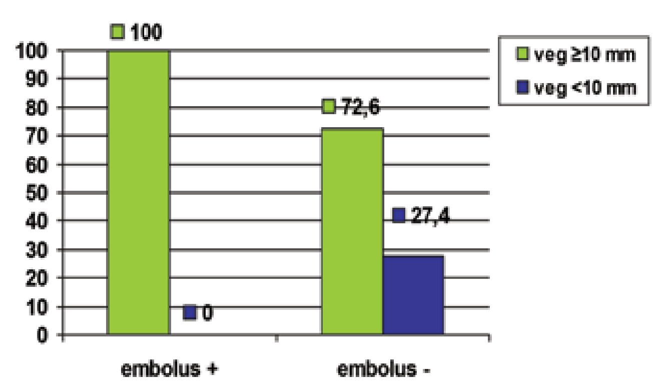
The mean size of the vegetation was >10 mm in all patients in embolization group (100% vs 72.6%, p=0.02) (Graphic 2). Vegetation mobility was also more frequent in the embolization group (82.1% vs 47.7%, p=0.001). The number of vegetations were similar in both groups (p>0.05).

Logistic Regression Analysis

The parameters which were significant in the univariate analysis were evaluated by stepwise logistic regression analysis to



Graphic 1. Distribution of embolic complications in patients with infective endocarditis



Graphic 2. Presence of embolic events with respect to size of vegetation (veg) (10 mm cut off)

determine the predictors of embolization. Presence of vegetation, size of vegetation, localization of vegetation, vegetation mobility, culture positivity, the causative pathogen, age, ejection fraction (EF), left ventricular end systolic diameter and chordal rupture were evaluated as potential variables; culture positivity, EF, presence of vegetation, size of vegetation, vegetation mobility and chordal rupture were identified as significant predictors of embolization. Other variables lost their statistical significance in the logistic regression analysis (Table 4).

DISCUSSION

Embolic events are observed in 10-50% of cases with IE(5,8-12). However the exact incidence of this complication is not identified. The incidence of embolization was 23.5% in our study population, which is comparable to other studies. Twenty patients admitted with embolization while 8 patients suffered from embolization during follow-up. The presence of embolization was evaluated by clinical and radiologic methods in our study. In some series, the presence of embolization was evaluated by computerized tomography which permitted diagnosis of silent embolization.

In a study by Di Salvo et al., the frequency of embolic events was 37% (n=68). The authors suggested that early surgical intervention could have resulted in reduced vegetation progression and embolic event rates(9) In our series most of the patients (76%, n=90) were surgically treated in addition to medical treatment. In the study of Di Salvo et al., the patients underwent surgical intervention after mean 10 days follow-up. However in our study, the duration was 22 days in the embolization group and 28 days in the non-embolization group.

One of the main objectives of our study was to investigate the significance of vegetation properties on embolic events. A vegetation was diagnosed as mobile when it is pedinculated and/or has fibrillary components at the edges.

In our study, the presence of vegetation on echocardiographic examination, vegetation size >10 mm and mobility of vegetation were identified as predictors of embolization(10). Di Salvo et al., identified only vegetation mobility and vegetation size as significant predictors of embolic events(9), while Rohmann et al., reported vegetation size >10 mm and mitral valve involvement as risk factors for em bolization in their prospective study which evaluated 118 patients(7). In another study by Lutas et al., size of vegetation was not identified as a predictor of embolization(4). However in their study, the authors did not apply TEE which could detect vegetations more precisely than TTE.

Age, sex and localization of vegetation were not significant predictors of embolization in the study of Di Salvo et al. In our study also these variables did not have any significant effect on embolization(9).

In our study, culture positivity had predictive value for embolic events. However the type of causative pathogen did not predict embolization. Staphylococcic endocarditis was significant in the univariate analysis of the study by Di Salvo et al., which lost its predictive value in the multivariate analysis. They also revealed that the frequency of embolic events reduced in the culture negative group(9).

In our study, chordal rupture was significantly more common in the embolization group. There was no relationship between embolization and leaflet or cuspal perforation, pericardial effusion and periannular abscess which shows periannular extention of IE.

We hypothesize that; motion amplitude of vegetation might increase the possibility of vegetation fragmentation. This suggestion merits to be evaluated by further researches.

Limitations of the Study

Routine computerized tomography, magnetic resonance imaging and ultrasonography was not performed, hence only clinically evident cases of embolization were included. As the frequency of silent embolization could not be detected, the true incidence of embolization might be more than reported.

In most of the study patients, embolic events occurred before admission to hospital which could have resulted in underestimation of the real size of vegetations.

In 8 of the study patients, embolic events happened after antibiotherapy and the effects of antibiotherapy over vegetation and embolic events could not be followed up in these patients.

Relatively low number of patients in the embolization group could have resulted in the significance of coincident findings in univariate analysis. These variables lost their significance in the multivariate analysis.

CONCLUSION

In patients with infective endocarditis, culture positivity, ejection fraction, presence of vegetation, vegetation size, vegetation mobility and the presence of chordal rupture are the variables with predictive value for embolization. Further prospective controlled trials are required in order to identify the predictive value of the presented data and other variables.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

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