Bacterial Endocarditis Complicating Mitral Annular Calcification: A Clinical and Echocardiographic Study

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Background and aim of the study: **Although described in a number of necropsy studies, endocarditis on mitral annular calcification (MAC) has rarely been reported during life. The study aim was to assess the frequency and specific features of bacterial endocarditis complicating MAC.**
Methods: **Data relating to 62 cases of infective endocarditis of the native mitral valve diagnosed with multiplane transesophageal echocardiography (TEE) over a five-year period were collected prospectively.**
Results: **Among 62 patients, 15 (24%) had vegetations originating from a calcified mitral annulus (group 1), while 47 had classic leaflet endocarditis (group 2). Group 1 patients differed significantly from group 2 patients with regard to: (i) higher incidence of diabetes mellitus and cancers; (ii) initial clinical presentation, with febrile coma or meningoencephalitis in 53% of cases; (iii) echocardiographic features, with significantly greater vegetations, presence of calcium-dense echoes within the vegetation, high frequency of ring abscess, and high frequency of para-annular ventriculoatrial leakage; and (iv) poorer clinical outcome, with 53% in-hospital mortality.**
Conclusion: **MAC appears to be an underestimated predisposing factor for a particularly severe type of bacterial endocarditis. The use of multiplane TEE should improve current knowledge of this disease.**

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Mitral annular calcification (MAC) is one of the most common cardiac abnormalities in elderly patients. It is found in 8.5 to 12.5% of adult autopsies (1,2), invariably in patients aged over 50 years, and in up to 47% of patients aged over 90 years (3,4). MAC is considered to be the result of a degenerative process within the cardiovascular fibrous skeleton. In younger patients, the condition can be seen in association with factors that accelerate this process, including connective tissue diseases (5), metabolic disorders (6,7), or conditions that increase mitral annular stress (8,9). MAC is generally considered as a benign finding, with systolic and/or diastolic murmurs as the only clinical consequence. Although heart block (2,8), valvular dysfunction (1,2,10) or stroke (11-14) have been described as complications of MAC, scant attention has been paid to infection in this respect.

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Bacterial endocarditis involving a calcified mitral annulus fibrosus seems to be very uncommon. Although this complication has been described in several autopsy series (3,15-17), only a few isolated cases have been documented during life (18-20). Therefore, a prospective study was conducted with the aim of assessing the actual incidence and specific features associated with this disease compared to 'classic' bacterial endocarditis involving the mitral leaflets.

Clinical material and methods

Patients

All consecutive patients referred to the present authors' ultrasound laboratory for clinical suspicion of infective endocarditis (IE) involving the native mitral valve during a five-year period were studied. Patients with valve prosthesis were excluded, and only those in whom the diagnosis of IE was considered definite were included.

Echocardiography

Echocardiographic examinations were performed using Hewlett-Packard Sonos 1500 and 2500 ultrasound systems; a 2-2.5 MHz transducer was used for

Table I: Patient medical history.

Parameter	Group 1 Annulus endocarditis (n = 15)	Group 2 Leaflet endocarditis (n = 47)	p-value
Age (years)*	70.8 ± 7.5	65.6 ± 14.2	NS
Age (years; range)	(58-80)	(30-92)	
Sex ratio (M:F)	1.14	3.3	NS
Rheumatic fever (%)	0	6.4	NS
Hypertension (%)	60	32	NS
Coronary heart disease (%)	20	21.2	NS
Diabetes mellitus (%)	80	17	<0.005
High serum cholesterol (%)	20	16.7	NS
Pacemaker (%)	20	0	NS
Congestive heart failure (%)	13	8.5	NS
Chronic renal failure (%)	20	6.4	NS
Cancers (%)	40	13	<0.05
Cirrhosis (%)	27	6.4	0.09

*Values are mean ± SD.
NS: Not significant.

transthoracic evaluation, and a 3.7-5 MHz omniplane probe for transesophageal assessment. Careful scanning of the mitral valve was performed by gradually rotating the imaging plane from 0 to 180° at different levels in the esophagus in order to determine precisely the attachment site of the vegetations.

The study population was divided into two groups according to the site of vegetations: group 1 consisted of patients with endocarditis of the mitral annulus, while group 2 patients had mitral leaflet endocarditis.

The following echocardiographic parameters were studied: prevalence and severity of MAC (graded as mild, moderate or severe); number and size of vegetations; severity and mechanism of mitral regurgitation; and associated infective lesions, with particular attention being paid to annular abscesses.

Clinical, biological (blood cell count, serum levels of C-reactive protein, fibrinogen, creatinine, calcium, phosphorus and glucose) and bacteriological data were also collected.

Statistical analysis

For qualitative data, a comparison between groups 1 and 2 was made using chi-square analysis. For quantitative data, variance distribution and homogeneity between the two groups were first assessed using Bartlett's test. If similar, ANOVA was used; if not, the non-parametric Wilcoxon test was used. A p-value <0.05 was considered to be statistically significant.

Results

During the study period, 62 cases of IE involving the native mitral valve were diagnosed. In 15 patients, transesophageal echocardiography (TEE) demonstrated the presence of infective lesions arising from a cal-

Table II: Pertinent clinical data on admission.

Parameter	Group 1 Annulus endocarditis (n = 15)	Group 2 Leaflet endocarditis (n = 47)	p-value
Mean temperature (°C)*	39.5 ± 0.83	38.8 ± 0.93	NS
Coma or mental confusion (%)	53	10.6	<0.005
Stroke (%)	33	17	NS
Heart murmur (%)	60	87	0.09

*Values are mean ± SD.
NS: Not significant.

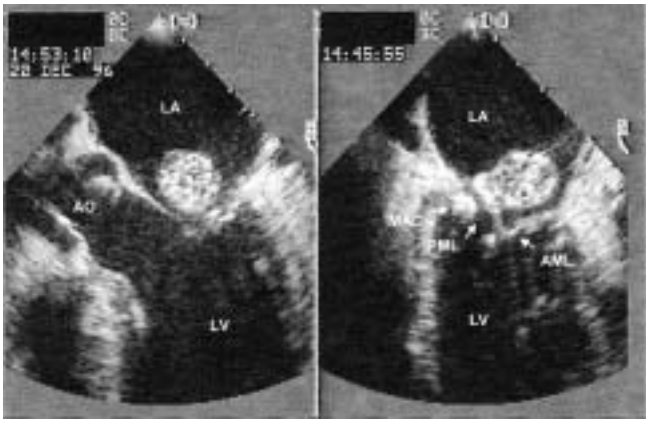

Figure 1: Transesophageal echocardiography showing a large vegetation, 'riddled' with microcalcifications. In the horizontal plane (left), the vegetation seems to be attached to the posterior mitral leaflet; in the 105° oblique plane (right), implantation on the calcified mitral annulus is obvious. AML: Anterior mitral leaflet; AO: Aorta; LA: Left atrium; LV: Left ventricle; MAC: Mitral annular calcification; PML: Posterior mitral leaflet.

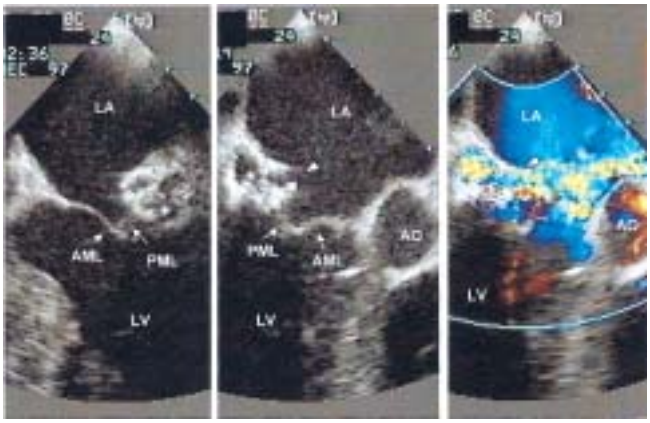

Figure 2: Same patient as Figure 1. Transesophageal examination conducted three weeks later. The vegetation has disappeared; instead, a partitioned abscess cavity is present within the annulus (asterisk), and color-flow Doppler study shows fistulization of the ring abscess into the left atrium (arrowhead). Left panel: Horizontal plane; middle and right panel: 115° oblique plane. AML: Anterior mitral leaflet; AO: Aorta; LA: Left atrium; LV: Left ventricle; PML: Posterior mitral leaflet.

cified mitral annulus (group 1), while in 47 patients vegetations were found attached to the mitral leaflets (group 2).

Comparisons between groups 1 and 2 with regard to medical history, together with clinical, biological and echocardiographic data are detailed in Tables I-V.

Associated diseases

Group 1 patients were slightly, but not significantly, older than group 2 patients, and carried a high prevalence of morbid conditions, including hypertension, diabetes mellitus, chronic renal insufficiency, cirrhosis, pacemaker usage, and recently cured or active malignant disorders (two colic adenocarcinomas, two rectal adenocarcinomas, one hepatocarcinoma, one myeloma). In addition, one patient had stage IV arteritis with leg amputation and stump chronic osteitis, and one had bullous pemphigoides and systemic sarcoidosis. All the patients had at least one debilitating condition, including diabetes, cirrhosis, neoplasia and chronic renal failure. The prevalence of both diabetes and cancer was significantly higher in group 1 than in group 2.

Table III: Hematological laboratory data on admission.[*]

Parameter	Group 1 Annulus endocarditis (n = 15)	Group 2 Leaflet endocarditis (n = 47)	p-value
Hemoglobin (g%)	10.4 ± 1	11.9 ± 2.3	<0.05
WBC count (per mm^3)	13,550 ± 5,197	11,516 ± 4,717	NS
Neutrophils (per mm^3)	11,400 ± 5,054	9,585 ± 4,707	NS
Platelets (per mm^3)	262,500 ± 204,716	214,418 ± 85,299	NS
CRP (mg/l)	157.8 ± 103.7	103.9 ± 79.3	NS
Fibrinogen (g/l)	6.28 ± 2.7	4.94 ± 1.5	<0.05
Calcium (mg/l)	83.6 ± 12.3	86.3 ± 7	NS
Phosphorus (mg/l)	44.5 ± 21.8	32.3 ± 11.1	NS
Creatinine (mg/l)	20.2 ± 18.2	12.8 ± 8.8	NS
Urea (g/l)	0.85 ± 0.14	0.59 ± 0.7	NS
Glucose (g/l)	2.53 ± 1.5	1.27 ± 0.4	<0.05

[*]Values are mean ± SD.
NS: Not significant.

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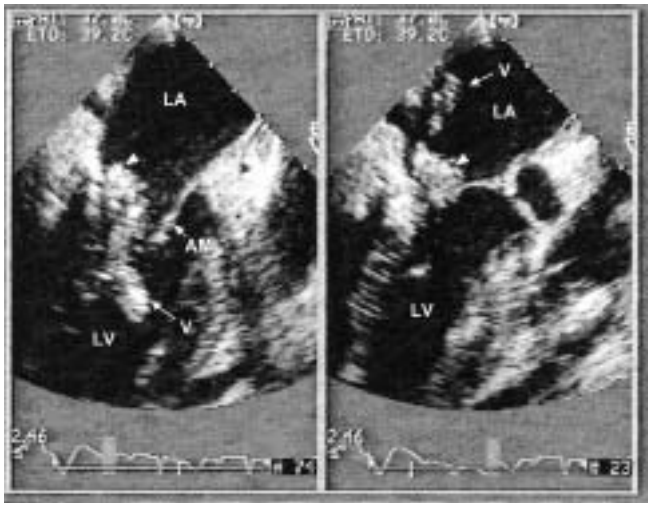

Figure 3: Transesophageal echocardiography. Example of a long vegetation, containing calcium-dense echoes, attached to the posterior part of the calcified mitral ring which takes on a 'puffed-up' appearance (arrowhead). (116° oblique plane; left: Diastole; right: Systole). AML: Anterior mitral leaflet; LA: Left atrium; LV: Left ventricle; V: Vegetation.

Figure 4: Transesophageal view at 130°. Left: Vegetation attached to the calcified mitral annulus. Right: Color-flow Doppler study showing perforation of the posterior mitral leaflet at the level of its insertion on the annulus. AML: Anterior mitral leaflet; AO: Aorta; LA: Left atrium; LV: Left ventricle; MAC: Mitral annular calcification; PML: Posterior mitral leaflet.

Clinical data on admission

Heart murmurs were absent in 40% of group 1 patients, and stroke was seen in 33% of group 1 patients versus 17% of group 2, though the difference was not significant (Table II). More importantly, febrile coma, or a clinical picture of meningoencephalitis associated with mental confusion, was the initial clinical presentation in 53% of group 1 patients, compared to 11% in group 2 ($p < 0.005$).

Table IV: Results of blood cultures.

Organism	Group 1 Annulus endocarditis (n = 15)	Group 2 Leaflet endocarditis (n = 47)	p-value
Staphylococcus sp.	10 (67)	16 (34)	0.07
Staph. aureus	7	10	
Staph. epidermidis	3	6	
Streptococcus sp.	3 (20)	22 (47)	NS
Strep. bovis or *enterococcus* (group D)	1	12	
Strep. equisimilis (group G)	1	0	
Strep. agalactiae (group B)	1	2	
Viridans group streptococci	0	8	
Other organisms	2 (13)	3 (6)	NS
Proteus mirabilis	1		
Escherichia coli	1		
Negative blood cultures	0	6 (13)	

Values in parentheses are percentages.
NS: Not significant.

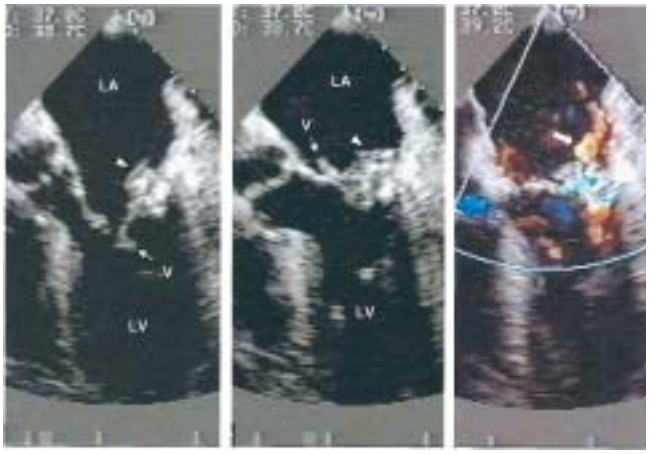

Figure 5: Transesophageal echocardiography. Left and middle panels (horizontal plane, diastole and systole): 'Puffed-up' aspect of the mitral annulus (arrowhead) associated with a vegetation (V). Right panel (10° oblique plane, systole): Perforation near the base of the posterior mitral leaflet (large arrow). LA: Left atrium; LV: Left ventricle.

Blood laboratory data

Group 1 patients were more anemic and had significantly higher serum fibrinogen and glucose levels than group 2 patients. Serum creatinine levels were higher in group 1, though the difference was not statistically significant (Table III).

Bacteriology

Bacteriological investigations showed 100% and 87% positive blood cultures in groups 1 and 2, respectively (Table IV). *Staphylococcus* was found to be the causative organism in 67% of group 1 patients, whereas *Streptococcus* was predominant in group 2. In patients with endocarditis on MAC, the portal of entry was identified in eight cases, suspected in two, and not found in five.

Echocardiography

Transthoracic echocardiography (TTE) showed the presence of moderate to severe MAC in all group 1 patients (by comparison, four group 2 patients had only mild MAC) (Table V). The diagnosis of infective endocarditis was suspected in only two group 1 patients due to the presence of a mobile mass which

Table V: Echocardiographic features.

Parameter	Group 1	Group 2 Annulus endocarditis (n = 15)	p-value Leaflet endocarditis (n = 47)
MAC (%)	100	11	<0.001
MAC severity	Moderate-severe	Mild	
Mitral regurgitation (%)			
None	6.6	0	NS
Grade 1-2	60	34	NS
Grade 3-4	33.3	66	NS
Vegetations*			
No. (range) of vegetations	0.9 ± 0.3 (0-1)	1.3 ± 0.7 (0-3)	0.055
Mean width (mm) (range)	11.7 ± 8.7 (7-34)	4.4 ± 8 (1-14)	<0.01
Mean length (mm) (range)	25.6 ± 16.5 (8-60)	11.9 ± 8 (3-32)	<0.01
Calcifications (%)	80	8.5	<0.01
Associated infectious lesions			
Mitral ring abscess (%)	60	0	<0.001
Aortic ring abscess (%)	0	4.2	NS
Other valve infected (%)	0	32	<0.05
Mitral perforation (%)	73	40	NS
Leaflet perforation (%)	33	40	
Annular perforation (%)	40	0	
Ruptured chordae (%)	0	40	<0.05
Pericardial effusion (%)	33	11	NS

*Values are mean ± SD (unless otherwise indicated).
MAC: Mitral annular calcification; NS: Not significant.

was suggestive of vegetation. TEE revealed a number of features that proved to be highly specific for IE on MAC, and significantly different from group 2 patients. A unique, large-sized vegetation containing calcium-dense echoes which was attached to the posterior, most calcified part of the annulus, was most frequently observed (Figs. 1, 3 and 4), while the infected annulus often showed a swollen, 'puffed-up' appearance (Figs. 3 and 5) that evolved to form an abscess cavity (Fig. 2). Fistulization subsequently occurred

Table VI: Previously published cases of infective endocarditis on calcified mitral annulus.

Reference	No. of patients	Infecting organism	Diagnosis	Age/ Sex	Ring abscess	Leaflet perforation	Systemic emboli
Pomerance (3)	3	*Staphylococcus* NA NA	Autopsy	-/3 F	-	-	1/3
Burnside and DeSanctis (15)	7	*Staph. aureus* (5/7) *Strep. pneumoniae* (1/7) *α-Streptococcus* (1/7) *E. coli* (1/7)	Autopsy	58-88 5F/2M	7/7	7/7	6/7 (3/7)
Watanakunakorn (16)	5	*Staph. aureus*	Autopsy	80, M 72, F 75, F 72, F 81, F	2/5	-	4/5
Case 5-1975 (24)	1	*Staph. aureus*	Autopsy	70, F	+	0	+
Arnett and Roberts (17)	1	NA	Autopsy	-	+	-	-
Mambo et al. (25)	5	*Staph. aureus* (3/5) Unknown (2/5)	Autopsy	60, M 69, F 75, F 90, F	5/5	4/5	4/5
Marier et al. (34)	1	*Serratia marcescens*	Autopsy	78, M	+	+	+
Fulkerson et al. (8)	3	*Staph. aureus* *α-Streptococcus* *Enterococcus*	Clinical	-	-	-	-
Chaitin et al. (26)	1	*E. coli*	Autopsy	84, M	+	0	0
Fernicola and Roberts (27)	9	*Staph. aureus* (7/9) *β-Streptococcus* (2/9)	Autopsy	45-85 3F/3M	2/9	-	4/9
Schecter et al. (23)	1	'Gram-+ organisms'	Autopsy	86, F	+	0	+
D'Cruz et al. (18)	1	*Staph. aureus*	TTE	40, F	+	0	+
Charney et al. (29)	1	*Strep. pneumoniae*	TEE	79, F	+	0	0
Tunick et al. (19)	1	*Strep. sanguis*	TEE	76, F	0	0	0
Shenoy and Chandrasekaran (30)	1	β-*Strep.* (Group G)	TEE	74, M	0	0	+
Eicher et al. (20)	1	*Staph. epidermidis*	TEE	73, F	+	+	0

with a ventriculoatrial communication (Fig. 2). The adjacent posterior leaflet was also frequently perforated at the level of its insertion on the annulus (Figs. 4 and 5).

Clinical outcome

The clinical outcome of group 1 patients was disappointing. Surgical treatment was undertaken in two patients because of uncontrollable sepsis despite antibiotic therapy; abscess evolution was associated with a submitral left ventricular mycotic aneurysm in one case, and with a very long, life-threatening vegetation in the other case. In both patients the echocardiographic description was confirmed by intraoperative findings: vegetation lay over a blister in the posterior part of the annulus, inside which the calcification was liquefied and disintegrated, and which led into an abscess cavity. In both cases there was a linear perforation at the base of the posterior mitral leaflet. The leaflets and vegetations were removed, the cavities drained and closed with autologous pericardium, and a prosthesis was inserted. Culture of the vegetations grew *Staphylococcus* sp. Both patients died postoperatively from multi-organ failure, presumably in relation to their very poor preoperative condition. Six other patients died during their hospitalization, four from intractable sepsis and multi-organ failure, one from decompensation of cirrhosis, and one from massive brainstem emboli. Finally, group 1 patients had a very high in-hospital mortality rate of 53% compared with that in group 2 (30%; p = NS). Seven patients were still alive at a follow up of between 20 and 45 months. One of these patients was considered to be healed, with moderate, central mitral regurgitation as the only sequela; the other six had fistulized annular abscesses or perforated leaflets with moderate to severe regurgitation. Of these patients, one underwent valve replacement at three months after recovery of sepsis, with good results, and one patient refused surgical treatment. The other patients were not considered for surgery as they were thought to be either asymptomatic or too old.

Discussion

Pathophysiology of infective endocarditis

Bacterial endocarditis usually occurs on valves previously damaged by other disease processes. Among these processes, the potential role of degenerative lesions should not be underestimated, considering their increasing incidence in the aging population. In a study of 63 cases of native valve endocarditis by McKinsey et al. (21), the underlying cardiac lesions were degenerative calcific valvular lesions in 21% (notably, MAC in 6%).

Pre-existing valvular abnormalities induce high-velocity jets that traumatize the endothelium ('jet lesions'); subsequently, aseptic thrombosis develops on these endocardial erosions, providing a nidus for infection (22). Mitral annular calcification may predispose to infection by a similar mechanism, although not involving regurgitant jets: when MAC is severe enough there may be a protrusion of calcium that results in turbulent blood flow and a denuded surface ideal for bacterial adherence (23). Alternatively, calcium may ulcerate through the left atrial endocardium and be responsible for thrombus formation (13,14), with possible subsequent colonization by an infectious organism.

Pathological reports

Several reports have been made concerning IE of the calcified mitral annulus, the majority having been based on autopsy studies. The present authors identified 34 anatomic descriptions (3,15-17,23-27,34) among 42 reported cases (Table VII). One important postmortem study of MAC, where endocarditis was first mentioned, was reported by Pomerance in 1970 (3). This author reviewed 258 cases of mitral ring calcification seen among 3,334 necropsies, and described a number of complications. In particular, bacterial endocarditis was seen in three patients, one of whom died from embolic staphylococcal meningitis. Burnside and DeSanctis (15) subsequently reported the pathological findings in seven cases of IE on MAC. In a study by Watanakunakorn (16), calcified mitral annulus fibrosus was the site of vegetations in five cases among 16 necropsy patients who died from *Staphylococcus aureus* endocarditis. Five other cases among 20 adults with fatal endocarditis were reported by Mambo et al. (25). Fernicola and Roberts (27) studied at necropsy 63 patients with active IE of the native mitral valve; among these patients, MAC was the pre-existing disease in nine cases (14%), with *Staph. aureus* being the infecting organism on seven occasions (78%). A few single cases of MAC have also been reported (17,23,24,26,34), and the pathological findings in these have been strikingly uniform. First, the infection is most often of the posterior leaflet, beneath which the calcification was the heaviest and deformity the greatest. Second, the vegetations were always found close to the origin of the valve and communicated with deep-seated abscesses in and around the calcified ring. Third, perforation of the leaflet adjacent to the infection was seen in most of the cases. Fourth, no patient had infection or rupture of mitral chordae; and fifth, systemic emboli were very frequently observed (15).

Frequency of sepsis on MAC

Clinical series about endocarditis and MAC are vir-

tually non-existent. Fulkerson et al. (8), when reviewing the clinical features of 80 patients with radiographically proven MAC, reported an incidence of endocarditis of 3.7% (3/80). In a prospective study, Aronow et al. (28) demonstrated a higher incidence of bacterial endocarditis in elderly patients with MAC (3%) than without MAC (1%) at a mean follow up of 39 months. Echocardiographic descriptions in the literature have been restricted to five isolated cases, one with use of TTE (18), and four with TEE (19,20,29,30). The scarcity of such reports contrasts with autopsy series, where this diagnosis represented 14% of 63 infective endocarditis isolated to the native mitral valve in the study of Fernicola et al. (27), 25% of 20 fatal endocarditis cases in the report by Mambo et al. (25), and 42% of 12 staphylococcal mitral endocarditis cases from the series of Watanakunakorn (16).

The present study is the first clinical and echocardiographic investigation to be conducted in this setting, and the diagnosis represented 24% of the non-prosthetic mitral endocarditis cases seen at the authors' institution over a five-year period. The present results confirm that the frequency of IE on MAC is undoubtedly underestimated, and difficulties in asserting a diagnosis, either clinically or echocardiographically, most likely account for this discrepancy.

Clinical features

The results of the present study have enabled a clinical picture of this disease to be outlined. Unlike formerly published cases, where the female:male ratio was 2.3:1, 53% of the present patients were male. The mean age was 71 years, compared to 66 years in patients with leaflet endocarditis; among the 32 published cases where information was available, the mean age was 72 years. In the study of Fernicola and Roberts (27), patients with IE and MAC were significantly older than those without MAC (mean age 66 versus 46 years).

Traditionally, elderly patients and those on hemodialysis are more likely to develop severe MAC. From the present data, important additional risk factors for developing IE on MAC appear to be diabetes mellitus, malignant disorders and cirrhosis. In previous publications, a number of predisposing conditions were similarly identified: cirrhosis and hepatobiliary disorders were present in 43% of cases in the study of Burnside et al. (15); hemodialysis patients represented 55% of the cases of Fernicola and Roberts (27), and 25% for Mambo et al. (25); 40% of the patients in the latter study had undergone abdominal surgery, compared with 20% in the present cohort.

With regard to initial clinical presentation, mental confusion or coma was the main feature in the present series (60%); the same observation was made in 60% of cases by Watanakunakorn (16), and in three isolated cases (18,23,25). This finding could be related to a high frequency of emboli. Among six of the present patients with such symptoms, three were shown to have cerebral emboli, and two had metastatic staphylococcal epidural infection with positive lumbar puncture. These findings were in agreement with the high frequency of cerebral and peripheral emboli found at autopsy in most studies, and were presumably related to the size of the vegetations.

Echocardiographic features

An echocardiographic diagnosis of IE in MAC is difficult to achieve. The sensitivity of TTE with regard to the diagnosis of IE has been reported to decrease to 45% in patients aged over 70 years as compared with 75% in patients aged <50 years, in relation to more frequent degenerative calcific valvular lesions and prosthetic valves (36). In the present patients, TTE usually showed the presence of moderate to severe annular calcification, but in most cases did not allow the identification of vegetations because of artifacts and shadowing in the vicinity of the calcification. TEE offers the same advantage over TTE as for prosthetic valve or annulus regarding analysis of the atrial aspect of the mitral valve; nevertheless, monoplane TEE does not allow optimal imaging of the posterior region of the annulus where the calcification is usually the thickest, and which is the most frequent attachment site of the vegetations. It is believed that, by using only the TEE transversal plane, a number of diagnoses of small vegetations may be missed, and a number of misdiagnoses of valvular leaflet endocarditis may be made. All of the present TEE examinations were conducted using an omniplane probe; in most cases, the precise attachment site of the vegetation was clear only in the 100-130° imaging planes (Figs. 1, 3 and 4).

The present echocardiographic findings completely matched the pathological descriptions, notably with regard to the two main features of mitral perforation, and ring abscess. Annular abscess is a well-known complication of aortic valve endocarditis, but is considered to be extremely rare in the course of endocarditis on the native mitral valve. In an analysis of 95 necropsy patients with active IE, Arnett and Roberts (17) identified 27 patients with ring abscess, with the aortic annulus being involved in 89% of the cases. Only two patients (7%) had an isolated mitral annular abscess, one of whom had the infection superimposed on a heavily calcified mitral annulus fibrosus. In the present authors' experience, mitral ring abscess is never seen except in association with MAC. The reason is probably that the infective process usually develops at the tip of the leaflets, near the line of closure. The mitral valve has a much greater surface area than aor-

tic cusps. Therefore, infection develops relatively distant from the mitral ring, and embolization or valvular destruction occur before sepsis can reach the annulus. In the case of MAC, the infection develops primarily within the annulus. Moreover, the calcification itself could represent a risk factor of abscess formation, because of the poor diffusion of antibiotics (31). In the mitral annulus, the abscesses usually evolve to fistulization on both the ventricular and atrial sides, producing left ventriculoatrial fistulas. If fistulization on the atrial side does not occur, the cavity may spread by dissecting the adjacent left ventricular or atrial myocardium. Extension within the left ventricular myocardium was observed in one of the present cases and was responsible for an acquired submitral left ventricular aneurysm (20). Otherwise, atrial myocardium may be involved, and two cases of dissecting hematoma of the left atrial wall with pulmonary vein obstruction have been reported (23,26).

Leaflet perforation was reported in all patients by Burnside and DeSanctis (15), and in 80% of cases by Mambo et al. (25), with a particular site being the base of the posterior leaflet, at the junction between leaflet and annulus. Among the present patients, 73% showed mitral regurgitation through a para-annular perforation, but only 33% had a basal leaflet perforation (Fig. 4), whereas in 40% of cases the mitral leak was rather a left ventricular to left atrial regurgitation through a fistulized annular abscess (Fig. 2).

Another important finding in the present study was the particular appearance of the vegetations. A unique, thick and long vegetation, 'riddled' with microcalcifications, seems to be the most characteristic picture (Figs. 1 and 3). The particularly large size is perhaps due to the lesser mobility of the supporting annulus compared to the leaflets, thereby facilitating growth of the vegetation. This may also explain the high embolic rate seen in association with this disease. The presence of calcifications within a 'fresh' vegetation is a specific feature that has not been previously reported. In the present authors' experience, it was almost constantly associated with a 'puffed-up' appearance of the underlying annulus with the same dotted pattern (Figs. 3 and 5). To explain this, the following pathophysiological hypothesis is proposed. First, infection developing within the calcified annulus induces liquefactive necrosis and swelling - the 'pop-corn' effect. Then, as the vegetation sprouts, it drags along some of the calcified matter which produces the echocardiographic appearance.

Prognostic implications

The particularly poor outcome in this series was striking, and may be due to several factors. First, all the patients had associated diseases which, in association with advanced age in some cases, hastened the evolution of sepsis to multi-organ failure. In the study of McKinsey et al. (21), patients with endocarditis on degenerative lesions also had a poorer prognosis than those in the other patient groups, reflecting the presence of coexistent serious medical illness in this patient population. Second, the diagnosis was often delayed, either because there was no heart murmur to call attention to the heart, or because TTE (or even monoplane TEE, as mentioned above) failed to provide adequate data. This left the opportunity for vegetations to grow, and for abscesses to develop. Intra-annular or peripheral metastatic abscesses usually worsen the clinical outcome because of uncontrolled infection and disseminated disease (32). Patients with mitral valve endocarditis and with vegetations >10 mm have been shown to have a higher risk of embolism and death (32,33). Finally, *Staph. aureus* infection has also been shown to be associated with early mortality (32).

Clinical implications

Degenerative calcific lesions - particularly MAC - are common in elderly persons, and are becoming one of the most frequent risk factors for IE; nevertheless, these lesions generally receive little attention as predisposing factors. Bacterial endocarditis on MAC is a dramatic disease that should be suspected when an unexplained sepsis is seen in patients who are either elderly, or who have diabetes mellitus, cancer, cirrhosis or chronic renal failure, so that antibiotic treatment could be started as early as possible. With regard to preventive treatment, there are currently no data available to recommend an antimicrobial prophylaxis for patients with MAC and undergoing dental procedures, considering that none of the patients in the present study, and almost none in the literature, was infected by organisms usually found in the oral cavity. Highly virulent organisms, mainly *Staphylococcus* sp., and some bacteria from the intestinal flora, usually appear to be involved. Therefore, the careful management of wounds, dermatoses and venous access for infusions or hemodialysis seems essential when MAC is present. Particular attention should also be paid to diabetic patients, patients with neoplasia, cirrhosis, and probably post-abdominal surgery. Finally, although a potential risk has not been clearly established, it seems reasonable to recommend antibiotic prophylaxis before digestive or urological endoscopic procedures are conducted in these patients.

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