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BRIEF REPORT

Mural Endocarditis: The GAMES Registry Series and Review of the Literature

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ABSTRACT

Introduction: Mural infective endocarditis (MIE) is a rare type of endovascular infection. We present a comprehensive series of patients with mural endocarditis.
Methods: Patients with infectious endocarditis (IE) from 35 Spanish hospitals were prospectively included in the GAMES registry between 2008 and 2017. MIEs were compared to non-MIEs. We also performed a literature search for cases of MIE published between 1979 and 2019 and compared them to the GAMEs series.
Results: Twenty-seven MIEs out of 3676 IEs were included. When compared to valvular IE (VIE) or device-associated IE (DIE), patients with MIE were younger (median age 59 years, $p < 0.01$). Transplantation (18.5% versus 1.6% VIE and 2% DIE, $p < 0.01$), hemodialysis (18.5% versus 4.3% VIE and 4.4% DIE, $p = 0.006$),

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catheter source (59.3% versus 9.7% VIE and 8.8% DIE, $p < 0.01$) and *Candida* etiology (22.2% versus 2% DIE and 1.2% VIE, $p < 0.01$) were more common in MIE, whereas the Charlson Index was lower (4 versus 5 in non-MIE, $p = 0.006$). Mortality was similar.MIE from the literature shared many characteristics with MIE from GAMES, although patients were younger (45 years vs. 56 years, $p < 0.001$), the Charlson Index was lower (1.3 vs. 4.3, $p = 0.0001$), catheter source was less common (13.9% vs. 59.3%) and there were more IVDUs (25% vs. 3.7%). *S. aureus* was the most frequent microorganism (50%, $p = 0.035$). Systemic complications were more common but mortality was similar.

Conclusion: MIE is a rare entity. It is often a complication of catheter use, particularly in immunocompromised and hemodialysis patients. Fungal etiology is common. Mortality is similar to other IEs.

Keywords: Endocarditis; Mural; Non-valvular endocarditis

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Key Summary Points

Mural endocarditis is a rare but increasingly recognized health care-associated disease that requires a high index of suspicion and a multidisciplinary approach to avoid a relevant morbidity and mortality.

It is associated with intravascular catheter use and immunocompromised patients such as transplantation, cancer and hemodialysis patients.

Fungal etiology and large vegetations are common in mural endocarditis.

INTRODUCTION

Mural infective endocarditis (MIE) is a rare type of endovascular infection that involves the non-valvular endocardium [1–6]. Cases of MIE have been described in *Candida* and *Aspergillus* endocarditis [2, 7–12] as well as in infective endocarditis (IE) caused by other microorganisms more characteristic of valvular endocarditis (VIE) such as *Staphylococcus aureus* and *Streptococcus*. Others have described MIE in intravenous drug users or associated with catheter use [1, 5, 7, 13–17].

Since valves are not involved, diagnosis is often delayed and made only when complications such as systemic or pulmonary embolisms occur, conveying a significant morbidity and mortality. Prognosis of MIE is usually poor according to the literature [3, 5, 18].

Information about MIE comes from isolated case reports or short series of selected cases. The actual epidemiology, relevance and prognosis are unknown. Data on MIE management and outcome are lacking.

We present a series of MIEs from the prospective GAMES registry and a comprehensive review of the literature.

METHODS

Study design

Between January 2008 and June 2018, consecutive patients with IE according to the Duke criteria were prospectively included in the "Spanish Collaboration on Endocarditis—Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España (GAMES)" registry, which is maintained by 35 Spanish hospitals. Multidisciplinary teams evaluated every case and completed standardized case report forms for each IE episode, including clinical, microbiologic and echocardiographic sections and follow-up data.

Literature search

Additionally, we performed a PubMed search that included the search term: "mural endocarditis." We filtered case reports and case series and omitted cases that included valvular or intracardiac device involvement. Inappropriate and inaccessible posts were excluded. A standardized form adapted from that of the GAMES registry was filled in for each literature MIE with enough available information and included in a database. The list of cases included in the literature review is accessible in Supplementary material.

Definitions

We considered *MIE* cases with non-valvular endocardium involvement. Cases with both mural and valvular involvement were excluded from the analysis, as were cases of endovascular infection that could be considered *endarteritis* (involving great vessels, ductus arteriosus, etc.). We considered as *non-mural endocarditis* those cases of infective endocarditis that involved valvular endocardial surfaces [valvular endocarditis (VIE) or those with vegetations involving intra-cardiac devices (pacemakers, implantable cardioverter defibrillators) device-associated endocarditis (DIE)]. IE was defined according to the modified Duke criteria [19].

Age-adjusted Charlson Comorbidity Index was used to quantify comorbidities [20].

Place of acquisition of IE was defined following ICE recommendations [21].

The catheter was considered as the source of endocarditis when the etiologic microorganism was detected in both the catheter and the blood cultures or surgical samples (vegetation, valve or implantable device), or when, from a clinical standpoint, the treating physician considered the catheter was the source.

All patients were evaluated by cardiac surgeons to determine the need for surgery according to international indications [22]. The final decision on surgery was made in agreement with the multidisciplinary endocarditis team at each center.

Both in-hospital mortality (overall mortality rate during the hospital stay) and 1-year mortality were analyzed.

Data analysis

Cases with MIE were compared to cases with non-valvular endocarditis in the GAMES registry (both VIE and DIE). MIEs from the GAMES registry were compared to cases of MIE from the literature.

The quantitative variables were expressed as mean and standard deviation or median and interquartile range; qualitative variables were expressed as frequency and percentage. Continuous variables were compared using the *t*-test, and categorical variables were compared using the χ^2 test or Fisher's exact test when the χ^2 test was not appropriate.

All statistical analyses were performed with SPSS version 25 software (IBM SPSS Statistics 22.0, Armonk, New York, NY: IBM Corp.).

Ethics

The study and the common case report form were approved by the local and national institutional review boards and ethics committees (Comité ético de Investigación Clínica Regional de la Comunidad de Madrid CEIC-R; EC 18/07; date 11/01/2008).

RESULTS

During the study period 3767 patients were included. Of them, 27 MIE (0.7% of total endocarditis) and 3649 non-mural endocarditis [407 (11.1%) DIE and 3242 (88.2%) VIE] were registered in the GAMES database. Moreover, 36 cases from the literature review that provided enough information to analyze were selected.

Differences between mural and non-mural endocarditis in the GAMES registry

General characteristics of mural (Fig. 1) and non-mural endocarditis from the GAMES registry are displayed in Table 1.

Compared to non-MIE, patients with MIE were significantly younger, and MIE was more prevalent in women. Patients with MIE presented a lower age-adjusted Charlson Comorbidity Index, were receiving hemodialysis more often and transplantation was more frequent as underlying disease.

Furthermore, in contrast with VIEs, which were mainly community-acquired (61.7%), the majority of MIEs were hospital-acquired (63%). DIEs were more common in a nosocomial setting and related to medical care.

A striking difference was found in the proportion of MIEs originating from the catheter, which was very high (59.3%) compared to non-MIEs with catheter source (8.8% and 9.7% in DIE and VIE, respectively) ($p < 0.01$).

The microorganisms most frequently implicated in endocarditis in all groups were *Staphylococci*, with a prevalence in MIEs of 29.6%, being 14.8% *S. aureus* and *S. coagulase* negative each, followed by *Streptococci* (25.9%). *Streptococci* were significantly more frequent in MIE and VIE (27.5%) than in DIE (8.1%). Significant differences were found between groups regarding *Candida* etiology (22.2% among MIE versus 2% in DIE and 1.2% in VIE, $p < 0.01$). *Aspergillus* was more common in MIE, though without statistical significance (3.7% among MIE vs. 0.2% in DIE and 0.3% in VIE, $p = 0.144$).

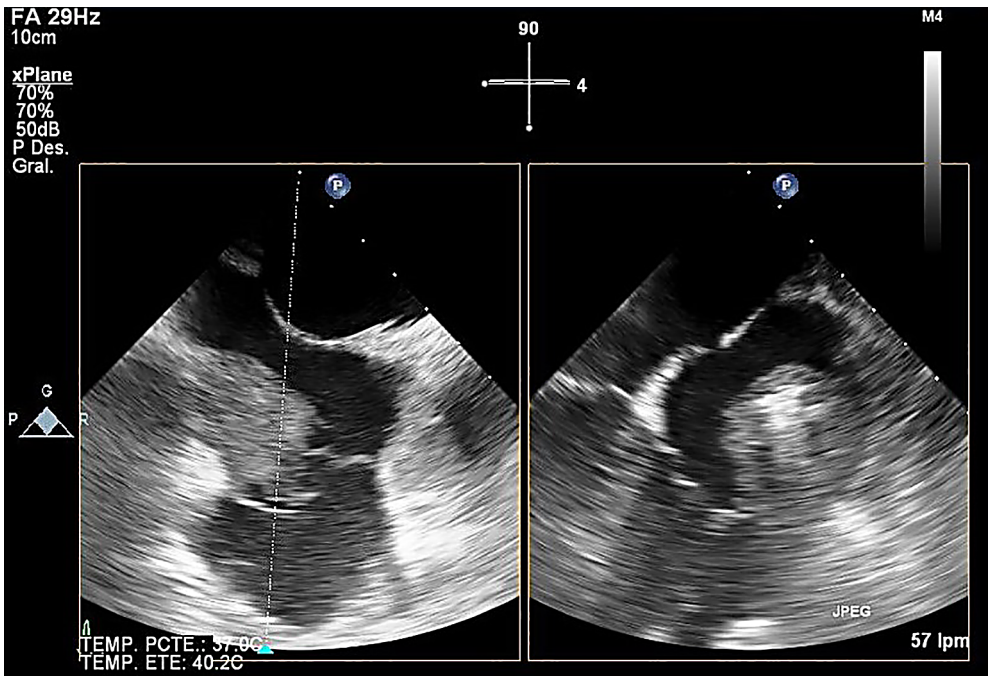

Fig. 1 Simultaneous bi-plane imaging by transesophageal echo showing a large sessile heterogeneous mass (3.9 × 2.8 cm) attached to the lateral and inferior wall of the right atrium, with irregular contour. The tricuspid valve and inferior vena cava were not affected

Table 1 Infective endocarditis in the GAMES registry: mural compared to valvular and device-associated endocarditis

Variables	A Mural (MIE) (*N* = 27)	B Device (DIE) (*N* = 407)	C Valvular (VIE) (*N* = 3242)	*p* value
Age, median (IQR)	59 (46–67)	71 (62–79)	69 (57–77)	< 0.01[a,c]
Sex (male)	11 (40.7)	297 (72.9)	2160 (66.6)	0.001[a]
Lung disease	8 (29.6)	94 (23.0)	570 (17.5)	0.167
Coronary disease	5 (18.5)	149 (36.6)	809 (24.9)	0.09
Heart failure	10 (37.0)	194 (47.7)	1022 (31.5)	0.001[b]
Diabetes	3 (11.1)	154 (37.8)	892 (27.5)	0.009[a]
Trasplantation	5 (18.5)	8 (2.0)	54 (1.6)	< 0.01[a,c]
Heart	2 (7.4)	1 (0.2)	3 (0.1)	0.002[a,c]
Lung	0	0	3 (0.1)	0.761
PM/ICD	2 (7.4)	407 (100.0)	262 (8.0)	< 0.01[a,b]
Peripheral arterial disease	2 (7.4)	49 (12.0)	341 (10.5)	0.678
Cerebrovascular disease	3 (11.1)	43 (10.6)	435 (13.4)	0.946
Neoplasm	6 (22.2)	36 (8.8)	528 (16.2)	0.001[b]
Congenital cardiopathy	3 (11.1)	16 (3.9)	181 (5.5)	0.202
Prior kidney disease	8 (29.6)	127 (31.2)	766 (23.6)	0.001[b]
Prior hemodialysis	5 (18.5)	18 (4.4)	140 (4.3)	0.006[a,c]
Liver disease	3 (11.1)	20 (4.9)	352 (10.8)	0.003[b]
IVDU	1 (3.7)	0	78 (2.4)	0.847
Age-adjusted-Charlson Index	4 (2–6)	5 (3–7)	5 (3–7)	0.006[a,c]
Place of acquisition				
Community acquired	7 (25.9)	156 (38.2)	2001 (61.7)	0.007[b,c]
Hospital acquired	17 (63.0)	184 (45.2)	874 (26.9)	< 0.01[b,c]
Health care associated	3 (11.1)	46 (11.3)	250 (7.7)	0.766
Catheter source	16 (59.3)	36 (8.8)	313 (9.7)	< 0.01[a,c]
Etiology				
Staphylococcus aureus	4 (14.8)	125 (30.7)	708 (21.8)	< 0.01[b]
CNS	4 (14.8)	123 (30.2)	515 (15.9)	< 0.01[b]
Enterococcus	1 (3.7)	20 (4.9)	482 (14.9)	< 0.01[b]
Streptococcus	7 (25.9)	33 (8.1)	893 (27.5)	< 0.01[a,b]
Candida	6 (22.2)	8 (2.0)	39 (1.2)	< 0.01[a,c]

Table 1 continued

Variables	A Mural (MIE) (N = 27)	B Device (DIE) (N = 407)	C Valvular (VIE) (N = 3242)	p value
Unknown etiology	0	35 (8.6)	296 (9.1)	0.795
Enterobacteriaceae	2 (7.4)	10 (2.4)	69 (2.1)	0.225
Neisseria spp.	0	0	2 (0.6)	0.533
Aspergillus spp	1 (3.7)	1 (0.2)	9 (0.3)	0.144
Polymicrobial	2 (7.4)	17 (4.1)	45 (1.4)	0.071
Clinical characteristic				
Vegetation size (mm), median (IQR)	22 (8–39)	12 (7–18)	10 (7–16)	< 0.01[a.c]
Intracardiac complication	1 (3.7)	15 (3.7)	1099 (33.9)	< 0.01[b.c]
Perforation/rupture	0	7 (1.7)	495 (15.2)	< 0.01[b]
Pseudoaneurysm	0	0	199 (6.1)	< 0.01[b]
Abscess	0	6 (1.4)	557 (17.1)	< 0.01[b]
Intracardiac fistula	0	1 (0.2)	88 (2.7)	0.004[b]
Vascular phenomena	3 (11.1)	9 (2.2)	310 (9.5)	0.033[a.b]
Heart murmur	4 (14.8)	35 (8.6)	1225 (37.7)	0.001[b.c]
Heart failure	5 (18.5)	76 (18.6)	1383 (42.6)	< 0.01[b.c]
Persistent bacteremia	5 (18.5)	51 (12.5)	374 (11.5)	0.408
Central nervous system involvement	1 (3.7)	18 (4.4)	705 (21.7)	0.041[b.c]
Embolism	6 (22.2)	60 (14.7)	683 (21.0)	0.003[b]
Kidney failure	5 (18.5)	140 (34.3)	1175 (36.2)	0.087
Septic shock	5 (18.5)	34 (8.3)	416 (12.8)	0.173
Sepsis	3 (11.1)	54 (13.2)	552 (17.0)	0.576
Surgical indication	9 (33.3)	337 (82.8)	2102 (65.3)	< 0.01[a.b.c]
Cardiac surgery	5 (18.5)	314 (77.1)	1382 (42.6)	< 0.01[a.b.c]
In-hospital mortality	5 (18.5)	58 (14.3)	913 (28.2)	< 0.01[b]
1-year mortality	2 (7.4)	22 (5.4)	206 (6.3)	0.863

[a] Significant differences between A–B
[b] Significant differences between B–C
[c] Significant differences between A–C

Table 2 Mural infective endocarditis: GAMES registry versus literature review

Variables (%)	Games (*N* = 27) (%)	Literature (*N* = 36) (%)	*p* value	T*otal* (*N* = 63)
Age, median (IQR)	56 (46–67)	45 (29–57)	0.001	52.5 (35.3–64)
Sex (male)	11 (40.7)	22 (61.1)	0.132	33 (52.3)
Lung disease	8 (29.7)	2 (5.6)	0.011	10 (16.4)
Coronary disease	5 (18.5)	0 (0)	0.010	5 (7.9)
Heart failure	10 (37)	0 (0)	0.000	10 (15.8)
Diabetes	3 (11.1)	3 (8.3)	1.000	6 (9.5)
Trasplantation	5 (18.5)	1 (2.8)	0.076	6 (9.5)
Heart	2 (7.4)	0		2 (33.3)
Kidney	0	1 (2.8)		1 (16.7)
PM/ICD	2 (7.4)	0 (0)	0.180	2 (3.1)
Peripheral arterial disease	2 (7.4)	1 (2.8)	0.572	3 (4.8)
Cerebrovascular disease	3 (11.1)	1 (2.8)	0.305	4 (6.3)
Neoplasm	6 (22.2)	4 (11.1)	0.303	10 (15.9)
Congenital cardiopathy	3 (11.1)	4 (11.1)	1.000	7 (11.1)
Prior kidney disease	8 (29.6)	2 (5.6)	0.014	10 (15.9)
Prior hemodialysis	5 (18.5)	1 (2.8)	0.076	6 (9.5)
Liver disease	3 (11.1)	6 (16.7)	0.720	9 (14.3)
IVDU	1 (3.7)	9 (25)	0.034	10 (15.9)
Age-adjusted Charlson Index	4.3 (DE 2.7)	1.3 (DE 2.2)	0.000	2.7
Place of acquisition			0.0001	
Community acquired	7 (25.9)	25 (69.4)		32 (50.8)
Hospital acquired	17 (63)	5 (13.9)		22 (34.9)
Health care associated	3 (11.1)	6 (16.7)		9 (14.3)
Catheter source	16 (59.3)	5 (13.9)	0.000	22 (34.9)
Etiology			0.342	
Staphylococcus aureus	4 (14.8)	18 (50)	0.035	22 (34.9)
CNS	4 (14.8)	0	0.074	3 (4.8)
Enterococcus	1 (3.7)	0	0.429	1 (1.6)
Streptococcus	7 (25.9)	8 (22.2)	0.772	15 (23.8)
Candida	6 (22.2)	3 (8.3)	0.155	9 (14.3)
Enterobacteriaceae	2 (7.4)	1 (2.8)	0.572	3 (4.8)
Aspergillus spp	1 (3.7)	4 (11.1)	0.381	5 (7.9)

Table 2 continued

Variables (%)	Games (N = 27) (%)	Literature (N = 36) (%)	p value	Total (N = 63)
Polymicrobial	2 (7.4)	0	0.180	2 (3.2)
Unknown etiology	0	2 (5.6)	0.502	2 (3.2)
Clinical characteristics				
Vegetation size (mm), median (IQR)	22 (8–39)	20 (13–33)	0.910	22 (12–22)
Vegetation location			0.0001	
Right ventricle	5 (18.5)	9 (25)		14 (22.1)
Left ventricle	1 (3.7)	17 (47.2)		18 (28.6)
Right auricular	14 (51.9)	4 (11.1)		18 (28.6)
Left auricular	2 (7.4)	6 (16.7)		8 (12.7)
Septum	1 (3.7)	0		1 (1.6)
Superior vena cava	3 (11.1)	0		3 (4.8)
Tendinous chords	1 (3.7)	0		1 (1.6)
Intracardiac complication	1 (3.7)	5 (13.9)	0.226	6 (9.5)
Perforation/rupture	0	2 (5.6)	0.502	2 (3.2)
Pseudoaneurysm	0	1 (2.8)	1.000	1 (1.6)
Abscess	0	2 (5.6)	0.502	2 (3.2)
Intracardiac fistula	0	0		0 (0)
Others	1 (3.7)	0		1 (1.6)
Vascular phenomena	3 (11.1)	8 (22.2)	0.332	11 (17.5)
Heart murmur	4 (14.8)	5 (13.9)	0.207	10 (15.9)
Heart failure	5 (18.5)	1 (2.8)	0.076	6 (9.5)
Persistent bacteremia	5 (18.5)	3 (8.3)	0.262	8 (12.7)
Central nervus system involvement	1 (3.7)	15 (41.7)	0.001	16 (25.4)
Embolism	6 (22.2)	24 (66.7)	0.002	31 (49.2)
Kidney failiure	5 (18.5)	11 (30.6)	0.383	16 (25.4)
Septic shock	5 (18.5)	10 (27.8)	0.552	15 (23.8)
Sepsis	3 (11.1)	10 (27.8)	0.128	13 (20.6)
Surgical indication	9 (33.3)	21 (58.3)	0.036	30 (47.6)
Cardiac surgery	5 (18.5)	14 (38.9)	0.101	19 (30.2)
In-hospital mortality	5 (18.5)	9 (25)	0.365	13 (20.6)
1-year mortality	2 (7.4)	1 (2.8)	0.577	3 (4.8)

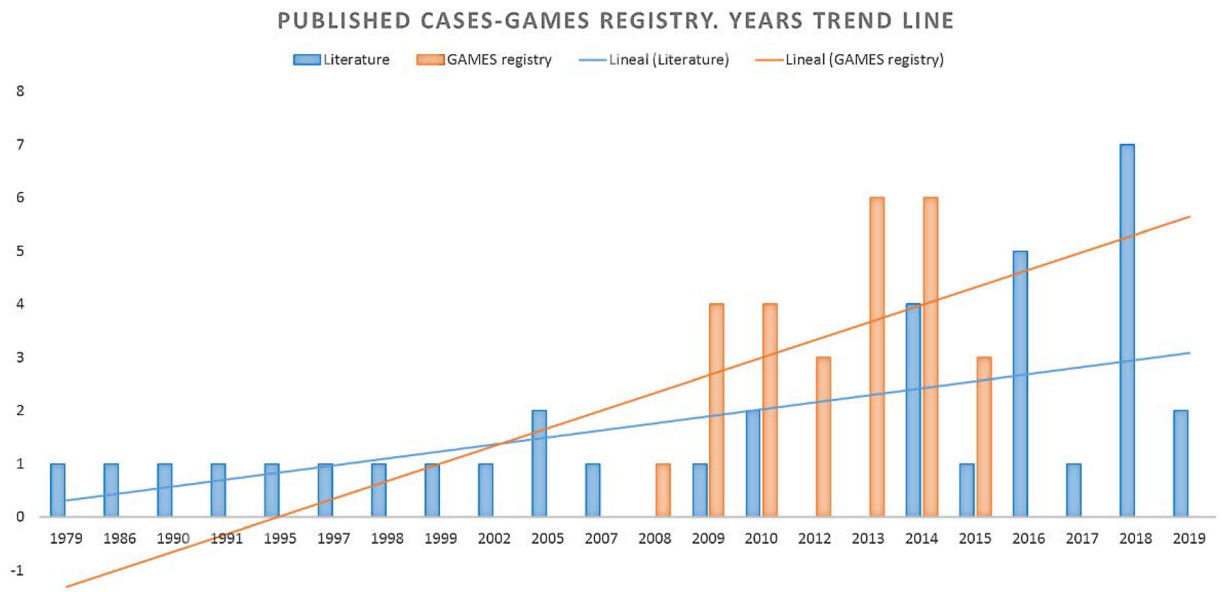

Fig. 2 Distribution by calendar year of the cases of mural endocarditis from the literature (blue) and those from the GAMES registry (orange)

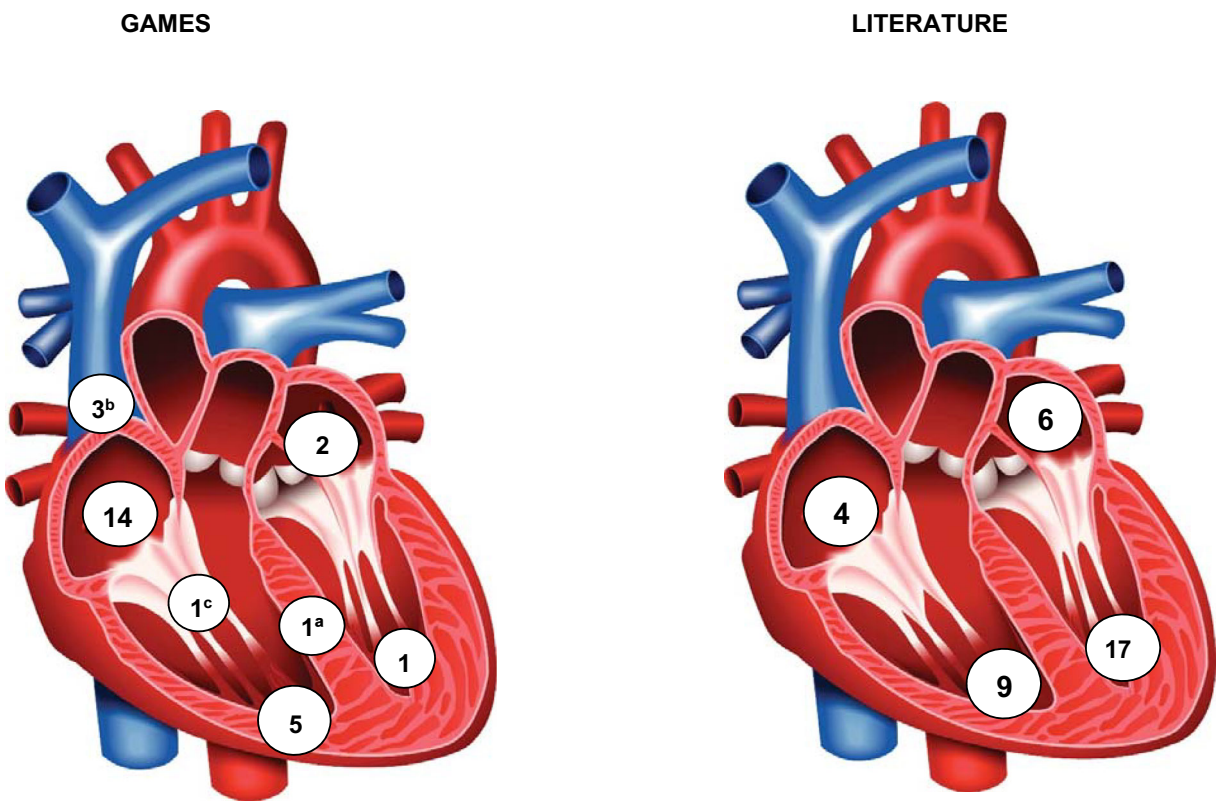

Fig. 3 Location of mural endocarditis. a: Septum. b: Vena cava. c: Tendinous chords. **A** GAMES, **B** literature

The vegetations were significantly larger in MIE, with a mean size of 22 mm compared to 12 and 10 mm in the DIE and VIE groups, respectively ($p < 0.01$).

Regarding complications associated with endocarditis, presence of intra-cardiac complications was significantly higher in VIE with 33.9% compared to 3.7% in MIE and in DIE each ($p < 0.01$). Likewise, systemic complications such as heart failure or central nervous system involvement were more frequent in VIE ($p < 0.01$ and $p = 0.041$); however, no differences were found in other complications such as acute renal failure, sepsis or septic shock.

Surgical indications were the same for all types of endocarditis and included: severe heart failure, septic shock, recurrent emboli, severe valve dysfunction, intracardiac complications (abscess), prosthetic valve infection, and large mobile vegetations or persistent bacteremia despite adequate antibiotic therapy. Non-MIEs more often had a surgical indication (65.3% in VIE and 82.8% in DIE vs. 33.3% in MIE, $p < 0.01$) and were operated on (42.6% in VIE and 77.1% in DIE vs. 18.5% in mural IE, $p < 0.01$).

No significant differences were found regarding in-hospital or 1-year mortality after the event.

Characteristics and differences between mural endocarditis from the GAMES registry and published cases of mural endocarditis

We retrieved 44 cases of MIE in the literature search, but only 36 had exclusive non-valvular involvement and enough information to analyze. General characteristics of MIE from GAMES and MIE published in the literature are given in Table 2. The column on the right side of the table summarizes the characteristics of both combined.

The time span for the collection of cases from the literature (1979–2019) was much broader than the study period of cases obtained from the GAMES registry (2008–2018), including a high proportion of cases (33.3%) diagnosed before the beginning of the GAMES registry. Figure 2 shows an increasing incidence of MIE along time.

Both series share some important characteristics such as a high proportion of fungal endocarditis and the presence of big vegetations. However, we found several relevant differences.

Patients in the literature group were younger than those in the GAMES series, with a mean age of 42.6 years versus 56.4 years ($p < 0.001$), had less frequent comorbidities as shown by a lower Charlson Index (1.3 literature vs. GAMES 4.3, $p = 0.000$). Of note, cases from the literature more frequently were users of intravenous drugs as a risk behavior for endocarditis compared to those from the GAMES registry (25% literature vs. 3.7% GAMES, $p = 0.034$). Acquisition of endocarditis in the community was more frequent in cases from the literature (69.4% vs. 25.9%) compared to those from GAMES, in which a nosocomial origin predominated (63% vs. 13.9%, $p = 0{,}0001$). Likewise, catheter as the source for endocarditis was more frequent in the GAMES series (59.3% vs. 13.9% in literature, $p = 0.000$). Regarding the etiology of endocarditis, *S. aureus* was more frequent in the literature group (50% vs. 14.8% in GAMES, $p = 0.007$) whereas coagulase-negative staphylococci were found in GAMES series but not in the literature series (14.8% vs. 0% in literature, $p = 0.035$), with significant differences. The most frequent location in the case of MIE in the literature was the left ventricle (47.2%), while in GAMES it was the right atrium (51.9%) (Fig. 3). Complications such as the presence of systemic embolisms and CNS involvement were more frequent in the literature group.

No significant differences were found regarding surgical indication, proportion of cases that received surgery or mortality.

DISCUSSION

Our results show that MIE represents 0.7% of endocarditis. It is often a complication of catheter use that appears in immunocompromised hospitalized patients, and fungal etiology is common. Surgery is performed less frequently

than in non-MIE, although mortality is similar to that of other types of endocarditis.

Our series provides information about MIE prevalence among total cases of endocarditis. There is no prior published large series of MIE. MIE is a rare disease, which has become easier to diagnose with the improvement in cardiac imaging techniques, which can explain in part an increasing incidence (Fig. 2). In view of the lack of prior MIE series, we decided to perform a literature review. The period of the literature review encompasses a larger period than the GAMES registry and, as such, includes earlier cases. When analyzing cases from the literature review, publication bias must be taken into consideration. Information from the GAMES together with the literature review offers a broad picture of the spectrum of MIE.

The combined data show that underlying transplantation, neoplasia and hemodialysis are prevalent in patients with MIE. The greater use of catheters in this type of subjects and a high use of hospital care could explain this finding. However, in the literature review, we observed a high proportion of community-acquired cases with a different clinical phenotype: intravenous drug users with *S. aureus* endocarditis. The high prevalence of parenteral drug users in case reports collected in the literature review may be related to the period in which the cases were described, a time when this activity was more common than nowadays. This suggests a shift in the epidemiology of MIE along time, with a decrease in IVDUs in favor of nosocomial endocarditis in which catheters appear to be implicated in the pathogenesis of MIE. The same applies to the change in the location of the vegetations in MIE [23, 24]. In contrast to VIE, where valvular endocardium is extensively exposed to damage from the bloodstream, we hypothesize that mural endocardium requires external damage, for instance, by the catheter jet, to start the process of developing a vegetation as has been described in other cases with endocardial damage caused by a jet [4, 17, 25–27].

In MIE, vegetations were larger compared to non-MIE. Regarding large vegetations, MIE diagnosis in earlier cases from the literature series often came only after embolism had already occurred. As the valvular apparatus is spared, heart failure symptoms cannot be expected to unveil the presence of endocarditis. The delay in the diagnosis of MIE implies a longer time of growth for the vegetations. The diagnostic delay in older cases, in keeping with worse imaging techniques, can explain a higher prevalence of embolisms and CNS involvement in the literature cases together with publication bias. It could be expected that, due to the larger size of the vegetations, significant differences between MIE and non-MIE regarding persistent bacteremia and systemic complications of endocarditis such as embolisms would be encountered; however, we did not find such differences.

Regarding etiology, the most common pathogens in MIE were *Staphylococci* and *Streptococci*, but we found a striking prevalence of fungi compared to non-MIE [23]. Fungal endocarditis was represented mainly by *Candida* and, to a lesser extent, by *Aspergillus* [2, 7–12]. In earlier cases of endocarditis associated with intravenous drug use, *Candida* has been related to injection of brown heroin diluted in fresh lemon juice [28]. In addition, candidemia is also prevalent among catheter users, leading to the development of endocarditis in the long term. Fungal endocarditis also develops in immunocompromised hosts; in particular, *Aspergillus* spp. endocarditis has been associated with transplantation [29]. Fungal IE often cause large vegetations [8, 12, 30, 31].

Heart failure and valvular dysfunction are relevant indications for surgery. We consider that, since MIE does not involve heart valves, these complications are less frequent, which is a possible explanation for the surgery not being indicated in as many cases of MIE as it was in other types of endocarditis. Although cardiac complications of MIE were less frequent and surgery was less commonly indicated, mortality was very similar to that of non-MIE, which underlines the importance of MIE diagnosis and correct management.

Strengths and limitations

The present study analyzes a multicenter series from the entire Spanish territory and over a long period of time and is complemented with a review of the literature. We believe it presents a comprehensive image of MIE. Cases from the GAMES registry are collected prospectively, according to pre-established criteria, and evaluated by a multidisciplinary team, which allows putting the prevalence of this rare disease in perspective and provides a broad set of data to describe this population. Regarding series of cases from the literature, incidence or prevalence data cannot be obtained, as the total population with endocarditis is unknown, and publication bias has to be considered, so that information obtained from these cases must be evaluated with caution. Information about published cases is seldom complete. Nevertheless, that series covers a large period and is a thorough sample, which provides very valuable information to enrich the information about MIE.

CONCLUSION

Mural endocarditis is a rare but increasingly recognized and reported health care-associated disease that requires a high index of suspicion and a multidisciplinary approach to avoid the relevant morbidity and mortality.

Our results highlight the importance of this type of endocarditis in association with intravascular catheters and immunocompromised patients and, as such, with a potential for prevention.

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REFERENCES

1. Patel M, Ahmad Z, Distler E, Swofford B. The use of cardiac MRI in a rare case of primary mural endocarditis. BMJ Case Rep. 2017; 2017

2. Lopez-Ciudad V, Castro-Orjales MJ, Leon C, Sanz-Rodriguez C, de Torre-Fernandez MJ, Perez de Juan-Romero MA, et al. Successful treatment of Candida parapsilosis mural endocarditis with combined caspofungin and voriconazole. BMC Infect Dis. 2006;6:73.

3. Ak K, Adademir T, Isbir S, Arsan S. Right ventricular mural endocarditis presenting as an isolated apical mass in a non-addict patient with congenital deafness and aphasia. Interact Cardiovasc Thorac Surg. 2009;8(4):498–500.

4. Hosokawa S, Okayama H, Hiasa G, Kawamura G, Shigematsu T, Takahashi T, et al. Isolated left atrial infective mural endocarditis. Intern Med. 2018;57(7):957–60.

5. Adel A, Jones E, Johns J, Farouque O, Calafiore P. Bacterial mural endocarditis. A case series. Heart Lung Circ. 2014;23(8):e172–9.

6. Tahara M, Nagai T, Takase Y, Takiguchi S, Tanaka Y, Kunihara T, et al. Primary mural endocarditis without valvular involvement. J Ultrasound Med. 2017;36(3):659–64.

7. Mullen P, Jude C, Borkon M, Porterfield J, Walsh TJ. Aspergillus mural endocarditis. Clin Echocardiogr Diagn Chest. 1986;90(3):451–2.

8. Kim KC, Choi HM, Yoon YE, Cho Y, Cho GY. A case of aspergillus mural endocarditis presenting with complete atrioventricular block after liver-kidney transplantation. CASE (Phila). 2019;3(6):267–71.

9. Lim ML, Oliver DH, Barasch E. Aspergillus mural vegetation identified by transesophageal echocardiography. Echocardiography. 1997;14(3):283–6.

10. Leung WH, Lau CP, Tai YT, Wong CK, Cheng CH. Candida right ventricular mural endocarditis complicating indwelling right atrial catheter. Chest. 1990;97(6):1492–3.

11. Granados JM, Ayestaran OS, Gaboli M, Fernandezde Miguel S, Gomezdeuero MP. Combined antifungal therapy. Treatment success in a case of mural endocarditis due to Candida glabrata. An Pediatr (Barc). 2009;71(4):368–9.

12. Pavlina AA, Peacock JW, Ranginwala SA, Pavlina PM, Ahier J, Hanak CR. Aspergillus mural endocarditis presenting with multiple cerebral abscesses. J Cardiothorac Surg. 2018;13(1):107.

13. Ruiz RS, San Roman JA, Alonso JR, Fernandez-Aviles F. Acute myocardial infarction secondary to left atrial mural endocarditis. Echocardiography. 2005;22(7):621–2.

14. Shirani J, Keffler K, Gerszten E, Gbur CS, Arrowood JA. Primary left ventricular mural endocarditis diagnosed by transesophageal echocardiography. J Am Soc Echocardiogr. 1995;8(4):554–6.

15. Rutlen C, Vallurupalli S. Chamber-made: mural endocarditis. Am J Med. 2018;131(8):918–21.

16. Neoh K, Khan JN, Albouaini K, Chenzbraun A. Biventricular mural vegetations without valvular involvement: an unusual presentation of *Staphylococcus aureus* endocarditis. Echo Res Pract. 2018;5(4):I11–3.

17. Fyfe B, Ianosi-Irimie M, Motavalli L. Infective endocarditis complicating hypertrophic obstructive cardiomyopathy: an unusual mural pattern. Cardiovasc Pathol. 2010;19(1):e5-7.

18. Wilson AM, Lu YR. Two cases of right atrial mural endocarditis caused by *Staphylococcus Aureus*. Heart Lung Circ. 2016;25(10):e119–21.

19. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis. 2000;30(4):633–8.

20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.

21. Murdoch DR, Corey GR, Hoen B, Miro JM, Fowler VG Jr, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med. 2009;169(5):463–73.

22. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. ESC Guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC). endorsed by: European association for cardio-thoracic surgery (EACTS), the European association of nuclear medicine (EANM). Eur Heart J. 2015;36(44):3075–128.

23. Ortega-Loubon C, Munoz-Moreno MF, Andres-Garcia I, Alvarez FJ, Gomez-Sanchez E, Bustamante-Munguira J, et al. Nosocomial vs. community-acquired infective endocarditis in Spain: location, trends, clinical presentation, etiology, and survival in the 21st century. J Clin Med. 2019;8(10):1755.

24. Hwang JW, Park SW, Cho EJ, Lee GY, Kim EK, Chang SA, et al. Risk factors for poor prognosis in nosocomial infective endocarditis. Korean J Intern Med. 2018;33(1):102–12.

25. Lee KY, Yi JE, Moon D, Jung HO, Youn HJ, Lim J, et al. Isolated right-sided mural infective endocarditis in a 32-year-old woman with muscular ventricular septal defect. Cardiology. 2014;129(1):65–8.

26. Ringer M, Feen DJ, Drapkin MS. Mitral valve prolapse: jet stream causing mural endocarditis. Am J Cardiol. 1980;45(2):383–5.

27. Gonzalez-Lavin L, Lise M, Ross D. The importance of the "jet lesion" in bacterial endocarditis involving the left heart. Surgical considerations. J Thorac Cardiovasc Surg. 1970;59(2):185–92.

28. Bisbe J, Miro JM, Latorre X, Moreno A, Mallolas J, Gatell JM, et al. Disseminated candidiasis in addicts who use brown heroin: report of 83 cases and review. Clin Infect Dis. 1992;15(6):910–23.

29. Ioannou P, Papakitsou I, Kofteridis DP. Fungal endocarditis in transplant recipients: a systematic review. Mycoses. 2020;63(9):952–63.

30. Badiee P, Amirghofran AA, Ghazi NM. Evaluation of noninvasive methods for the diagnosis of fungal endocarditis. Med Mycol. 2014;52(5):530–6.

31. Leite-Andrade MC, Inacio CP, Calixto F, Feitosa M, Sepulveda DPL, Santos FAG, et al. Large aortic prosthesis fungal vegetation due to candida parapsilosis: an uncommon presentation. Mycopathologia. 2019;184(6):795–6.