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Pseudoaneurysm of the mitral–aortic intervalvular fibrosa

A new comprehensive review

Abbreviations

LVOT	Left ventricular outflow tract
MAIVF	Mitral–aortic intervalvular fibrosa
P-MAIVF	Pseudoaneurysm of the mitral–aortic intervalvular fibrosa
TEE	Transesophageal echocardiography
TTE	Transthoracic echocardiography

The mitral–aortic intervalvular fibrosa (MAIVF) is an avascular structure located adjacent to the left ventricular outflow tract between the aortic and mitral valve providing functional and anatomical integrity.

Pseudoaneurysm of the MAIVF (P-MAIVF) is a rare but potentially life-threatening condition. With the increasing incidence of infective endocarditis and cardiac surgery, a likely increment in the frequency of pseudoaneurysm is expected. Transesophageal echocardiography (TEE) has facilitated the visualization of this area and enhanced the detection and assessment of pseudoaneurysm.

P-MAIVF is often associated with infection or surgical trauma. A congenital origin and blunt chest trauma are among the other causes. While it is likely to follow an asymptomatic course, symptoms of endocarditis, heart failure, chest pain, shortness of breath, and cerebrovascular events are common clinical presentations.

The recommended treatment is surgery. However, conservative therapy is an alternative approach for high-risk patients or those who refuse surgery with a reasonable follow-up period with echocardiography of 6–12 months.

Methods

We found 487 articles in the PubMed database by searching the keywords "pseudoaneurysm of the mitral–aortic intervalvular fibrosa," "left ventricular outflow tract aneurysm," "left ventricular pseudoaneurysm," and "subvalvular aneurysm". All of the articles were screened manually and 101 were selected due to their relevance to P-MAIVF. These articles were published between 1960 and March 2014, and one was in French. A total of 161 cases were evaluated in 104 articles. The cases were classified according to their age, sex, etiology, clinical presentation, diagnosis, complication, treatment, and survival status. Besides these 161 patients collected in our literature review, our hospital established a definite diagnosis in another series of eight patients (**Tab. 1**). Since only five of them remained unpublished, we included them in our comprehensive review, thereby reaching a total of 166 cases.

Etiology and pathophysiology

The MAIVF is bounded by the left and right fibrous trigones, thus gaining a functional and anatomical integrity between the aortic valve and mitral valve. The roof is formed by the pericardium, while its base is situated adjacent to the left ventricular outflow tract (LVOT). Half of the noncoronary cusp, some part of the left coronary cusp, and the anterior mitral leaflet constitute an immediate vicinity of this area.

Since the MAIVF is relatively avascular, it becomes more prone to infections and traumas. Infection of this area may result in abscess or pseudoaneurysm formations. The opening of the abscess formation into the LVOT creates a suitable milieu for the formation of P-MAIVF.

The most common causative factors are infective endocarditis and surgical trauma. Aortic valve infections may extend directly into the MAIVF area. The relatively avascular nature of the MAIVF renders it more prone to infectious insults and hence abscess formations. Should the abscess sac communicate with the LVOT, a pseudoaneurysm can possibly be generated.

Aortic regurgitation is another entity that contributes to the formation of pseudoaneurysm. Infected aortic regurgitation jet impinging on this innately sensitive region may also predispose to the development of pseudoaneurysm. The combination of bicuspid aortic valve and PMAIVF seems a common condition because of the congenital compromise in this area (bicuspid/native valve ratio: 0.44 in our review).

Additional material online: This article includes an additional Table. You will find this supplemental at dx.doi.org/10.1007/s00059-014-4185-z.

Tab. 1 Clinical and imaging features of our patients

Case	Gender	Age (years)	Time from diagnosis to surgery	Size	Diagnostic method	Aortic valve	Endocarditis	Causative microorganism	Comorbidity	Treatment	Surgical details
1	Female	35	No surgery	2.1×1.1 cm	TTE/3D TTE	Native	–	–	Takayasu	Refused surgery; lost to follow-up	–
2	Female	23	No surgery	1.2×3.1 cm	TTE/3D TTE	Native	Aortic valve endocarditis	*S. aureus*	–	Exitus	–
3	Male	43	38 months	3.2×1.9 cm	MDCT/TTE/TEE	AVR	–	–	–	Surgery	AVR + closure of pseudoaneurysm with synthetic graft
4	Female	42	26 months	1.6×2.3 cm	TTE/TEE	AVR	–	–	–	Surgery	Closure of pseudoaneurysm with synthetic graft
5	Male	68	108 months	0.9×2.1 cm	TTE/TEE	AVR	–	–	MVR	Surgery	Simple closure of pseudoaneurysm neck
6	Male	71	No surgery	2.7×2.1 cm	TTE/TEE/3D	Native	Aortic valve endocarditis	*S. aureus*	–	Refused surgery; noncardiac exitus	–
7	Male	55	14 months	2.8×1.6 cm	TTE/TEE	Bioprosthesis	–	–	Severe MR	Surgery	AVR + MVR + closure of pseudoaneurysm with pericardial graft
8	Male	72	76 months	1.1×1.4 cm	MDCT/TTE/TEE	AVR	Metallic aortic valve endocarditis	*S. aureus*	–	Surgery	AVR + simple closure of pseudoaneurysm neck

TTE transthoracic echocardiography, *TEE* transesophageal echocardiography, *MDCT* multidetector computed tomography, *AVR* aortic valve replacement, *MVR* mitral valve replacement

In the selected articles, 68 patients had active endocarditis (40%), whereas 30 patients had a history of previous endocarditis (18%). The causative microorganisms were reported to be *Staphylococcus* species in 22 patients [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 102, 104], *Streptococcus* species in 14 patients [1, 7, 17, 18, 19, 20, 21, 22, 23, 103], *Bacillus* species in one patient [24], *Brucella suis* in two patients [25, 26], *Escherichia coli* in one patient [27], and *Enterococcus* species in four patients [17, 28, 29, 30]. Fungal infections were the associated etiology in two patients, in one of whom it was *Paecilomyces lilacinus* [31] and in the other, *Monilia albicans* [32].

MAIVF can become subject to damage due to valvular surgery. Not only valvular surgeries, but other surgical and interventional procedures such as cardiac catheterization, radiofrequency ablation, and ventricular septal defect repair in the vicinity of this area can also result in P-MAIVF. In our literature review we found that P-MAIVF developed in 87 patients (52%) following aortic surgery, among whom 52 also had had a history of active or prior infective endocarditis.

Congenital heart diseases are another causative factor of P-MAIVF. Cardiovascular defects such as ventricular septal defect, atrial septal defect, patent ductus arteriosus, aortic coarctation, and bicuspid aortic valve may be detected at the time of diagnosis [47, 73].

Clinical presentation

P-MAIVF often remains asymptomatic in the absence of complications. It is usually diagnosed during a routine examination. The most commonly encountered clinical situations are symptoms related to an active infection, shortness of breath, and symptoms/signs of heart failure [16, 32, 33]. Chest pain, cerebrovascular events, and systemic embolism are other likely clinical presentations [16, 32, 33]. The most common clinical presentation in the reviewed articles was active en-

docarditis, with 68 patients in this clinical situation [2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 14, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 102, 103, 104], 36 patients had been admitted with shortness of breath and/or other heart failure-related symptoms/signs [6, 27, 29, 30, 31, 32, 34, 41, 46, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60]. Five patients had presented with cerebrovascular events [4, 7, 10, 21, 46], and 19 patients had described typical or atypical angina [9, 16, 20, 58, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72]; 17 patients had been asymptomatic at the time of diagnosis [1, 49, 60, 61, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83]. In 33 patients the reports did not reveal adequate information regarding the symptomatology. A chest wall mass gained attention as an unusual clinical presentation in one patient [84].

Complications

Impingement by the pseudoaneurysm of the surrounding tissues leads to a number of complications. Specifically, progressive enlargement of the pseudoaneurysm may compress the coronary arteries, thus resulting in angina or even myocardial infarction [12, 21, 62, 64, 65, 67, 72, 79, 85]. The most common compression is on the left circumflex coronary artery. Other coronary arteries can also be affected. Compression of the pulmonary artery [47] may result in pulmonary hypertension. Compression of the mitral annulus and anterior mitral valve leaflet is likely to result in mitral regurgitation [51].

Fistula formations into adjacent cardiac structures constitute another complication. A fistula may develop between the LVOT and the left atrium or the aorta. Upon formation of a fistula between the LVOT and the left atrium, an eccentric flow can be visualized mimicking a mitral regurgitant jet. Accordingly, any new eccentric mitral regurgitation detected in addition to a previous or recent aortic valve replacement should raise suspicion of fistula formation.

If the pseudoaneurysm ruptures into the pericardium, fatal complications may ensue [78, 102]. The most typical example of this situation is pericardial tamponade. Purulent and hemorrhagic pericarditis is another complication of P-MAIVF. In one case report, P-MAIVF was reported to have ruptured into the anterior chest wall, generating a pulsatile mass in the chest wall [84].

Clots may occur within the cavity of the pseudoaneurysm, and they may be associated with cerebrovascular events and systemic emboli.

Diagnosis

Echocardiography is the most widely used method in the diagnosis of the pseudoaneurysm. Transthoracic echocardiography (TTE) was performed in 152 of 166 cases (92%) (**Fig. 1, 2**). Using TTE, a definitive diagnosis could be made in 60 patients (36%); suspicious lesions were observed in 24 patients; and P-MAIVF was not evident in 68 patients. Moreover, transesophageal echocardiography

Abstract · Zusammenfassung

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Pseudoaneurysm of the mitral–aortic intervalvular fibrosa. A new comprehensive review

Abstract

Pseudoaneurysm of the mitral–aortic intervalvular fibrosa (P-MAIVF) is an infrequent but potentially life-threatening condition. Both transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) can detect P-MAIVF with sensitivity rates of 43 and 90%, respectively. The typical finding of echocardiography is a pulsatile echo-free sac that expands in systole and collapses in diastole. Our review comprises 166 patients with P-MAIVF, including eight cases in our hospital and 158 cases from the literature. P-MAIVF is often associated with infection or surgical trauma. While it is likely to maintain an asymptomatic course, symptoms of shortness of breath, heart failure, valvular disease, chest pain, endocarditis, and cerebrovascular events are common clinical presentations. The recommended treatment is surgery. However, conservative therapy is an alternative approach for high-risk patients or when surgical treatment is refused. With the increasing incidence of cardiac surgery and infective endocarditis, a likely increment in the new diagnosis of pseudoaneurysm is expected.

Keywords

Pseudoaneurysm · Mitral–aortic intervalvular fibrosa · Transthoracic echocardiography · Transesophageal echocardiography · Therapy

Pseudoaneurysma der mitral-aortalen intervalvulären Fibrosa. Eine neue umfassende Übersicht

Zusammenfassung

Das Pseudoaneurysma der mitral-aortalen intervalvulären Fibrosa (MAIVF, aortomitraler Übergang) ist nicht häufig, aber potenziell lebensbedrohlich. Sowohl mit der transthorakalen Echokardiographie (TTE) als auch mit der transösophagealen Echokardiographie (TEE) kann ein Pseudoaneurysma der MAIVF (P-MAIVF) mit einer Sensitivitätsrate von 43 bzw. 90% diagnostiziert werden. Typischer Befund bei der Echokardiographie ist ein pulsierender echofreier Sack, der sich in der Systole ausdehnt und in der Diastole zusammenfällt. In die Studie wurden 166 Patienten mit P-MAIVF, darunter 8 Fälle aus der Klinik der Autoren und 158 Fälle aus der Literatur, aufgenommen. Oft geht ein P-MAIVF mit einer Infektion oder einem chirurgischen Trauma einher. Es ist zwar wahrscheinlich, dass der Verlauf asymptomatisch ist, aber Symptome wie Luftnot, Herzinsuffizienz, Herzklappenerkrankungen, Schmerzen in der Brust, Endokarditis und zerebrovaskuläre Ereignisse sind häufige klinische Zeichen. Zumeist wird die chirurgische Behandlung empfohlen. Die konservative Therapie ist jedoch ein alternativer Ansatz für Hochrisikopatienten oder in Fällen, in denen die Operation abgelehnt wird. Mit Zunahme der Häufigkeit von Herzoperationen und infektiöser Endokarditis ist auch von einem Anstieg der neuen Diagnose des Pseudoaneurysmas auszugehen.

Schlüsselwörter

Pseudoaneurysma · Mitral-aortale intervalvuläre Fibrosa · Transthorakale Echokardiographie · Transösophageale Echokardiographie · Therapie

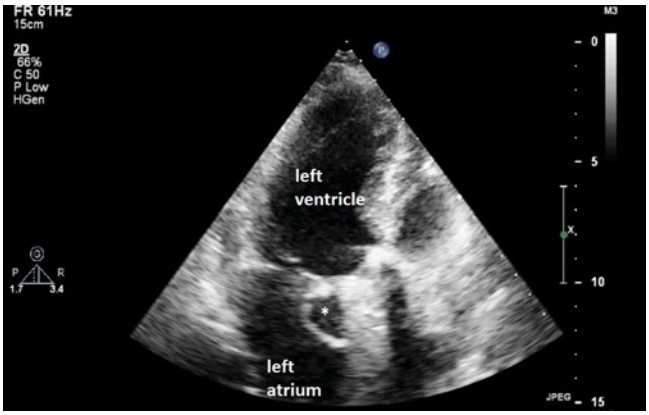

Fig. 1 ▲ Four-chamber view of a pseudoaneurysm (*asterisk*)

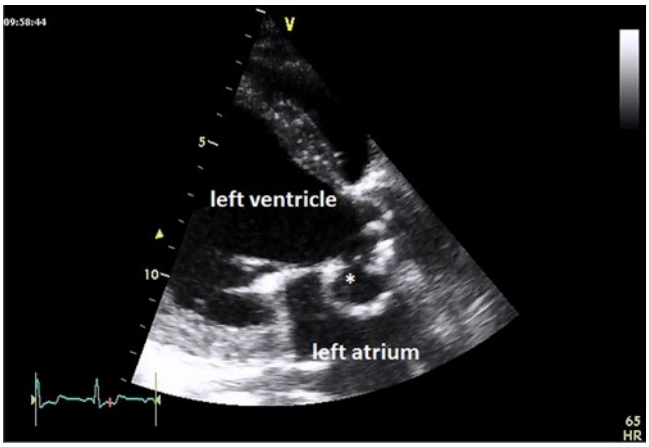

Fig. 2 ▲ Parasternal long-axis view of a pseudoaneurysm (*asterisk*)

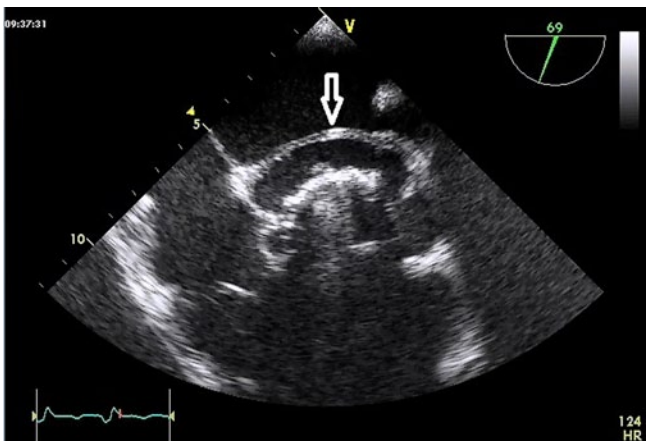

Fig. 3 ▲ Transesophageal echocardiographic view of a pseudoaneurysm (*arrow*)

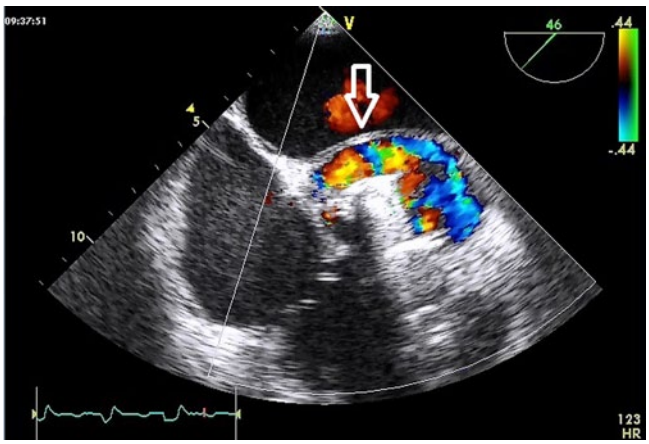

Fig. 4 ▲ Color Doppler view of a pseudoaneurysm (*arrow*)

(TEE) was also implemented for a further detailed examination in most of the patients (66%) undergoing TTE. P-MAIVF was evident in all patients who were evaluated using TEE. Even if a large pseudoaneurysm could be depicted in TTE, TEE was necessary for the definitive diagnosis and detection of the complications. TEE proved superior to TTE in identifying the pseudoaneurysm (**Fig. 3**). One study demonstrated that the diagnostic sensitivity of TTE was markedly lower than that of TEE (43% vs. %90, $p<0.05$) [46].

The typical finding of echocardiography is a pulsatile echo-free sac that expands in systole and collapses in diastole. This almost always plays a major role in the definitive diagnosis of P-MAIVF [6].

Color Doppler imaging can help establish the diagnosis on the basis of forward blood flow into the pseudoaneurysm during systole and backflow into the LVOT during diastole (**Fig. 4**). In addition, color Doppler imaging helps demonstrate the relationship between the pseudoaneurysm and other heart structures [6]. Color Doppler examination relies on the turbulent flow inside the cavity and can prove useful in revealing any communication between the echo-free space, namely, the pseudoaneurysm, and the LVOT. The source and direction of the blood flow can be defined more clearly using color Doppler TEE imaging, which further facilitates the diagnosis of any complications.

Furthermore, compared with two-dimensional echocardiography, three-dimensional echocardiography provides a better anatomic and morphological visualization of the cardiac structures (**Fig. 5**). Three-dimensional echocardiography is likely to be more useful, especially if two-dimensional views are insufficient for identifying the patho-anatomic structures in recognizing the complications of endocarditis [35, 74].

Other diagnostic methods are computed tomography, magnetic resonance imaging, and left ventricular catheterization. Computed tomography was used for the purpose of a definitive diagnosis in 24 patients (**Fig. 6**, [9, 12, 15, 29, 36, 37, 48, 59, 61, 65, 66, 69, 71, 72, 73, 78, 80, 82, 87, 88]); magnetic resonance imaging in 11 patients [2, 37, 51, 62, 77, 81, 83, 89, 90]; and, the diagnosis was confirmed by left heart catheterization in 19 patients [12, 21, 32, 37, 46, 47, 52, 64, 67, 69, 70, 76, 85, 89, 91, 92, 103].

Differential diagnosis

Aortic root abscess should be kept in mind in the differential diagnosis. The characteristic echocardiographic feature of P-MAIVF, namely, the pulsatile echo-free pouch, is not evident in aortic root

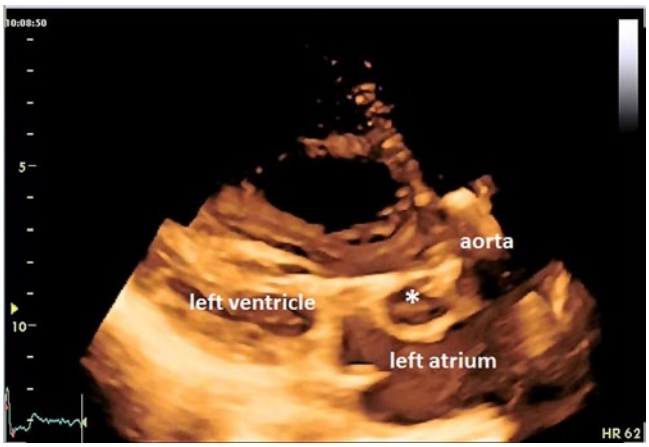

Fig. 5 ◀ Three-dimensional view of a pseudoaneurysm (*asterisk*)

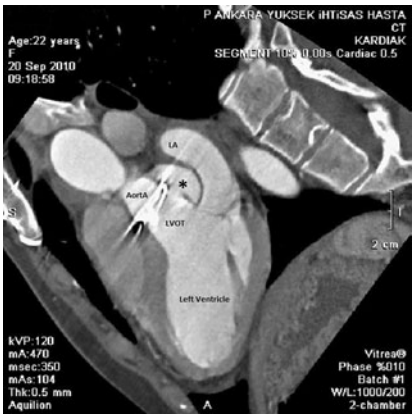

Fig. 6 ▲ Computed tomography view of a pseudoaneurysm (*asterisk*)

abscess. Moreover, Color Doppler imaging demonstrates no inflow to the aortic root abscess. Furthermore, such kinds of abscesses are prone to be smaller than P-MAIVF.

Characteristic ante- and retrograde blood flow visualized using color Doppler imaging P-MAIVF may also be confused with aortic stenosis and aortic regurgitation.

When the pseudoaneurysm communicates with the left atrium, its flow can be confused with mitral regurgitation jet. Accordingly, suspicions regarding P-MAIF should rise whenever an eccentric jet has been visualized within the left atrium, especially in patients with the history of a previous infective endocarditis or aortic valve replacement surgery. Furthermore, the origin of such a jet is likely to be elucidated more thoroughly using TEE thanks to its better spatial and temporal resolution.

Management and treatment

Surgery

The clinical outcome of P-MAIVF is hard to predict. Rupture of the pseudoaneurysm into the pericardium may be fatal and hence when the pseudoaneurysm is diagnosed, surgical treatment should be recommended to all patients even if they are asymptomatic. A number of surgical procedures have been used, including: simple closure of the aneurysm neck; closure using pericardial or synthetic graft materials; and complete removal of the pseudoaneurysm sac from the LVOT. In most of the cases, aortic valve replacement or aortic root surgery were included in the surgical repair of P-MAIVF.

Successful percutaneous closure attempts were preferred in some cases, with uneventful follow-ups reported [27, 65, 77].

Type of surgery

Most of the reviewed patients underwent surgical treatment. Pseudoaneurysm repair encompassed concomitant aortic surgery including aortic valve replacement and/or aortic root replacement in 71 patients [2, 6, 7, 8, 9, 12, 13, 14, 15, 19, 20, 21, 22, 23, 24, 26, 30, 31, 32, 38, 41, 42, 43, 45, 46, 48, 49, 51, 52, 53, 62, 63, 64, 67, 68, 88, 92, 93, 94, 95, 104]; concomitant aortic valve replacement and mitral valve replacement in 11 patients [2, 5, 7, 14, 18, 33, 50, 54, 55, 56]; and concomitant mitral valve replacement in only one patient [29]. On the other hand, pseudoaneurysm repair was implemented without any concomitant valve surgery in 23 patients [3, 16, 17, 33, 37, 47, 59, 69, 70, 72, 76, 82, 83, 84, 87, 91, 96, 97, 98, 103]; coronary arterial by-pass grafting was added to the repair procedure in two patients [64, 67]. One patient had a successful orthotropic cardiac transplantation [67].

Follow-up without surgery

An alternative approach to surgical correction is conservative therapy. Surgical correction might be high risk for various reasons. In particular, comorbidities could cause contraindications for surgery, and these patients should be followed up with medical treatment. The natural course of P-MAIVF remains to be clearly elucidated. For this reason, close clinical and echocardiographic follow-up is essential. The combination of TTE and TEE should be recommended in all follow-ups. Pseudoaneurysm rupture has been reported only rarely, but one must be vigilant in terms of complications. Surgical treatment was not used in 29 patients [1, 4, 17, 29, 33, 36, 39, 46, 47, 49, 60, 61, 71, 73, 74, 78, 80, 81, 99]. The follow-up periods for these patients ranged from 10 months to 9 years, with a mean of 30 months. The dimensions of the pseudoaneurysm did not change in ten patients. On the other hand, the size of the pseudoaneurysm increased progressively in some patients. In one patient with a 9-year follow-up, the size of the pseudoaneurysm increased from 0.6 cm to 4.9×7.8 cm [1]. Interestingly, this patient remained asymptomatic.

Mortality

Mortality occurred in 29 patients during follow-up, which was due to: heart failure in five patients [34, 58]; coronary arterial disease or coronary artery compression-related complications in three patients; [1, 21, 79]; P-MAIVF rupture into the pericardium in three patients [33, 44, 102]; infection and/or sepsis in five patients [2, 4, 17, 28, 40]; cerebrovascular accident in one patient [35];and intraoperatively or postoperatively in 11 patients [2, 14, 17, 21, 30, 41, 47, 59, 60, 64]; in one case autopsy was refused by the patient's family [60].

Sixteen patients had active infective endocarditis or a history of endocarditis;

of these patients, eight had aortic valve surgery, five were diagnosed at autopsy, and one had congenital heart disease. The cause of death in two patients could not be found in the articles.

Discussion and conclusion

As mentioned, P-MAIVF is a rare clinical entity. Postmortem reports regarding some African patients were the first documents to which we ever gained access in the literature, wherein the exact etiology had remained unknown [58]. Thinks to the increasing recognition and usage of echocardiography modalities around the world, the number of diagnoses has been rising progressively so that increasing insights into the etiology are being gained.

The most common causes are infection and surgical trauma. Both native and prosthetic valve endocarditis may result in P-MAIVF. In some cases the pseudoaneurysm develops due to the opening of an abscess formation through the LVOT. P-MAIVF was also suggested to be associated with insult incurred by the aortic regurgitation jet trauma toward the MAIVF area.

The most common traumatic surgery is aortic valve replacement. Since MAIVF is closely knitted with the aortic root anatomy, it may be easily damaged during such surgeries. Therefore, any eccentric mitral regurgitation identified in a patient with previous or recent aortic valve replacement should be further evaluated for a probable P-MAIVF. Aortic valve replacement is not the only reason of surgical trauma. The same may hold true following a mitral valve replacement surgery. Additionally, ventricular septal defect repair, intracardiac radiofrequency catheter ablation, and other cardiac structural repair operations are also likely to result in P-MAIVF during follow-up. Such patients, therefore, should be regarded as high risk and be approached in the relevant manner.

Surgical repair is the treatment of choice, and the most frequently preferred surgical method comprises pseudoaneurysm repair together with aortic surgery. Simple closure, repair using a graft, and percutaneous repair are among the alternative treatment methods. A conservative approach is preferred when surgery is not considered. Patients should be monitored regularly in reasonable time lines, namely, 6–12 months, using a combination of TTE and TEE.

The increasing incidence of infective endocarditis and aortic surgeries in recent years is expected to expand the current series of P-MAIVF cases. Therefore, clinicians should always bear in mind the likelihood of P-MAIVF developing in such cases.

Study limitations

Our study was limited by some incomplete or and/or missing patient reports and the relatively small sample size. Furthermore, we only reviewed the English- and Turkish-language literature and one French article regarding this rare disease entity.

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Compliance with ethical guidelines

Conflict of interest. E. Şahan, M. Gül, S. Şahan, E. Sokmen, Y.A. Guray, and O. Tufekçioglu state that there are no conflicts of interest.

The accompanying manuscript does not include studies on humans or animals.

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