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Cavitation phenomenon in mechanical prosthetic valves: Not only microbubbles

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Abstract

Introduction: Microbubbles (MBs) or cavitation is high-velocity, echo-bright findings present during the closing or opening of a mechanical valve (MVP). Cavitation bubble growth or gas emboli are less frequently described. We evaluated the hemodynamic parameters involved in the formation of gas emboli and the impact of gas emboli on requests for additional investigations.

Methods and Results: Transthoracic echocardiographic studies (TTE) of 57 patients (31 males, mean age 46.8 ± 13.8 years) with gas emboli were evaluated after heart valve replacement surgery. The majority (72%, n = 42) had a mitral or combined mitral/aortic MVP, with 28% (n = 16) an aortic MVP. The last TTE with and without gas emboli were considered for the same patient and the no emboli group was the control group (42 patients). The patient's blood pressure (BP) and heart rate (HR) were available for each TTE. Comparing the two TTEs, the systolic and diastolic BP, transmitral and aortic gradients, and left ventricular ejection fraction were similar but the HR (80.9 ± 18.7 vs 72.5 ± 13.9 bpm, $P = .02$) was significantly higher in the group with gas emboli. A TEE was performed 52 times in 27 patients, due to gas emboli, with one case positive for thrombus/vegetation. For 19 patients, a brain CT was requested. In two patients, the indication for the brain CT was gas emboli but the result was negative.

Conclusion: Gas emboli are frequently present and associated to an increased HR. They can cause the misdiagnosis of endocarditis or thrombus formation with significant additional requests for diagnostic examinations.

KEYWORDS
echocardiography, mechanical prosthetic valves, microbubbles

1 | INTRODUCTION

Annually, approximately 280 000 cardiac valve substitutes are implanted globally, of which half are mechanical valve prostheses (MVP). MVP implants can cause cavitation, a well-known and described phenomenon associated with the presence of microbubbles (MB). The MBs are visible as a discontinuous flow of rounded, echogenic, and fast-moving echoes occurring from the left ventricular (LV) side of the MVP.[1] The development of the microbubbles typically occurs during the prosthetic valve closure, due to the Venturi effect caused by a high-velocity flow within the narrow gap between the leaflets and valve housing.[2] When pressure returns to normal, the cavitation MB can collapse (implode) causing high stress on the surrounding elements. According to experimental data, particularly in a bi-leaflet MVP, MBs are positively associated with heart rate and valve closure velocity. It is assumed that MB formation over time predisposes to growth cavitation bubbles or gas emboli.[3]

The phenomenon of MB was first described in the 1980s after a series of prosthetic valve failures (Edwards Laboratories, USA). It was hypothesized that cavitation might be responsible for erosion during valve closure, prosthetic valve failure, hemolysis, transient ischemic attacks, stroke, and subtle changes in higher cerebral functions, such as speech and memory.[4–11] MB can also coalesce and form gas emboli, which can resemble a vegetation or thrombus on the echocardiogram and be the cause of the observed transient ischemic attacks or strokes.[7]

Although the cavitation phenomenon has been extensively studied with in vitro models, in vivo results are mostly limited to case reports.[12,13] The aim of the current study was to evaluate the echocardiographic characteristics of patients with an MVP exhibiting gas emboli, their hemodynamic status and complications that may be related to gas emboli formation.

2 | METHODS

This was a retrospective study, conducted in 2018, evaluating the transthoracic echocardiograms (TTE) of 174 consecutive patients with a mitral valve replacement, aortic valve replacement, or both. The group with gas emboli were included in the study. Spontaneous MBs are defined as a small (less than 1 mm), bright, high-velocity echo finding, in the LV during valve leaflet closure (Figure 1).[14] The gas emboli were larger in appearance, but also high-velocity echo findings within the LV (Movie S1). Unlike MB, gas emboli dissolved into MB within the LV or disappeared into the left ventricular outflow tract or ascending aorta (LVOT, Figures 2 and 3). In these patients, the serial TTEs were reviewed until the first TTE without gas emboli was found. Transesophageal echocardiograms (TEEs) were also reviewed when available. The studies were evaluated by two experienced physicians (MA and OV) and one experienced sonographer (FA).

Patient characteristics such as age, weight, height, body surface area (BSA), time of cardiac surgery, number of cardiac surgeries done, number and type of MVP, comorbidities, and drug therapy were derived from the patient`s electronic record and/or echocardiographic reports. Blood pressure values were taken from the echo study report. The heart rate was either obtained from the echo study reports when there were no gas emboli, or from the corresponding echoframe where gas emboli were seen.

All the patients had a comprehensive TTE evaluation. The echocardiographic studies were performed with a commercially available ultrasound system (GE Norway-E-9/E-95- and Philips Medical System, -E33/Epic-) equipped with a broad band S5-1 transducer. A standard clinical protocol was followed for all echocardiograms, according to ASE recommendations.[15] The TTE studies included all structural and functional parameters of the cardiac chambers, including structural valvular deterioration that resulted in stenosis or regurgitation. An estimation of the prosthetic pressure gradients and flow velocity Doppler measurements were performed using ultrasound assessment (continuous wave -CW- and pulsed wave -PW-) of aortic and mitral MVPs. The measurements were obtained from the apical, right parasternal, suprasternal, and sub-costal views (to measure the highest velocities) for the aortic valve and CW Doppler recordings from the apical position for the mitral valve.[1] The mobility of the prosthetic disks and the presence of regurgitant jets were also evaluated. TEE was performed if there was any suspicion of MVP malfunctioning, thrombosis or endocarditis, pannus, or another reason that required a TEE evaluation. Prosthetic valve thrombi/vegetations were recognized as soft and homogeneous, independent motion masses located at the valve occlusion or valve disks, while pannus was suspected in a small mass, mostly involving the suture line, beneath the disks. TEE was performed using a 5-MHz multiplane after oropharyngeal anesthesia (10% lidocaine spray) and conscious sedation (intravenous midazolam 1-5 mg, fentanyl 25-50 mg IV).

For each patient, the last echocardiographic examination, with and without gas emboli, was compared, with the no emboli group serving as the control group. In this way, the two groups were automatically stratified for valve type, re-do sternotomies, numbers of prosthetic valves, and overall cardiovascular risk factors. The blood tests included the hemoglobin level, the last INR value, and pro-BNP.

2.1 | Statistical analysis

Categorical data are summarized as frequency and percentage. Continuous variables are expressed as mean ± standard deviation. Nominal variables were compared by using the Chi-square test. An unpaired *t* test was used to compare variables between TTE studies with and without gas emboli. The statistical analysis was done with SPSS 15.0 (SPSS, Inc). A value of $P < .05$ was considered to be statistically significant.

3 | RESULTS

In total, 174 patients had valve replacement surgery due to rheumatic heart disease. The gas emboli group (n = 57) (31 males, 26 females) had gas emboli in the LV (32.7%). Of this patient subset, 41 patients had an isolated mitral or combined mitral/aortic valve replacement and 16 patients had an isolated aortic valve replacement (Table 1).

All patients were on warfarin, and supplemental aspirin (81 mg/d) was prescribed for 17 patients. In seven cases, the INR was below the therapeutic range. The clinical characteristics corresponding to the last TTE with gas emboli are reported in Table 2. All except two patients were seen as outpatients. The two inpatients presented with fever and positive blood cultures, and a TTE or TEE was

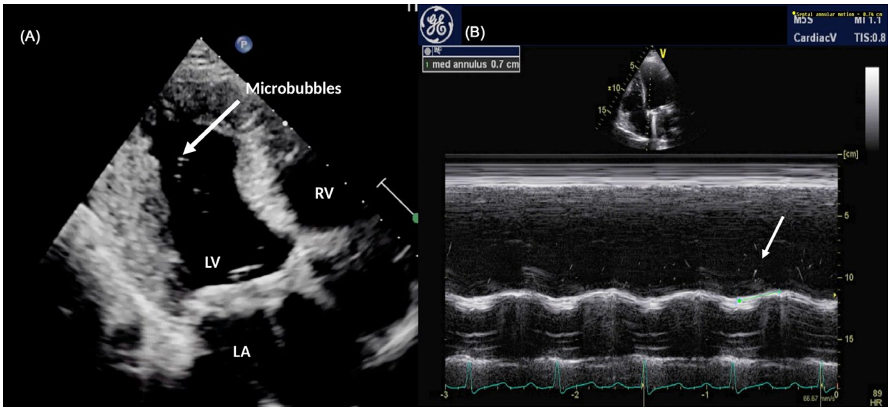


FIGURE 1 Panel A: The arrow indicates the microbubble (cavitation) from 4CH. Panel B: bright spots detected by M-Mode on the LVOT (left ventricular outflow tract). LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; RA = right atrium

requested to rule out endocarditis. MBs could be seen constantly during the echo study, with the gas emboli seen intermittently or during an increase in heart rate (eg, during atrial fibrillation or during a dobutamine stress echo, (Figure 4)). Most of the time, the increase in the heart rate was mild. The previous TTE studies were reviewed until a study was found with no gas emboli. In 26% (n = 15), all the reviewed TTEs showed gas emboli. In total, 52 TEEs were performed for 27 patients, ranging from 1 to 6 TEEs. The indication for the TEEs was gas emboli (seven patients) with one case positive for thrombus/vegetation, suspicion of prosthesis malfunction (nine patients), assessing a thrombus/endocarditis (eight patients) and for five patients, other reasons. In five cases, the TEE was positive for a mass or endocarditis.

A third of the group (33%, n = 19) had a cerebral CT to rule out cerebral lesions. The indication for the brain CT was to rule out brain hemorrhage after trauma (4 patients), clinical signs of stroke (3 patients), unusual headache (2 patients), supratherapeutic INR (1 patient), endocarditis (1 patient), gas emboli (2 patients), and possible gas emboli (6 patients). The CT revealed ischemic lesions (including a case of very small lacunar infarcts) in seven patients, a cavernous lesion in one patient, and subarachnoid hemorrhage in two patients. The cerebral CT was negative in nine cases.

The TTE studies with gas emboli were compared with the TTE without emboli for the same patient (n = 42). The gradients across the mitral and aortic valve, left ventricular ejection fraction, and blood pressure were similar in the two groups. The mitral valve peak

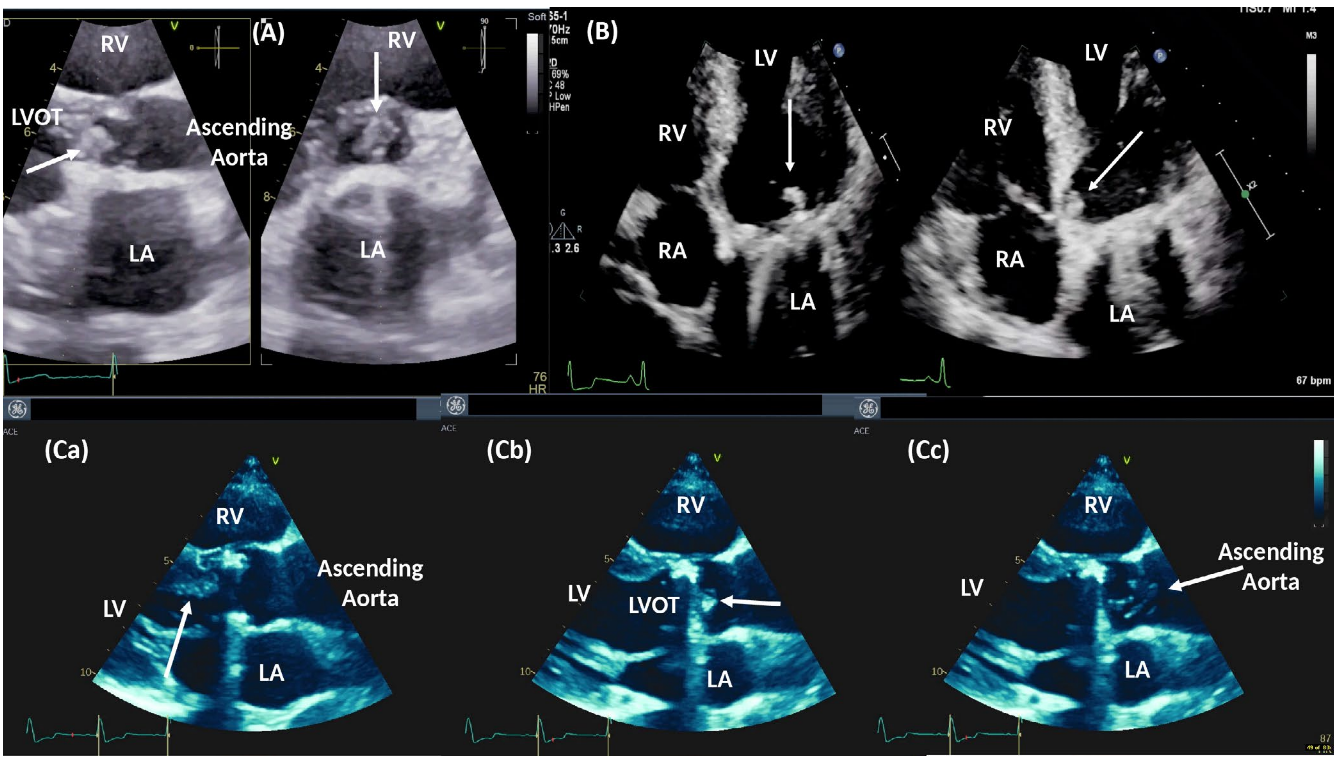
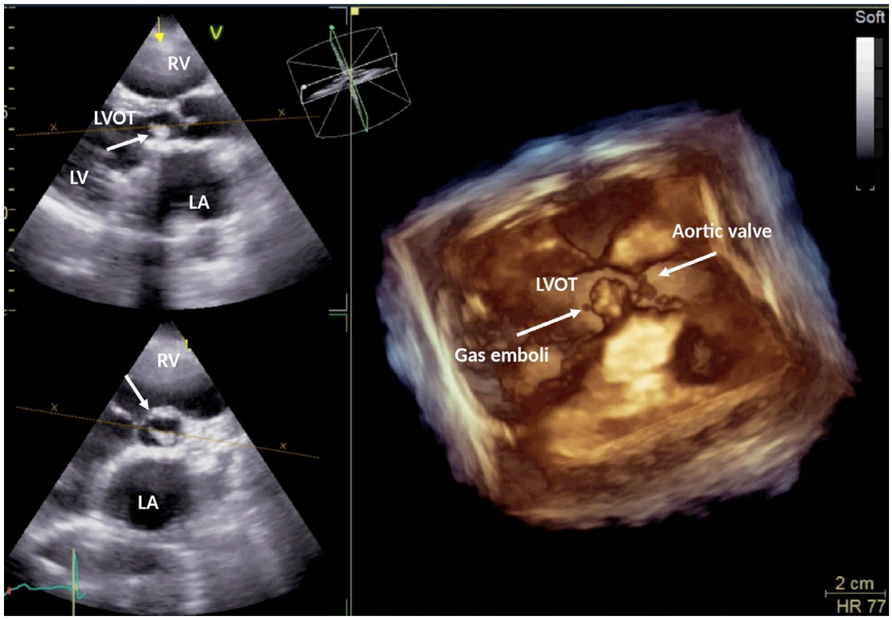


FIGURE 2 Mechanical valve in mitral position. Panel A: long axis and in short axis by x-plain showing gas emboli in the LVOT (arrow). Panel B: gas emboli on the mitral MVP and then in the LVOT (arrow). Panel C: Mechanical valve in aortic position. Gas emboli in the LVOT (Ca), across the aortic valve (Cb) and then it tends to dissolve in the ascending aorta (Cc), (arrow). LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; RA = right atrium; RV = right ventricle

FIGURE 3 Mechanical valve in mitral position. 3D echocardiography: gas emboli in the LVOT (arrow). LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; RV = right ventricle



gradients (11.9 ± 3.9 vs 11.7 ± 4.1 mm Hg, *P* = .8) and mean gradients (4.6 ± 1.9 vs 4.1 ± 1.6 mm Hg, *P* = .3) were similar in the TTEs with and without gas emboli, respectively. The aortic valve peak gradients (30 ± 12 vs 28.4 ± 20 mm Hg, *P* = .09) and mean gradients (11.8 ± 7.7 vs 16.7 ± 12.3 mm Hg. *P* = .1) were similar in the TTEs of both groups. Of all the parameters, only the HR was significantly higher in the group with gas emboli (Figure 5).

4 | DISCUSSION

Valve prosthesis implantation is a life-saving procedure but it has potential complications, such as anticoagulation-related bleeding and cerebral hemorrhage, thromboembolism, and mechanical prosthesis valve failure. Depending on the type of MVP, MB can be considered a normal echocardiographic finding. However, gas emboli are considered less prevalent and the consequences are not clear.[14]

TABLE 1 MVP characteristics and number of cardiac surgeries

		Size prosthesis
Number of prosthetic valves	1 valve: 34 2 valves: 18 3 valves: 5	
Type of valve in aortic position	23 Carbomedics 2 ATS	19–27
Type of valve in mitral position	38 Carbomedics 11 ATS 2 others	27–33
Number of cardiac surgeries	39 had 1 cardiac surgery 16 had 2 cardiac surgeries 3 had 3 cardiac surgeries	

In the current study, we found that: (a) gas emboli were present in a significant number of patients with MVP; (b) gas emboli were related to HR and associated with even a mild increase in HR; (c) gas emboli were present in patients who received anticoagulation or anticoagulation plus antiplatelet therapy; (d) gas emboli resulted in a significantly increased rate of requests for TEE to assess for thrombus/vegetations; (e) the association between cerebral CT results and gas emboli could not be determined.

Cavitation is a hydrodynamic phenomenon, which develop when a fluid undergoes very high acceleration in a spatially limited region, causing a sharp drop in pressure. When pressure falls below the fluid vapor pressure, bubbles of vapor emerge spontaneously. Cavitation can develop in cardiac blood flow in the presence of mechanical valve prostheses, more frequently during valve closure and in mitral valve replacements. Cavitation is never seen with bioprosthetic valves. Although most MBs last for a few milliseconds, some of them can last longer, especially if the heart rate increases. Longer lasting MBs have more time to interact and coalesce, resulting in gaseous emboli, which have the possibility to damage surrounding materials, from biological tissues to metallic elements. In addition to heart rate and the velocity of closure of the valve disks, other factors that can contribute to cavitation include the patient's age, gender, valve orientation, method of valve implantation, myocardial contractility, and oxygen therapy.[16–19]

There are different hypotheses about cavitation and the gas emboli phenomenon. The most accepted hypothesis is that gas emboli form due to a local transient pressure drop between the prosthetic ring and leaflet during valve closure. However, as this is accepted as a short-lived phenomenon, other authors suggested that the observed cavitation is associated with *degassing*, the liberation of CO^2 contained in water that is durable and occurs under much lower pressure drops. A third hypothesis is that MBs and gas emboli are solid microemboli. Valve designs always generate local flow characterized

Variables	Mean ± SD		Variables	Mean ± SD
Age (y)	46.8 ± 13.8		LVIDD (mm)	49.7 ± 6.6
Gender (M/F)	31/26		IVSD (mm)	9.2 ± 1.7
Height (cm)	161.9 ± 10.4		PWTD (mm)	8.8 ± 1.4
Weight (Kg)	73.2 ± 16		EF (%)	53.7 ± 10.7
BSA (m^2)	1.9 ± 0.2		LVMI (g/m^2)	
SBP (mm Hg)	123.3 ± 12.4		RWT	36.2 ± 8.5
DBP (mm Hg)	70.8 ± 11.4			
HR (bpm)	80.9 ± 18.8		MV Peak gradient (mm Hg)	11.9 ± 3.9
Sinus rhythm (n)	35		MV Mean gradient (mm Hg)	4.6 ± 3.9
Atrial fibrillation (n)	18			
Pace maker (n)	4		Aortic valve peak gradient (mm Hg)	21 ± 12.1
Laboratory data	**Mean ± SD**	**Range**	Aortic valve mean gradient (mm Hg)	11.9 ± 7.6
Hemoglobin (g/L)	123.3 ± 24.7	11–16	TR (m/s)	2.5 ± 0.81
INR (last determination)	2.6 ± 0.9	1–5	PASP (mm Hg)	33.2 ± 12.7
pro-BNP pmol/L	269.6 ± 184.1	23–749	TAPSE (mm)	14.3 ± 3.4

Abbreviations: BSA = body surface area; DBP = diastolic blood pressure; EF = ejection fraction; HR = heart rate; IVSD = interventricular septum in diastole; LVIDD = left ventricular diameter in diastole; LVMI = left ventricular mass index; MV = mitral valve; PASP = pulmonary artery systolic pressure; PWTD = posterior wall thickness in diastole; RWT = relative wall thickness; SBP = systolic blood pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

TABLE 2 General and echocardiographic characteristics of the 57 patients with gas emboli

by high shear stresses, turbulent fluctuations, regions of recirculation of blood, and stasis that enhance the risk of thrombus formation by inducing platelet activation, aggregation, and deposition.[20] The last hypothesis is probably the least likely.

The present evaluation compared echocardiographic examinations of the same patient with and without gas emboli. As a result, the case–control groups had identical characteristics in terms of type of valve, type of surgical intervention, number of surgeries, number of prosthetic valves, and cardiovascular risk factors. We found that gas emboli were present in a high proportion of patients and the presence was strictly associated with heart rate. Generally, gas emboli are observed at mean heart rates of 81 bpm vs 72 bpm for the control baseline examination. Gas emboli are also observed in patients with a sudden increase in heart rate, such as atrial fibrillation or during a dobutamine stress echocardiogram. Other hemodynamic parameters such as blood pressure, ejection

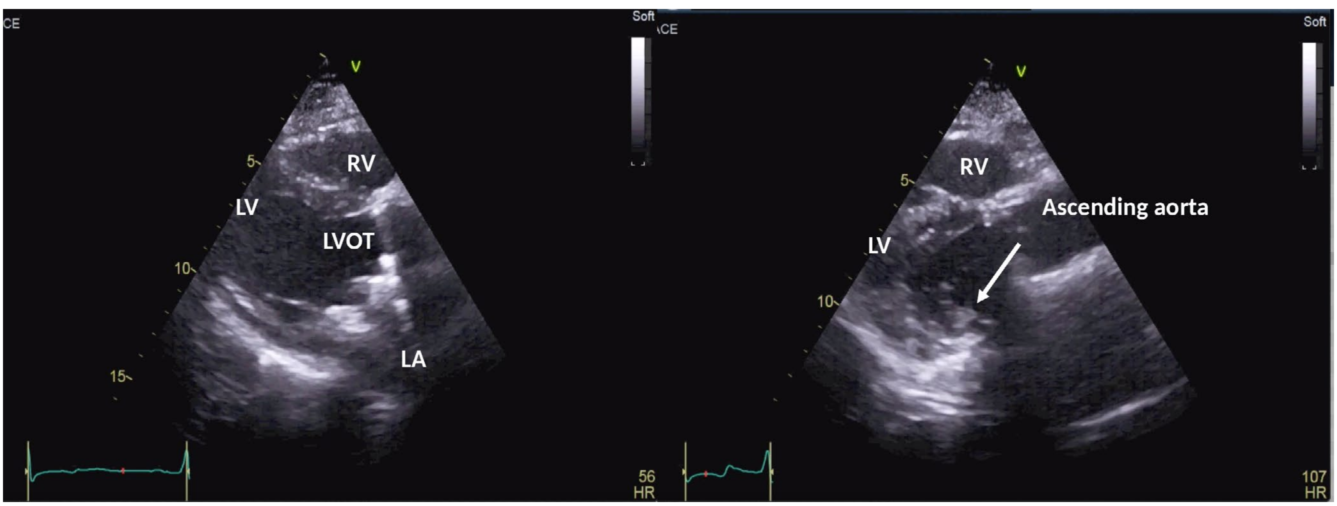


FIGURE 4 Mechanical valve in mitral and aortic position. Dobutamine stress test. Long axis view: gas emboli formation at HR of 107 bpm. HR = heart rate; LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; RV = right ventricle

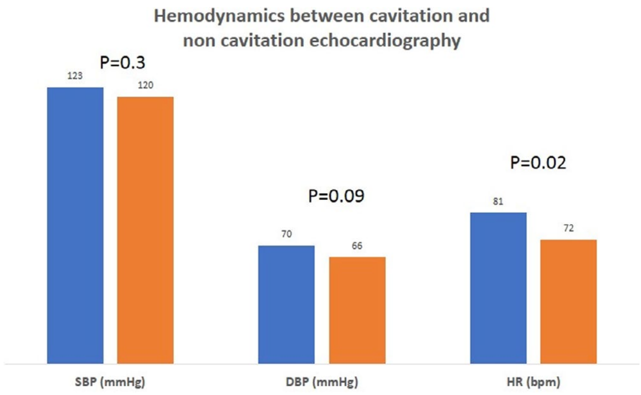


FIGURE 5 Difference in hemodynamics between the 42 patients with TTE with gas emboli (blue bars) and without gas emboli (orange bars). DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure

fraction, and gradients across the aortic and mitral valve did not differ between the two groups. A possible explanation could be the instantaneous pressure drops during rapid blood acceleration and deceleration, which correspond to valvular opening and closure in relation to HR.[21–23] This means that patients with mechanical valves may have multiple episodes of gas emboli related to an increase in the heart rate during daily life, and they occur more frequently than observed during echocardiographic studies. Most of the time, when the gas emboli reach the ascending aorta, they dissolve in microbubbles.

Patients had a significant number of TEE procedures. The most frequent indication was to rule out vegetation/thrombus in the absence of clinical or laboratory findings. Reviewing the studies, in some cases differentiating gas emboli from masses was quite difficult and, although we were aware of the characteristics of gas emboli, we did not feel confident to release the patients without a definitive diagnosis.

Cerebral CT was done in 33% of the sample, which was positive in 52% of cases. The CT was requested for different indications. In two cases, the indication was gas emboli with a negative result. For brain lesions related to gas emboli, an MRI would have been more sensitive than a CT. Brain involvement, due to circulating microbubbles, has been reported during cardiac surgery associated with a decline in cognitive performance.[24] Deklunder et al[25] found that patients with MVPs had higher rates of microemboli detected by transcranial Doppler and impaired working memory performance, compared to patients with bioprosthetic valves and normal patients. Telman et al[26] compared the microbubbles from agitated saline in patients with PFO to those of patients with MVP. They did not find any difference in duration and mean relative velocity between the bubbles in PFO and MVP patients. There are also some reports describing ischemic complications after a bubble test in PFO during TTE.[27–29] It can be speculated that the injected agitated saline with air for the PFO diagnosis has more bubbles reaching the brain for each time unit than the bubbles due to an MVP, but we cannot exclude that chronic gas emboli can have some effect on the brain.

4.1 | Limitations

To our knowledge, this is the largest collection of echo studies performed during regular follow-up with gas emboli related to LV mechanical valves. There are several limitations to our study. As this is a retrospective study, we could only register and describe the incidence of gas emboli as well as the additional diagnostic examinations requested for these patients. Also, we could not find any association between gas emboli and complications such as cerebral arterial occlusion or chronic microvascular ischemic changes because a cerebral MRI, which is more sensitive than CT, was not used. In addition, our findings can be ascribed to the Carbomedics leaflet valve only, since this valve was most frequently used in our center.

5 | CONCLUSIONS

Microbubbles are constantly associated with MVP and gas emboli are considered a rare phenomenon. In our group of patients, gas emboli were observed in 32.7% of the patients who had valve replacement surgery. Of this patient subset, 26% had gas emboli present in all echocardiographic studies. The presence of gas emboli was highly correlated to an increase in heart rate. We reported that gas emboli significantly increased the number of requests for additional diagnostic tests such as TEE and brain CT. In the current study, we were not able to find an association between gas emboli and brain involvement, and additional research is required to verify the possible association between MVP-induced gas emboli and brain injury.

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CONFLICT OF INTERESTS

The authors have no conflicts of interest.

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SUPPORTING INFORMATION

Movie S1. Parasternal long axis (left side) and short axis (X-plain with the cutting point in LVOT, on the right side). Gas emboli from the mechanical mitral valve (site of formation) to the LVOT and aortic root. AV = aortic valve; LA = left atrium; RV = right ventricle.