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Evaluation of the Systolic Pulmonary Pressure during stress Doppler Echocardiography in Mitral Stenosis

Saléha Lehachi[1]*; Fadila Daimellah[1]; Djohar Hannoun[2]; Youcef Laid[2]; Rachid Mechmeche[3]; Mohand Said Issad[1]

[1]Cardiology Department, University Hospital Center Beni Messous, Algiers, Algeria.

[2]National Institute of Statistics, Algiers.

[3]Cardiology Department at Rabta Hospital, Tunis.

***Corresponding Author(s): Saleha Lehachi**

Cardiology Department, University Hospital Center Beni Messous, Algiers, Algeria.

Email: leyas10@live.fr

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Keywords: Mitral stenosis; Systolic pulmonary artery pressure; Exercise doppler echocardiography.

Abstract

Background: In Mitral Stenosis (MS), the international recommendations favor the indication of Percutaneous Mitral Commissurotomy (PMC) if Systolic Pulmonary Artery Pressure (SPAP) reaches or exceeded 60 mmHg in Doppler echocardiography stress (Grade C).

Objective: Study of the SPAP during exercise Echocardiography in patient with Mitral Valve Area (MVA) of ≤ 2 cm^2.

Results: 300 patients were included. The mean age was 42.7±1.3 years, the sex ratio of 0.23. According to the MVA, three groups were defined. G1 (severe MS): MVA ≤ $1cm^2$ (n =72), G2 (moderate MS): $1cm^2$ < MVA < $1.5cm^2$ (n = 128) and G3 (mild MS): MVA ≥ 1.5 cm^2 (n=100). The mean MVA was 0.8 ± 0.1 cm^2 (G1), 1.3 ± 0.1 cm^2 (G2) and 1.7 ± 0.1 cm^2 (G3) ($p < 10^{-6}$). At rest, from the 1st to the 3rd group, mean heart rate/min was respectively 71.5 ± 2.7, 76.3 ± 1.7 and 73.6 ± 2.1, and means transmittal gradient were respectively to 11.6 ± 0.8 mmHg, 8.8 ± 0.5mmHg and 5.1 ± 0.3mmHg ($p < 10^{-6}$). At peak exercise, mean heart rate/min was 152.3 ± 2.9 (G1), 150.7 ± 2.2 (G2), 148.7 ± 2.4 (G3) (p = 0.20), and SPAP effort was 95.7 ± 3.6 mmHg (G1), 81.2 ± 2.2 mm Hg (G2) and 61.8 ± 1.2 mm Hg (G3) ($p < 10^{-6}$). At peak exercise, SPAP was above 60 mm Hg in 58 patients (58%) in G3 despite MVA ≥ 1.5 cm^2, 123 patients (86.2%) in G2 and 71 patients (98.6%) in G1.

Conclusion: At maximum exercise, most of our patients have increased their SPAP beyond 60 mm Hg, even those who had mild MS (MVA ≥ 1.5 cm^2). Therefore, in stress echo-Doppler, the SPAP at peak exercise justifying percutaneous mitral commissurotomy is probably greater than 60 mm Hg.

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Introduction

The Mitral Stenosis (MS) is the most frequent rheumatic valvulopathies, and its hemodynamic upstream explains the symptom (dyspnea of effort and crises of acute pulmonary oedema) and the evolutionary complications so rhythmic (atrial fibrillation in particular) that thrombo-embolic stroke in particular).

The cardiac echo-Doppler at rest is the examination by far the most useful, in particular to estimate the degree of severity of the MS based on the calculation of the Mitral Valve Area (MVA) and to appreciate its hemodynamic effects by the study of the mitral gradients and the Systolic Pulmonary Artery Pressure (SPAP).

The indication of the mitral intervention, the pair Percutaneous Mitral Commissurotomy (PMC) in particular, basses on the functional symptom (degree of the dyspnea), the risk thromboembolic and on results of the cardiac echo-Doppler at rest. The existence of a discrepancy between these different parameters, frequently observed in clinical practice, complicates the therapeutic decision.

The stress echo Doppler cardiac which allows to study the hemodynamic response after exercise or after injection of Dobutamine, in particular the rise of the mitral gradient and the SPAP was introduced in 1998 into the American Recommendations (ACC / AHA) to directed the therapeutic strategy, in particular in the cases where there is a conflict between the degree of severity of the dyspnea and the results of the cardiac echo-Doppler at rest [1].In front of these clinical situations, the American Scientific Society recommend a mitral intervention when in the cardiac echo Doppler of stress, the mean gradient exceed 15 mmHg (or double its resting value) and /or when the SPAP is superior to 60 mm Hg in the peak of the stress[1-3].The level of proof of the values recommended by the American is low(grade C).they are based , on old studies, with a small number of patients (20-60 patients) and hemodynamic values were recorded in the post-stress or in stress under maximal [4,5].

Objective

Was to study the evolution of the Systolic Pulmonary Artery Pressure (SPAP) of MS Echo Doppler cardiac during effort.

Materials and Methods

Study Type: Prospective, descriptive, study.

Location: Cardiology Department, UHC Béni Messous, Algiers. Duration of recruitment was of 34 months.

Patients

Patients with MS and a mitral valve area (MVA) ≤ 2 cm², in New York Heart Association (NYHA) functional classes I, II, and III, with a systolic pulmonary artery pressure (SPAP) ≤ 60 mm Hg on resting echo-Doppler, were included. Patients with mitral and/ or aortic regurgitation grade 3-4, aortic stenosis with a mean gradient > 30 mmHg, heart conditions that increase left ventricular diastolic pressure (ischemic heart diseases, hypertension...), conditions that raise SPAP (pulmonary pathologies...), and those leading to tachycardia (anemia, thyroid disorders...) , poor echogenicity and difficulties in recording the flow of tricuspid regurgitation were excluded.

Protocol

A resting cardiac echo-Doppler: Was performed in all patients before their inclusion. Mean and maximal mitral gradient and SPAS at rest were recorded. Based on MVA, patients were divided into 3 groups: G1 (very tight MS = MVA ≤ 1 cm²), G2 (tight MS = MVA between 1 and 1.5 cm²), and G3 (moderately tight MS = MVA ≥ 1.5 cm²).

Exercise testing: To identify dyspneic subjects objectively, an exercise test was performed on a treadmill using according the Bruce protocol (30 Watts/3 minutes). The Dyspnea was stratified in the following way:

Stage I: onset of dyspnea motivating effort to stop a load level greater than 90 watts or beyond the third level.

Stage II: onset of dyspnea motivating effort to stop a load level between 30 and 90 watts or, which corresponds to the second and third level.

Stage III: onset of dyspnea motivating effort to stop a load level less than 30 watts, that is to say from the first level.

The patients not dyspneic (asymptomatic) corresponded to those who were at the stage I and dyspneic patients to those stratified stage II and III.

The doppler cardiac stress (effort)

Has been performed on an echocardiography table tilting, the patient pedal half-sitting position at 45°. The exercise was stopped when the maximum frequency theory (TMF = 220 - age) was reached or before the onset of symptoms requiring cessation of exercise (severe dyspnea cyanosis or severe pain in the lower limbs). This is the Bruce protocol was used (30 Watt/3 minutes). The ECG recording was continuous. Heart rate, MMG and SPAP were measured at rest and at the end of each level to the peak stress and recovery.

Endpoints

The evaluation criteria is represented by the average of the SPAP recorded at the end of the first level and at peak effort. These values are accompanied by their corresponding 95% Confidence Intervals (CI).

Statistical Analysis

The results are presented as Mean (m) ± CI 95% for continuous variables and number (percentage) for categorical variables. Group comparisons were conducted using the following tests: Student's t-test, ANOVA, Kruskal-Wallis, Chi-square and Fisher's exact test. A p value less than 0.05 was considered to be statistically significant. cfr EPI INFO version 6.04 released by the CDC was used.

Results

Characteristics of patients

Three hundred patients were included. The mean age was 42.7±1.3 years, the sex ratio of 0.23. The anatomical average MA is 1.34 ± 0.04cm² on 300 patients, G1= 72 patients (24%) had a MA < 1.00cm²; G2= 128 (42.7): 1.00cm² < MA <1.50 cm²; and G3= 100 (33.3%) : MA ≥ 1.50 cm². Patient characteristics and results of Doppler echocardiography rest in all three groups (G1,G2,G3) depending on the degree of severity mitral stenosis (Table 1).

Stratification of effort dyspnea (NYHA versus Exercise Testing)

This analysis shows that the evaluation of effort dyspnea using the Ergometric test is more objective than that based on the NYHA (Figure1).

Results of stress Doppler echocardiography

Charge level reached

The effort was maximal (≥80% of the TMF) in most patients (92% of cases). Nearly 2/3 of the patients arrived at a load 90 Watts: third tier and this regardless of the severity of MS (Table 2).

Evolution of Heart rate

(Table 3) shows no relationship between the severity of MS and increased Heart Rate (HR) recorded in the first level ($p=0.24$) and at peak exercise ($p=0.20$).

The rise in heart rate was higher during the first level 55 % to 59 %) and similarly in the three groups of patients ($p = 0.16$). Thus, 55- 59 % of this increase occurred at the end of the first level.

Evolution of Systolic Pulmonary Artery Pressure (SPAP)

Relationship between SPAP and mitral area

In (Table 4), during the effort, the SPAP increased in a proportional way with the severity of the MS as well in the 1^{er} landing as in the peak of the effort ($p < 10^{-6}$). In Three groups, about 60 % of the increase of the SPAP were recorded during the first landing and in a similar way in three groups of patients ($p=0.42$).

Relationship between SPAP and dyspnea

❖ In the general population

The SPAP is higher in symptomatic patients (stage II, III), both at rest ($p < 10^{-6}$), at the end of the first level ($p < 10^{-6}$) and at maximum of effort ($p < 10^{-6}$) (Table 5).

At the first level, the increase in SPAP was 60% and 59% respectively dyspneic subjects and asymptomatic subjects ($p= 0.50$).

❖ In groups G1 and G2 (SM <1.5 cm ²)

In severe or moderate MS (n = 200), SPAP is higher in patients with dyspnea: at rest ($p < 10^{-6}$), at the end of the first stage ($p < 10^{-6}$) and peak effort ($p < 10^{-6}$) (Table 6).

The increase of the SPAP is early (57 % to 60 %) at the end of the first level and similar between the subjects dyspneic and subjects without dyspnea ($p = 0.49$).

Predictive value of SPAP peak effort with the value of 60 mm Hg (threshold AHA / ACC)

❖ General population

In our study population, 83.6% of patients have increased SPAP beyond 60 mmHg at maximum effort (threshold in the U.S Recommendations: Table 7).

At peak effort, the predictive value of Doppler stress in the onset of dyspnea justifying the PMC is low with values of 60 mmHg.

❖ Predictive value of SPAP peak effort with the value of 60 mmHg according to severity of mitral stenosis and dyspnea

Figures 2 and 3 show that in the peak effort, in the group of MVA ≥1.5 cm², more of one a patients on two exceeded in the peak of the effort the threshold of 60 mmHg and in the group of the asymptomatic patient (stage I), 2/3 of these patients increased their SPAP beyond 60 mmHg in the peak exercise (high number of false positives).

Example of a PAPS profile in exercise Doppler echocardiography (Figure 4).

Table 1: Patient characteristics in all three groups depending on the degree of severity mitral stenosis.

Parameters (N = 300) m ± CI 95% n(%)	Group 1 MVA ≤ 1cm² (N = 72)	Group 2 1cm²< MVA < 1.5cm² (N = 128)	Group 3 MVA ≥ 1.5cm² (N = 100)	p
Sex (Women)	53 (73.6)	(84.4)	83 (83 .0)	0.15
Age	36.2 ± 2.9 (17-71)	43.2 ± 1.7 (21-69)	46.8 ± 2.0 (21-72)	10^{-6}
NYHA I II III	 7 (9.7) 56 (77.8) 9 (12.5)	 39 (30.5) 88 (68.8) 1 (0.8)	 80 (80.0) 19 (19.0) 1 (1.0)	10^{-6}
FA	19 (26.3)	25 (19.5)	17 (17.0)	0.80
Beta- blocker Diuretic IEC/ARAII Nitrates	40 (55.5) 42(58.3) 42 (58.3) 16(22.2)	54 (42.1) 34(26.5) 66 (51.5) 3 (2.3)	30 (30.0) 5 (5.0) 19 (19.0) 0 (0.0)	2.10^{-2} 10^{-2} 10^{-4} 10^{-3}
MA anatomic (cm²)	0.8 ± 0.1	1.3 ± 0.1	1.7 ± 0.1	10^{-6}
Score de Wilkins > 8	8.8 ± 0.3	8.7 ± 0.2	7.5 ± 0.2	10^{-6}
LA Area (cm²) ≥ 20	29.3 ± 7.8	27.9 ± 6.1	24.8 ± 7.1	7.10^{-5}
MVA functional / PHT (cm²)	0.8 ± 0.1	1.2 ± 0.1	1.7 ± 0.1	10^{-6}
MMG (mm Hg)	11.6 ± 0.8	8.8 ± 0.5	5.1 ± 0.2	10^{-6}
SPAP (mm Hg)	41.3 ± 1.7	34.6 ± 1.2	28.7 ± 0.7	10^{-6}
TR grade 3-4	12 (16.7)	17 (13.3)	7 (7.0)	0.05*
MR grade 3-4	11 (15.3)	31 (24.2)	25 (25.0)	0.28

NYHA**:** New York Heart Association; MVA: Mitral Valve Area; PHT: Pressure Half-Time; LA: Left Atrium; MR: Mitral Regurgitation; TR: Tricuspid Regurgitation; MMG: Mean Mitral Gradient; SPAP: Systolic Pulmonary Artery Pressure. Qualitative variables expressed as n (%) and quantitative variables as mean ± standard deviation.

Table 2: Load level achieved by patients in the Doppler effort.

Watts	N = 300 n (%)
30 (1st level)	2 (0.7)
60 (2nd level)	97 (32.3)
90 (3rd level)	184 (61.3)
120 (4th level)	17 (5.6)

Table 3: Profile of heart rate during effort according to the severity of the MS.

Heart rate (beats/min) m ± CI 95%	G1 N = 72	G2 N = 128	G 3 N = 100	P
Rest	71.5 ± 2.7	76.3 ± 1.7	73.6 ± 2.1	
1st level (30W)	118.7 ± 3.3	117.0 ± 2.6	114.7 ± 3.3	0.24
Peak effort	152.3 ± 2.9	150.7 ± 2.2	148.7 ± 2.4	0.20
[First level- rest] / [peak stress-rest]	0.59 ± 0.03	0.55 ± 0.03	0.55 ± 0.04	0.16

Table 4: Profile of SPAP during effort according to the severity of the MS.

SPAP (mmHg) m ± IC 95%	G1 N = 72	G2 N = 128	G 3 N = 100	p
Rest	41.2 ± 1.7	34.6 ± 1.1	28.7 ± 0.7	$< 10^{-6}$
1st level(30W)	74.1 ± 3.7	62.0 ± 2.4	49.1 ± 1.7	$< 10^{-6}$
Peak effort	95.7 ± 3.6	81.2 ± 2.2	61.8 ± 1.2	$< 10^{-6}$
[1st level – rest] / [Peak effort – rest]	0.60 ± 0.03	0.59 ± 0.03	0.62± 0.03	0.42

Table 5: Comparison between the mean SPAP in patient with dyspnea and patients without dyspnea in the study population to the Doppler stress.

SPAP (mmHg) m ± IC 95%	G1 N = 72	G2 N = 128	G 3 N = 100	p
Rest	41.2 ± 1.7	34.6 ± 1.1	28.7 ± 0.7	$< 10^{-6}$
1st level(30W)	74.1 ± 3.7	62.0 ± 2.4	49.1 ± 1.7	$< 10^{-6}$
Peak effort	95.7 ± 3.6	81.2 ± 2.2	61.8 ± 1.2	$< 10^{-6}$
[1st level – rest] / [Peak effort – rest]	0.60 ± 0.03	0.59 ± 0.03	0.62± 0.03	0.42

Table 6: Change of the SPAP according to the presence or not the dyspnea in groups G1G2.

PAPS (mm Hg) m ± CI 95%	Dyspnea (-) N = 34	Dyspnea (+) N = 166	p
Rest	30.7 ±1. 6	38.3 ± 1.1	$< 10^{-6}$
1st level	51.6 ± 2.9	69.4 ± 2.3	$< 10^{-6}$
Peak effort	67.7 ± 2.5	90.3 ± 2.1	$< 10^{-6}$
[1st level – rest] / [Peak effort – rest]	0.57 ± 0.06	0.60 ± 0.02	0.42

Table 7: SPAP Sensibility and Specificity with the value of 60 mmHg.

Tests	Peak Effort		
Index	Sensitivity	Spécificity	PPE (false +)
SPAP ≥ 60mmHg	95.6%	33.9%	66%

PPE: Positive Predictive Error.

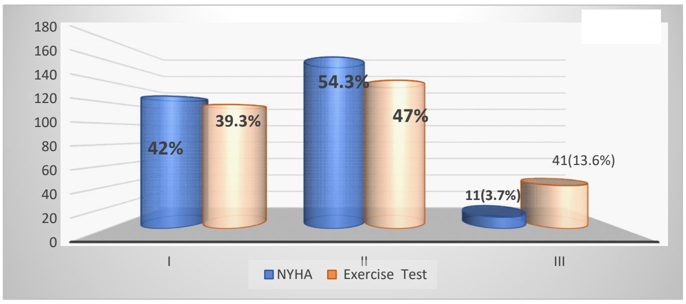

Figure 1: Stratification of effort dyspnea (NYHA versus Exercise Testing).

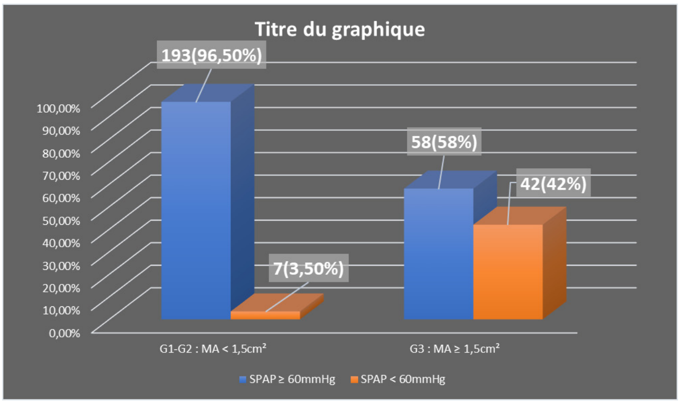

Figure 2: Predictive value of SPAP with the peak value of 60 mmHg according the severity of mitral stenosis.

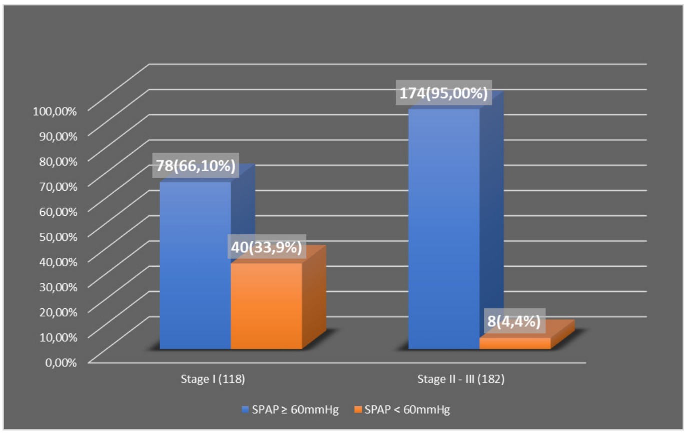

Figure 3: Predictive value of SPAP with the peak value of 60 mmHg according the severity of dyspnea.

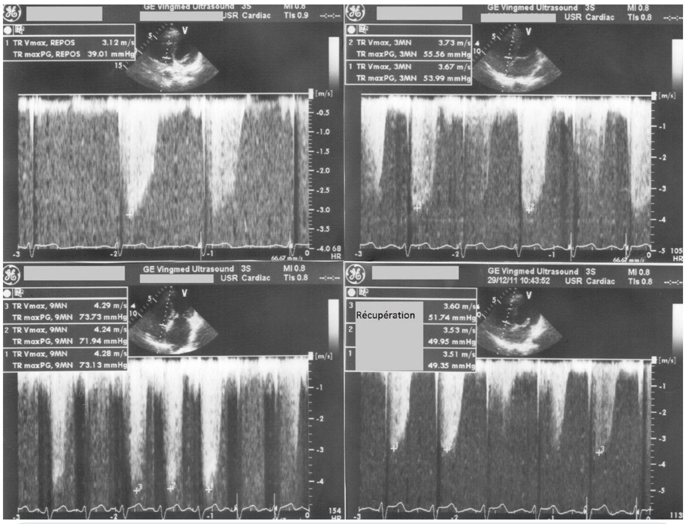

Figure 4: Profile of SPAP in effort Doppler echocardiography.

Discussion

In our population, our finding are:

- The stress test stratifies more precisely and objectively the severity of dyspnea versus NYHA classification (p=2. **10**$^{-6}$).
- Absence of link between the cardiac frequency and the degree of severity of the MS during the effort.
- At the first level and the peak of the effort, the SPAP is higher than MS is tighter (p=10^{-6}).
- The speed of the increase of the SPAP was not linear, it was the most important during the first level. So, more than 50% of the increase occurred during the first three minutes, whatever the degree of severity of the MS on the one hand, to the subjects dyspneic and to the subjects not dyspneic on the other hand.
- At the first level, the elevation of SPAP is similar regardless of the severity of (p=0.42) and functional symptoms (an identical increase in dyspneic subjects and subjects without dyspnea (p=0.50).
- In MS severe and moderate MS (SM<1.5 cm^2), the SPAP is more important in dyspneic patients both at rest (p= 10^{-6}), the first level (p= 10^{-6}), that at peak exercise (p= 10^{-6}), but the rate of increase in SPAP first level is similar between patients with dyspnea and asymptomatic patients (p= 0.49).
- At the most of the exercise, it is the subjects most dyspneic that increased in a more important way their SPAP (p=10^{-6}).
- This study shows the low specificity of the SPAP with the value of 60 mmHg at peak (33.9%).

Compared to the international literature:

The number of patients included in this study is significantly higher (300 patients). Indeed in various publications, the number of patients is generally low (10-60 subjects), which reduces the power of the results of this studies [4-9].

Brochet showed on 48 patients judged not dyspneic at the end of the interview (stage I of the NYHA), 22 (46%) were in reality dyspneic and developed during the echo Doppler effort an important dyspnea which motivated to stop the test. This observation joins our results and confirm the subjective character of the stratification of the dyspnea based on the classification of the NYHA, in particular when it is about stage I, II and III). However, our results and those of Brochet highlight the importance of quantifying dyspnea on exercise test, especially in patients with a discrepancy between the severity of dyspnea in the interrogation (NYHA) and the degree of MS evaluated according to the mitral area measured by echocardiography [9].

Most study have used physical effort as stress [5-7,9-15]. It was realized on a treadmill or bicycle and the majority of authors did not register the SPAP during effort, but more often in post effort, beyond the first minute after cessation of exercise [6,7-10]. Others realized the recordings in the "peak of the stress", but it is necessary to say that this one was in reality under maximal, lower than 75% of the TMF [5,15]. Thus, the values were recorded when the heart rate and hemodynamic variables down , it is the reason for which , in the majority of the publications, we notice that the average of the cardiac frequency , the SPAP registered in the stress are lower than our results [7-11]. In our work, the effort was maximal , $\geq$ 80% of the TMF in most patients (92% of cases).In the literature , only Brochet used a protocol that is similar to ours(bicycle, half- sitting position and recording of variables at each level until the TMF or until the appearance of dyspnea (20W/3 minutes).

Cheriex, which restarted his population in three groups according to the MA, obtained similar results to ours that is existence of a relation between the severity of the MS and the increase of the SPAP at stress echo Doppler [7].

In the MS, few authors have studied the hemodynamic changes and their relation with the, of dyspnea during stress. Using Doppler recordings in post exercise in 17 patients with M, Tunick showed that the onset of dyspnea during exercise was related to a significant increase in SPAP [4]. So, the results of these stadies join ours. In the work of Brochet, the rate of increase of SPAP was faster in patients who developed dyspnea during echo Doppler of effort versus those who remained asymptomatic [9]. In contrast, the average recorded in the SPAP peak effort was not different between the two groups (p=0.58). This difference with the profits of Brochet is explained by the category of patients included. Indeed, Brochet took only 48 patients, who were at the stage I of the NYHA and who had a mitral area less than 1.5 cm^2.

In the MS, the first recommendations which validated the stress cardiac echo Doppler in case of conflict between the symptoms and the severity of the MS are Guidelines Americans which were published in 1998 by the AHA/ACC [1]. In these recommendations and those published in 2006 [3], the mitral dilation is indicated when the mean gradient mitral upper to 15 mmHg and /or SPAP superior to 60mmHg in the peak stress. It should be noted that the level of evidence of these thresholds is low (grade C). Indeed, in our study, on 118 patients not dyspneic in exercise test, in Doppler cardiac stress, the SPAP was greater than 60 mmHg in 78% (66.1%) (high rate of false positives). So, in the peak of the effort, 2/3 the asymptomatic patients exceeded thresholds proposed by the International Recommendations for the CMP. This threshold value remains disputed, moreover, it was not retained in the Recommendations of the European Society of Cardiology (ESC) published, since. 2007 [13,14,16.]. In his article published in. 2011, Brochet questioned this thresholds, highlighting the lack of specificity of the SPAP with the value of 60 mmHg at maximum exercise, and he underlined the need to define the true predictive thresholds of the dyspnea of effort asking indication of the CMP.

Abbreviations

AF: Atrial Fibrillation; AR: Aortic Regurgitation; AS: Aortic Stenosis; CI: Confidence Intervals; HR Heart Rate; LA Left Atrial; MR: Mitral Regurgitation; MS: Mitral Stenosis; MVA: Mitral Valve Area; NYHA: New York; Heart Association; PMC: Percutaneous Mitral Commissurotomy; SDE: Stress Doppler Echocardiography; SPAP: Systolic Pulmonary Artery Pressure; HR: Heart Rate; TR: Tricuspid Regurgitation; W: Watts.

Conclusion

We hold in this work:

- Proportional relation between the importance of the SPAP recorded in the first landing and in the peak of the effort with the severity of the MS and the dyspnea.
- No relation between the speed of increase of the SPAP in the 1er landing with the severity of the MS and the dyspnea.
- At peak effort, the predictive value of Doppler stress in the onset of dyspnea justifying the PMC (threshold proposed by the AHA) is low with values of 60 mm Hg.

Conflicts of interest: None.

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