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Mitral Valve Abnormalities during Hypertrophic Cardiomyopathy: Study on a Cohort in Dakar

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Abstract

INTRODUCTION: Mitral valve abnormalities in hypertrophic cardiomyopathy (HCM) are becoming increasingly well defined, and their role in intra-ventricular obstruction is well defined. The aim of this study was to evaluate mitral valve abnormalities in patients with HCM. **PATIENTS AND METHODS:** We conducted a descriptive cross-sectional study from May 1 to July 1, 2022 in the Cardiology Department of Aristide Le Dantec Hospital. All patients with HCM aged at least 18 years old were included. The parameters studied concerned mainly the mitral valvular apparatus (papillary muscles abnormalities, leaflet length, mitral insufficiency). **RESULTS:** A total of 10 patients were included. Mean age was 58.3. On Doppler echocardiography, mean interventricular septal thickness was 20.6 mm. The mean maximum intra-ventricular gradient was 21.06 mmHg. Two patients had significant intra-ventricular obstruction. The mean length of the anterior mitral valve leaflet was 28.7 ± 3.55 mm, with extremes of 22 and 33 mm. The posterior mitral leaflet averaged 14.8 ± 3.16 mm. Nine (9) out of 10 patients had an elongated anterior valve leaflet. Elongation of the posterior leaflet was noted in 6 patients. With regard to papillary muscle position, 6 patients had an anterolateral ascending pillary muscle. These patients had a mean intra-ventricular gradient of 25 mmHg, compared with 16.5 mmHg in the others cases. We found no direct insertion on the mitral valve. Mitral insufficiency was noted in 9 patients, including 5 with mild insufficiency and 4 with moderate one. **CONCLUSION:** Mitral valve abnormalities in HCM appear to be frequent. They should be analyzed for a better diagnostic and therapeutic approach.

Keywords

Hypertrophic Cardiomyopathy, Mitral Valve, Obstruction

1. Introduction

Hypertrophic cardiomyopathy (HCM) is a primary condition defined, according to European guidelines [1], by the presence of increased left ventricular parietal thickness that cannot be explained by abnormal loading conditions. It is usually asymmetrical, often septal, and inconsistently with ventricular obstruction. It is the most common genetic heart disease, with a prevalence of 1/500 [2]. It is a genetically heterogeneous disease, inherited in the autosomal dominant mode. Obstruction is a prognostic factor [3] [4]. It is generally due to systolic anterior motion (SAM) of the mitral valve, producing an intraventricular gradient at rest or during exercise. This generates a turbulent flow sucking in the medial part of the large valve, sticking it or bringing it closer to the left interventricular septum. In the left ventricular outflow chamber, systolic anterior motion produces a sub-valvular obstruction, with the distal part of the large valve prolapsing into the outflow chamber opposite the septal bead and obstructing ejection flow [5]. In addition, morphological abnormalities of the mitral valve as mitral valve elongation, ascended papillary muscles and direct insertion of mitral valve leaflet, even in the absence of hypertrophy, may be the cause of this obstruction. Classical dogmas concerning the dynamic nature of obstruction are tending to change in the direction of a mechanical origin [6]. Thus, we proposed to study the mitral valve apparatus in patients with HCM in a cohort of patients followed for this pathology in our unit.

2. Patients and Methods

We conducted a descriptive cross-sectional study from May 1 to July 2022 in the Cardiology Department of Aristide Le Dantec Hospital. The study population concerned all patients followed for HCM at the Cardiology Department of Aristide LE DANTEC Hospital. A cohort of all consecutive cases of HCM has been set up there since 2015. The positive diagnosis was made on the basis of echocardiography and MRI in some cases. It was confirmed with the presence of a left ventricular wall thickness of ≥15 mm unexplained by abnormal loading conditions or unexplained left ventricular wall thickness of ≥13 mm in relatives of individuals with HCM. All patients with HCM aged at least 18 years were included in this study. Those who refused to participate were not included. With regard to the parameters studied, we were first interested in the general characteristics of our population: age, sex, history and symptoms. We then looked at echocardiographic data: type of HCM, presence of obstruction. Mitral valve abnormalities were studied in particular: we looked for mitral insufficiency, we measured the length of the mitral leaflets with standards of 22 - 23 mm for the

anterior leaflet and 12 - 13 mm for the posterior leaflet [7]; we analyzed the insertion of the papillary muscle, the position of the pillary muscles to.

We used a General Electric (GE) Vivid E9 XD clear with 3Sc probe. The examination was carried out by a cardiologist qualified in echocardiography and experienced in HCM. In addition, the recorded loops were reviewed by a second echocardiographer. In some cases, MRI was performed to confirm HCM and check for mitral abnormalities.

We used Word 2021 and Excel 2021 software for data entry. Data analysis was performed using SPSS (Statistical Package for Science Social) version 23.0. For quantitative variables, results were presented as mean, standard deviation, minimum and maximum; qualitative variables were described by frequency.

3. Results

A total of 10 patients were included out of the 44 in the registry.

General characteristics of the population

The mean age was 58.3 years, with extremes of 26 and 92 years. Symptomatology was dominated by dyspnea and chest pain (7 cases respectively). Syncope and lipothymia occurred in 02 patients. The electrocardiogram showed regular sinus rhythm in all patients. Left ventricular hypertrophy was found in 5 patients, and negative T waves in 6. Q-waves of lateral pseudonecrosis was found in 3 patients. On Doppler echocardiography, the mean interventricular septal thickness was 20.60 mm, with extremes of 09 and 23 mm. Maron type IV predominated (5 cases). This was followed by Maron type III (4 patients) and I (1 patient). The mean maximum intra-ventricular gradient was 21.06 mmHg, with extremes of O and 90 mmHg. Two patients had a resting gradient greater than or equal to 30 mmHg. Mean LVEF was 65.8% measured at SB. The median was 65%, with extremes ranging from 54% to 79%.

Table 1 summarizes the general characteristics of our population.

Table 1. General characteristics of the population.

Parameters	Number (/10)	Frequency
Dyspnea	7	70
Chest pains	7	70
Syncope and lipothymia	2	20
Negative T waves (ECG)	6	60
Q-waves (ECG)	3	30
Maron Type		
Type IV	5	50
Type III	4	40
Type I	1	10
Intraventricular Obstruction	2	20

Abnormalities of mitral Leaflet length

The mean length of the anterior mitral valve was 28.7 ± 3.55 mm, with extremes of 22 and 33 mm. The mean length of the posterior valve was 14.8 ± 3.16 mm, with a minimum of 10 mm and a maximum of 21 mm. Nine out of 10 patients had an elongated anterior valve (Figure 1). As for the posterior valve, elongation was noted in 6 patients. Table 2 summarizes the data concerning mitral valve leaflet length.

Papillary muscles position

Four (4) patients had papillary muscles in normal horizontal position. On the other hand, 6 presented ascended papillary muscles (Figure 2). It was noted that

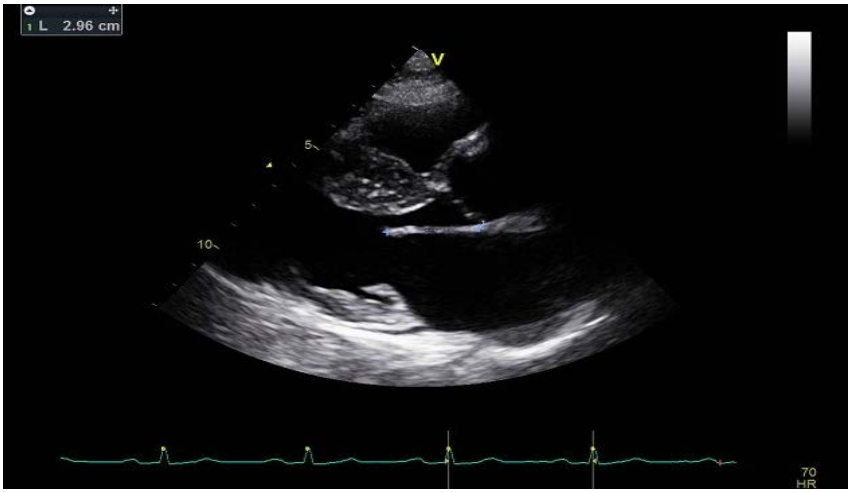

Figure 1. Echocardiography picture showing anterior mitral valve elongation.

Table 2. Measurement of mitral leaflets.

Parameters	Minimum	Maximum	Mean ± standard deviation
Anterior leaflet (mm)	22	33	28.7 ± 3.55
Posterior leaflet (mm)	10	21	14.8 ± 3.16

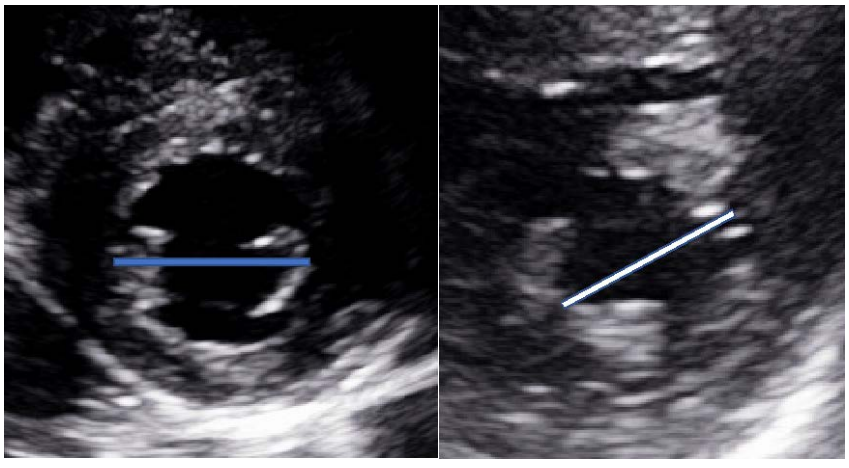

Figure 2. Echocardiography picture showing ascended antero-lateral papillar muscle (white line) compare to the normal position (Blue line).

the mean gradient in patients with anterolateral ascended papillary muscle was 25 mmHg, whereas the mean in the others was 16.5 mmHg.

Papillary muscle insertion and SAM

We found no direct papillary muscle insertion or SAM.

Mitral insufficiency

We found mitral insufficiency in 9 patients. Of these, 5 had mild insufficiency and 4 moderate one.

Strain

Overall strain averaged −15.4% ± 3.59% for a minimum of −8.8% and a maximum of −22.0%. Three (3) patients had a strain less than or equal to −14%.

The two patients with intraventricular obstruction at rest had the following characteristics:

- the first one had elongation of the anterior mitral valve and minimal septal hypertrophy (15 mm).
- the second one had greater morphological abnormalities, with elongation of both mitral valves, ascension of the anterolateral papillar muscle associated with an LV diameter of less than 45 mm, and a greater septal hypertrophy (19 mm).

Table 3 summarizes the mitral anomalies noted in our population.

4. Discussion

Limitation of the study

Our study was limited by the small number of cases which reduces the power of the results. However, this is about a rare disease and these results could serve as basis for a multicenter study in Africa.

Characteristics of our population

The most represented age group was 55 - 60 years, with an average age of 58.3 years. Although hypertrophic cardiomyopathy has long been considered as a disease of the young, it is increasingly diagnosed in adults. In a study published in 2020, Canepa [8] analyzed the temporal evolution of patients' age at diagnosis of hypertrophic cardiomyopathy between 1961 and 2019. Patients diagnosed with hypertrophic cardiomyopathy were increasingly older, with an average age of 40 before 2000 and 51 after 2010. This may be due to the development of diagnostic tools, in particular MRI, but also to greater awareness on the part of practitioners of the diagnosis of this pathology [6]. We noted 4 female and 6

Table 3. Summury of mitral valve abnormalities.

abnormalities	Number	Pourcentage (%)
Mitral insufficiency	9	90
Anterior mitral valve elongation	9	90
Ascended papillary muscles	6	60
Posterior mitral valve elongation	6	60

male patients. This male predominance has been reported in several studies. Olivotto *et al.*, in a study published in 2005 including 969 HCM patients in Italy and the USA, noted a male predominance (59%) [9]. Maron in a study including 51 patients in Tanzania reported 67.9% men [10].

Mitral valve abnormalities

We found a mean anterior mitral valve length of 28.7 ± 3.55 mm and posterior of 14.8 ± 3.16 mm. Among our patients, 9 out of 10 had an elongated anterior valve. Elongation of the posterior valve was noted in 6 patients. These measurements are similar to those reported by Maron [11] in 2011. This study included 172 patients with HCM and 172 without. Indeed, a length of 26 ± 5 versus 19 ± 5 mm for the anterior valve and 14 ± 4 versus 10 ± 3 mm for the posterior valve was reported for the HCM patient and control groups respectively. Klues *et al.* [12], in a study including 37 HCM patients, reported mitral valve elongation in 84% of cases. These measurements can be made on echocardiography or MRI. In MRI, mitral valve measurement is part of the overall HCM work-up, as can be seen in Maron's study [11]. Evidence for the existence of primary rather than acquired mitral leaflet changes derives mainly from comparative results between the affected group and an unaffected control group, showing that leaflet length was increased in HCM patients. Furthermore, in the subgroup of patients affected by this pathology, there was no difference in anterior mitral valve length between obstructive and non-obstructive HCM patients. The MRI findings in the preclinical HCM group suggest that changes in anterior mitral leaflet tissue occur early in the disease process and are not necessarily caused by a direct effect of the sarcomeric gene mutation. As postulated by Maron *et al.* [11] in the same study, other mechanisms, such as growth factors, modifier genes and environmental factors, probably play a major role in shaping the phenotype. A number of ideas and theories have been put forward on this subject. Some authors have argued for a link between mitral leaflet changes and genotype. For example, Hagège *et al.* suggested that posterior leaflet elongation of 14 mm was observed in carriers of a morbid HCM mutation, but without hypertrophy or obstruction [13]. The presence of an elongated leaflet in HCM patients without hypertrophy or obstruction suggests that changes in valve geometry are not due to leaflet stress or ventricular remodeling, but depend on a genetic defect (a mutation in the sarcomere gene). Indeed, a study by Judge *et al.* of MYBPC3 mutations showed that MYBPC3-mutated knockout mice with diagnosed LVH had longer, thicker mitral leaflets than controls. This abnormality was noted in the absence of obstruction or MAS [14].

Normally, the papillary muscle is aligned and horizontal. During HCM, however, they may become elevated, towards the interventricular septum [6], with the result that the mitral valve becomes verticalized, hindering ventricular ejection because of its position relative to the septum. In our study, the mean gradient in patients with anterolateral papillary muscle ascent was greater than that in patients without this anomaly (25 mnmHg versus 16.5 mmHg). In a study by Austin *et al.* [6], 66 HCM patients were included. They were divided into 4

groups: septal thickness less than 20 mm with normal papillary muscle position, septal thickness less than 20 mm with displaced anterior papillary muscle, septal thickness greater than 20 mm with normal papillary muscle position, septal thickness greater than 20 mm with displaced anterior papillary muscle. It was in patients with a septal thickness of less than 20 mm and a displaced anterior papillary muscle that he reported the greatest obstruction ($p = 0.03$). This shows the importance of this malposition on obstruction, even with minor septal hypertrophy. In our study, we did not observe any abnormal insertion on the mitral valve, probably due to the small number of patients. Other studies have found this anomaly. Klues *et al.* [15] showed that 9 out of 94 HCM patients had this abnomaly. This represented around 10%, reflecting the low proportion of this abnomaly in this group of patients. In another study conducted by Klues *et al.* [16] analysis of 78 excised mitral valves in patients with obstructive HCM showed 13% abnormal insertion of one or both left ventricular papillary muscles directly into the anterior mitral leaflet.

5. Conclusion

Mitral valve abnormalities during hypertrophic cardiomyopathy are frequent and are dominated by elongation of the leaflets. They should be analyzed for a better diagnostic and therapeutic approach. They appear to be linked to significant intraventricular obstruction. Multicenters studies are needed in Africa for more data.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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