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The Role of Clefts and Cleft-Like Indentations in Mitral Regurgitation Etiology Detected by Three-Dimensional Echocardiography in Patients with Hypertrophic Cardiomyopathy

Hipertrofik Kardiyomiyopati Hastalarında Üç Boyutlu Ekokardiyografi ile Tespit Edilen Mitral Yetersizliği Etiyolojisinde Kleft ve Kleft Benzeri İndentasyonların Rolü

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: Mitral regurgitation (MR) is a critical determinant in patients with hypertrophic cardiomyopathy (HCM). Three-dimensional (3D) echocardiography has transformed the imaging of the mitral valve by enabling real-time, direct visualization. This study aims to determine the frequency of clefts and cleft-like indentations (CLIs) and assess their contribution to MR in HCM patients.

Method: A total of 50 patients with HCM and moderate or severe MR who underwent 3D transesophageal echocardiography (TEE) were enrolled. For the control group, 200 patients with moderate or severe MR but without HCM were selected. The two groups were compared in terms of demographic characteristics, echocardiographic findings, and cardiac magnetic resonance imaging results.

Results: Patients with HCM were younger and had higher regurgitant volumes and effective regurgitant orifice areas compared to the control group. Clefts or CLIs were present in 14 patients (28%) in the HCM group compared to 31 patients (15.6%) in the control group (P = 0.041). Evaluation of MR jet direction in relation to the presence of clefts or CLIs revealed a significant association between anteriorly directed jets and the presence of clefts (P = 0.003).

Conclusion: In this study, the frequency of clefts or CLIs was higher in patients with HCM compared to the control group. Clefts influence the direction of MR jets (anteriorly), whereas CLIs do not. 3D-TEE can aid in the differential diagnosis of HCM in patients with anteriorly directed MR jets. However, using 3D-TEE to identify CLIs alone has no significant impact on the management of MR.

Keywords: Cleft-like indentation, cleft, hypertrophic cardiomyopathy, mitral regurgitation, three-dimensional transesophageal echocardiography

ÖZET

Amaç: Hipertrofik kardiyomiyopati (HKMP) hastalarında mitral yetersizlik en önemli bulgulardan biridir. Üç boyutlu (3B) ekokardiyografi, gerçek zamanlı doğrudan görüntülemeye izin vererek mitral kapağın görüntülenmesinde devrim yarattı. Bu çalışmanın amacı hipertrofik kardiyomiyopati hastalarında kleft ve kleft benzeri indentasyonların (KBI) sıklığını tanımlamak ve mitral yetersizliğine katkısını belirlemektir.

Yöntem: Orta veya ileri mitral yetersizliği olan ve 3B transözofageal ekokardiyografi (TÖE) yapılan toplam 50 HKMP hastası çalışmaya alındı. Kontrol grubunda HKMP tanısı olmayan orta veya ileri mitral yetersizliği olan 200 hasta seçildi. İki grup demografik, ekokardiyografik özellikler açısından birbirleriyle karşılaştırıldı. HKMP hastalarının kardiyak manyetik rezonans görüntüleme bulguları kaydedildi.

Bulgular: Kontrol grubuyla karşılaştırıldığında HKMP hastaları daha gençti ve regürjitan volümleri ile efektif regürjitan orifis alanları daha fazlaydı. HKMP grubunda kleft veya kleft benzeri indentasyon 14 hastada (%28'i) saptanırken, kontrol grubunda 31 hastada (%15,6'sı) saptanmıştır (P = 0,041). Mitral yetersizlik jet yönünün kleft veya kleft benzeri indentasyon varlığına göre değerlendirilmesinde anterior jet yönü ile kapakta kleft varlığı arasında anlamlı ilişki vardı (P = 0,003).

Sonuç: Bu çalışmada HKMP hastalarında kleft veya kleft benzeri indentasyon sıklığı kontrol grubuna göre daha sıktır. Kleftler mitral yetersizliği jetinin yönünü (öne doğru) etkilerken kleft benzeri indentasyonlar etkilememektedir. Öne doğru mitral yetersizliği jeti olan HKMP hastalarında 3B-TÖE ayırıcı tanıda yardımcı olabilir. Yalnızca kleft benzeri indentasyonları tanımlamak için 3B-TÖE'nin kullanılmasının mitral yetersizliği yönetiminde anlamlı bir etkinliği yoktur.

Anahtar Kelimeler: Kleft benzeri indentasyon, kleft, hipertrofik kardiyomiyopati, mitral yetersizliği, üç boyutlu ekokardiyografi

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Hypertrophic cardiomyopathy (HCM) is a common hereditary disease with an incidence of approximately 1 in 500 individuals.[1] Left ventricular outflow tract (LVOT) narrowing, myocardial ischemia, diastolic dysfunction, and mitral regurgitation (MR) constitute the core pathophysiological features of HCM.[2] MR may arise secondary to left ventricular outflow tract obstruction (LVOTO) or due to primary mitral valve pathologies. Systolic anterior motion (SAM) of the mitral valve's anterior leaflet during LVOTO impairs coaptation between the anterior and posterior leaflets, typically resulting in a posteriorly directed MR jet. When the MR jet is central or anteriorly directed, SAM cannot be excluded, but primary mitral valve pathologies should also be considered.[3] Advancements in imaging modalities and their broader applications have faciltated the identification of mitral valve anomalies in patients with HCM.[4] With the increased use of transesophageal echocardiography (TEE) and three-dimensional (3D) echocardiography for evaluating the anatomical structure of the mitral valve, it has become easier to identify pathologies of the mitral valve leaflets, such as clefts and indentations.[5] While there is no universally accepted consensus on the definition of clefts and cleft-like indentations (CLI), the description provided by Narang et al.[5] in 2018 is commonly referenced. According to this definition, clefts and CLIs are identified based on their location on the mitral leaflets and their distance from the annulus if located posteriorly. Physiologically occurring clefts on the posterior leaflet are excluded from this definition, whereas any indentation on the anterior leaflet is considered pathological. The presence of color Doppler flow originating from these indentations is included as part of the diagnostic criteria. Especially, severe MR, the cause of which cannot be explained on two-dimensional (2D) echocardiography, is often associated with a cleft identified on 3D examinations.[6] Moreover, in patients with HCM and moderate or severe MR for whom surgical myectomy is being considered, preoperative TEE and the evaluation of clefts or cleft-like indentations in the mitral valve leaflets are crucial for determining the appropriate surgical procedure.

The aim of this study is to assess the frequency of clefts and CLIs and their impact on MR in patients with HCM and moderate or severe MR using 3D echocardiograhy imaging.

Materials and Methods

Patient Population

This study is a single-center, retrospective study conducted at our tertiary center between August 2018 and May 2022. A total of 74 patients diagnosed with HCM in accordance with current guidelines[7,8] were included in the study group. All patients underwent TEE. To minimize the influence of confounding factors and selection bias, the control group consisted of 200 cases of mitral valve regurgitation, each attributed to one of four distinct etiological causes: rheumatic mitral valve disease, degenerative mitral valve disease, secondary MR, and cases of MR for which the etiology could not be determined with transthoracic echocardiography (TTE). Patients with the following conditions were excluded from the study: ventricular arrhythmia and pacemaker rhythm (six patients), moderate to severe mitral stenosis (three patients), and inadequate 3D echocardiographic imaging of the mitral valve (15 patients). The study received approval from the İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (Approval Number: 2022.03-16, Date: 15.03.2022), and was conducted in accordance with the principles outlined in the Declaration of Helsinki. No artificial intelligence-assisted technologies, such as large language models, chatbots, or image creators, were used in the production of this study.

The basic demographic information of the patients was obtained by retrospectively reviewing the hospital's electronic information system (Panates Hospital Information Management System). Age, gender, smoking status, comorbidities, 12-lead electrocardiogram (ECG), TTE, TEE, and cardiac magnetic resonance imaging (CMR) parameters of the subjects included in the study were recorded.

Echocardiographic Evaluation

TTE, TEE, and 3D images were retrieved from the hospital records of all patients. The images were retrospectively assessed by a physician certified in echocardiography using the Hospital Picture Archiving and Communication System (PACS). All procedures were performed using the Philips EPIQ7 Echocardiography device (Philips Medical Systems, Andover, USA).

MR was evaluated using qualitative, semi-quantitative, and quantitative measurements in accordance with established guidelines.[9] The direction of the jet (anterior, central, or posterior) and its eccentricity were recorded. For the measurement of vena contracta, two separate measurements were made in magnification mode with the Nyquist limit set to 50-60 cm/sec using the apical four-chamber and parasternal long-axis images, and the average was calculated. When calculating the effective regurgitant orifice area (EROA) using the current convergence method, the Nyquist limit was reduced to 20-40 cm/sec. The radius was measured at the region where the proximal isovelocity surface area (PISA) radius (r-cm) was largest during systole. MR peak velocity and MR velocity-time integral (VTI) were calculated by placing the continuous-wave (CW) Doppler sample volume on the MR jet. EROA was calculated using the formula: $2\pi r^2 \times V$ aliasing = EROA x MR velocity where r represents the maximal PISA radius, and V aliasing is the aliasing velocity of the proximal flow convergence. The maximum radius was measured from the tip

ABBREVIATIONS

2D	Two-dimensional
3D	Three-dimensional
CLIs	Cleft-like indentations
CMR	Cardiac magnetic resonance imaging
CW	Continuous-wave
HCM	Hypertrophic cardiomyopathy
LVOTO	Left ventricular outflow tract obstruction
MR	Mitral regurgitation
PISA	Proximal isovelocity surface area
RV	Regurgitant volume
TEE	Transesophageal echocardiography
VTI	Velocity-time integral

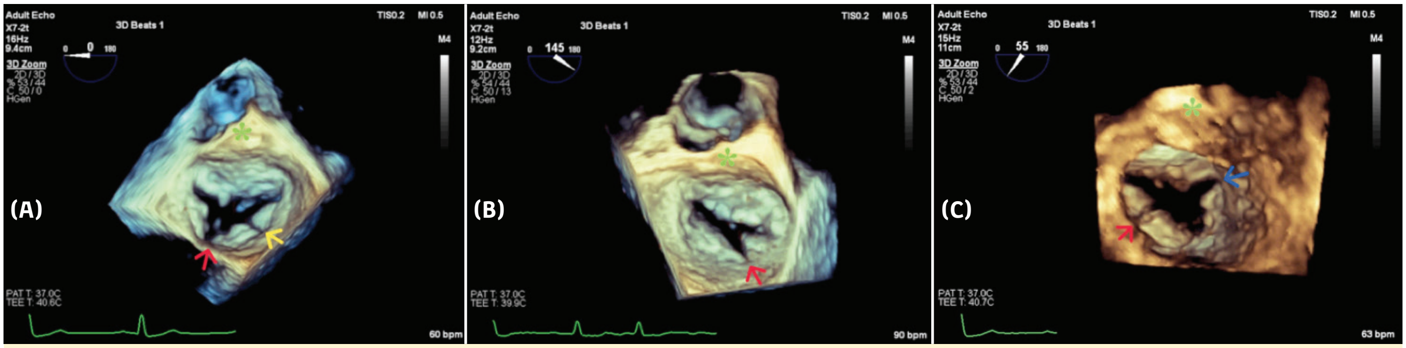

Figure 1. Three-dimensional (3D) zoom images of a hypertrophic cardiomyopathy (HCM) patient with mitral regurgitation: (A) Surgical view of the mitral valve showing a cleft on P1 (red arrow) and an indentation on P3 (yellow arrow). (B) Cleft located between P2 and P3 (red arrow). (C) Left ventricle view of the mitral valve showing a cleft on P1 (red arrow) and the lateral commissure (blue arrow). (The green "*" indicates the position of the aorta.)

of the leaflets to the point of first color aliasing. Regurgitant volume (RV) was calculated by multiplying the EROA value by the MR velocity-time integral.

In TEE, the mitral valve was evaluated in mid-esophageal windows using 3D zoom or live 3D modes. Clefts and indentations with visible tissue defects on 3D echocardiography were assessed during the systolic phase. The definitions of clefts and CLIs were based on the criteria published by Narang et al.[5] in 2018. According to these criteria, the classification is as follows:

- If an indentation is less than 50% of the distance to the annulus of the posterior leaflet and regurgitant flow is observed on color Doppler imaging, it is defined as a cleft-like indentation.
- When the indentation depth of a posterior scallop exceeds 50% of the depth of the adjacent scallop or reaches the annulus, the diagnosis of a cleft is confirmed.
- Since a cleft is not anatomically expected in the anterior leaflet, any indentations found in the anterior leaflet are defined as clefts regardless of their depth.

Posterior leaflet-related structures that did not meet these definitions were considered normal variants and were not included in the pathological group.[6]

Figure 1 illustrates clefts and cleft-like indentations on mitral valve scallops in 3D zoom mode.

Statistical Analyses

The normal distributions of the variables were evaluated visually using histogram curves and the Skewness-Kurtosis test. Continuous variables with normal distributions are presented as mean ± standard deviation (SD), while those without normal distributions are presented as median (interquartile range). Categorical variables are expressed as percentages (%). For statistical analysis of numerical variables between independent groups, an unpaired t-test was used for normally distributed data, and the Mann-Whitney U test was used for non-normally distributed data. Analysis of categorical variables was performed using Yates' Continuity Correction or Fisher's exact test. Unadjusted multinomial logistic regression was used to analyze the relationship between MR jet direction and valve pathology.

Table 1. Baseline Clinical and Demographic Characteristics of Patients in the HCM and Non-HCM Groups

	HCM Group (n = 50)	Non-HCM Group (n = 200)	P
Age (years)	54.5 ± 14	61 ± 14	0.001
Female sex, n (%)	24 (48)	89 (44.5)	0.656
Smoking history, n (%)	10 (20)	64 (32)	0.096
Hypertension, n (%)	29 (58)	135 (67.5)	0.206
Diabetes mellitus, n (%)	8 (16)	51 (25.5)	0.157
Atrial fibrillation, n (%)	11 (22)	76 (38)	0.034

HCM, Hypertrophic Cardiomyopathy.

A p value of <0.05 was considered statistically significant. Statistical analyses were performed using R software version 3.6.3 (R Project, Vienna, Austria).

Results

Our final patient population consisted of 50 patients with HCM after applying the exclusion criteria. The mean age of the HCM group was 54.5 ± 14 years, and 24 patients were female (48%). The control group comprised 200 patients with a mean age of 61 ± 14 years, including 89 female patients (44.5%). The baseline clinical, demographic, and echocardiographic characteristics of the patients are summarized in Tables 1 and 2.

The left ventricular end-diastolic and end-systolic diameters were significantly lower in the HCM group compared to the control group (P < 0.001). The interventricular septum thickness was significantly higher in the HCM group (P < 0.001). The left atrial diameter was similar between the two groups. However, systolic pulmonary artery pressure and left ventricular ejection fraction were significantly lower in the HCM group. EROA and RV parameters were used for the quantitative evaluation of MR. Both EROA and RV values were significantly higher in the HCM group (P < 0.001). The presence of clefts or CLIs was observed in 28% (n = 14) of the HCM group, compared to 15.6% (n = 31) in the control group. The frequency of clefts or CLIs was significantly higher in the HCM group (P = 0.041).

Table 2. Echocardiographic Characteristics of Patients with Moderate or Severe Mitral Regurgitation in the HCM and Non-HCM Groups

	HCM Group (n = 50)	Non-HCM Group (n = 200)	P
LVESD, mm	47.2 ± 5	54 ± 7	**<0.001**
LVEDD, mm	30.4 ± 5	38.6 ± 8	**<0.001**
IVS, mm	17.1 ± 3	10 ± 1.8	**<0.001**
LA anteroposterior diameter, mm	47 ± 6.9	47 ± 6.3	0.996
SPAP, mmHg	35 ± 11.6	45 ± 15.4	**0.001**
EF, %	55 (43-60)	60 (60-65)	**<0.001**
MR VC, cm	0.49 ± 0.19	0.59 ± 0.17	**0.001**
MR EROA, cm^2	0.42 (0.3-0.7)	0.3 (0.23-0.42)	**<0.001**
MR RV, mL	58 (47-76)	40 (32-69)	**<0.001**
Cleft and/or indentation, n (%)	14 (28)	31 (15.6)	**0.041**

HCM, Hypertrophic Cardiomyopathy; EF, Ejection Fraction; EROA; Effective Regurgitant Orifice Area; IVS, Interventricular Septum; LA, Left Atrium; LVEDD, Left Ventricular End-Diastolic Diameter; LVESD, Left Ventricular End-Systolic Diameter; MR, Mitral Regurgitation; RV, Regurgitant Volume; SPAP, Systolic Pulmonary Artery Pressure; VC; Vena Contracta.

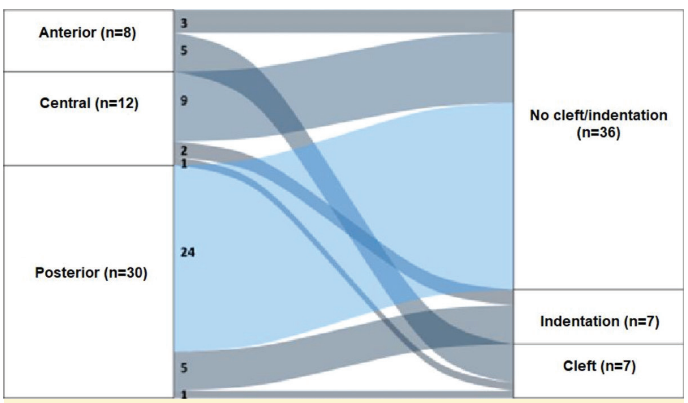

Figure 2. The distribution patterns of mitral regurgitation jet direction and the frequency of clefts or cleft-like indentations exhibit variability.

The echocardiographic and CMR imaging findings of patients with HCM are presented in Table 3. Among the HCM group, asymmetric septal hypertrophy was observed in 44 patients (88%), while reverse curve septal morphology was noted in six patients (12%). SAM of the anterior leaflet was present in all patients in the HCM group, and SAM of the posterior leaflet was detected in 22% of HCM patients. Mitral valve anterior leaflet elongation was observed in 28 patients (56%), while posterior leaflet elongation was identified in 12 patients (24%). Apical displacement of the papillary muscles was found in 24 patients (48%), and papillary muscle bifidity was detected in six patients (12%). Late gadolinium enhancement was observed in 38% of HCM patients on CMR images. An apical aneurysm was identified in two patients (14%). The rates of clefts (n = 7, 14%) and CLIs (n = 7, 14%) were similar among patients with HCM.

Table 3. Echocardiographic and Cardiac Magnetic Resonance Imaging Findings in HCM Patients

	n (%)
Asymmetric septal hypertrophy	44 (88)
Reverse curve septal morphology	6 (12)
Systolic anterior motion of anterior mitral leaflet	50 (100)
Systolic anterior motion of posterior mitral leaflet	11 (22)
Mitral valve anterior leaflet elongation	28 (56)
Mitral valve posterior leaflet elongation	12 (24)
Right ventricular hypertrophy	6 (12)
Papillary muscle apical displacement	24 (48)
Papillary muscle bifidity	6 (12)
Chordal rupture	1 (2)
Mitral valve prolapse	4 (8)
Apical aneurysm	2 (4)
CMR/late gadolinium enhancement	19 (38)
Presence of mitral valve cleft	7 (14)
Presence of mitral valve indentation	7 (14)

HCM, Hypertrophic Cardiomyopathy; CMR, Cardiac Magnetic Resonance.

The jet direction of MR and the frequency of clefts and CLIs are shown in Figure 2. A mitral valve cleft was identified in five out of eight patients with an anterior MR jet. Additionally, mitral valve prolapse (MVP) was observed in two patients, while MVP with chordae rupture was present in one patient. A significant relationship was found between the presence of a cleft and the anterior jet direction (P = 0.003), whereas no notable relationship was observed between the central jet direction and the presence of a cleft (P = 0.504). There was no relationship between the presence of a CLI and either the anterior jet (P = 0.994) or the central jet direction (P = 0.944). In the control group, the presence of clefts or CLIs did not significantly affect the jet direction of MR. Figure 3 illustrates an anterior eccentric MR jet associated with a cleft. In our study, 14 patients with clefts or CLIs were identified in the HCM group. Of these, seven patients had a cleft, and seven had a CLI. Regarding the localization of clefts, five out of seven patients with a cleft were located on the anterior mitral leaflet, and two out of seven patients with a cleft were located on the posterior mitral leaflet. Additionally, six out of seven patients with a CLI were localized on the posterior mitral leaflet. These findings highlight the association between the presence of a cleft and an anteriorly directed MR jet in HCM patients. Systolic anterior motion of the posterior mitral leaflet was detected in 22% of HCM patients. It was observed that the MR jet was central in patients with SAM of the posterior mitral leaflet.

Discussion

In this study, we investigated the frequency of clefts and CLIs, which are among the causes of mitral valve abnormalities, and their impact on the direction of the MR jet in HCM patients. The main findings of our study are as follows:

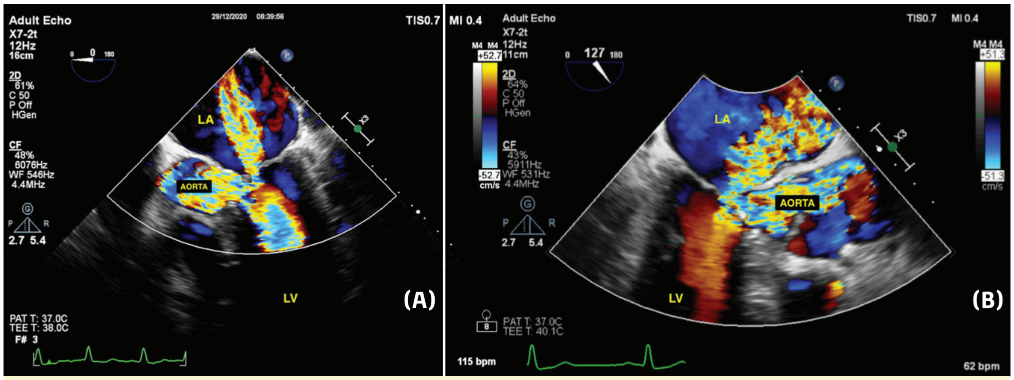

Figure 3. (A) Central mitral regurgitation jet observed in the mid-esophageal five-chamber view. (B) Anteriorly directed eccentric jet of severe mitral regurgitation due to a cleft, observed in the mid-esophageal long-axis view.

LA, Left Atrium; LV, Left Ventricle.

1. The frequency of clefts or CLIs was 28% in patients with HCM and moderate or severe MR, compared to 15.6% in patients without HCM.
2. The presence of a cleft was found to influence the direction of the MR jet, leading to an anterior direction. However, in this study, the presence of CLIs was not associated with the direction of the MR jet, whether central or anterior.

HCM is a complex and hereditary disease. SAM of the mitral valve or chordae is observed in 30-60% of cases.[10] The mitral valve leaflets are pushed towards the septum by the drag effect. During strong ventricular contraction, blood flow is often directed posteriorly to areas with abnormal ring geometry, including a small cavity, thickened wall structure, and a narrow LVOT.[11] In summary, LVOT due to systolic anterior motion occurs as a result of strong ventricular contraction, abnormal annular ring geometry, and impaired mitral valve leaflet coaptation.[12]

MR can arise from SAM of mitral valve structures or from primary mitral valve pathologies. As a result of SAM of the mitral valve leaflet during LVOT, coaptation between the anterior and posterior leaflets is impaired, typically resulting in a posterior or external MR jet.[3] In addition to SAM, abnormalities in mitral valve anatomy influence both the degree and direction of the MR jet. The presence of primary mitral valve pathology should be investigated, particularly in cases with anterior MR jets. In 2D TTE, short-axis images are limited in evaluating clefts due to artifacts or dropouts. With advances in 3D echocardiography, the anatomical structure of the mitral valve can now be more accurately defined. However, 3D echocardiography is a method that requires significant expertise and is not universally available. Therefore, it is crucial to identify which patients should undergo 3D TEE. In an echocardiographic study conducted in the general population, the incidence of isolated mitral clefts was reported to be 0.11%.[13] In a study by Mantovani et al.[6] involving patients scheduled for surgery due to myxomatous mitral valve disease, no patients were diagnosed with cleft-like indentations using 2D echocardiography, whereas 3D echocardiography identified CLIs in 35% of the patients in this group.[6] In a study by Narang et al.,[5] patients with severe MR identified on 2D echocardiography were further evaluated with 3D echocardiography, revealing an incidence of isolated mitral valve clefts of 3.3%. In addition, isolated mitral clefts were predominantly localized in the anterior scallop, specifically between A1 and A2. When comparing anterior and posterior clefts, the morphology of the mitral valve annulus was found to be similar.[5] As demonstrated, factors such as study design, patient population, evaluation method, and lesion definition influence the reported rates of clefts and CLIs. To better reflect real-world conditions, we included a control group in our study with a proportionate representation of patients from different etiologies. Specifically, our control group comprised patients with isolated clefts (1%), rheumatic etiology (24%), degenerative mitral valve disease (34%), secondary etiology (29%), senile degenerative mitral valve disease (8.5%), and mixed (organic and secondary) etiology (3.5%). The frequency of clefts or CLIs in this control group was 15.6%, which appears to accurately reflect clinical practice.

Mitral valve clefts are rare in HCM and are more commonly associated with congenital heart diseases, including ostium primum atrial septal defect, mitral valve prolapse, myxomatous mitral valve diseases, Marfan syndrome, and papillary muscle malrotation.[14,15] Although there is limited literature on mitral valve clefts in patients with HCM, a study published by Ye et al.[16] provided significant data on this topic. In that study, CLIs in the mitral valve were evaluated using intraoperative 3D TEE in HCM patients undergoing myectomy. A total of 90 HCM patients were compared with 59 controls. The analysis revealed that CLIs in the mitral valve were detected in 93.3% of the HCM patient group, compared to 39% in the control group. In our study, the frequency of clefts or CLIs was 28% in patients with HCM and grade 3 or higher MR. In the control group, the frequency was 15.6%. This difference highlights that mitral anatomy is also affected in patients with HCM and underscores that, in addition to the presence of SAM, primary valve pathologies contributing to MR should not be underestimated.

A crucial aspect of MR assessment in HCM patients is evaluating the direction of the MR jet. In SAM-related MR, the jet direction is typically posterior eccentric and, less commonly, central.[3] In patients with an anterior eccentric MR jet, it is important to consider the possibility of a mitral valve pathology other than SAM, and the evaluation should be conducted accordingly. In our study, MVP was observed in two out of five patients, and MVP with chordal rupture was observed in one out of five patients with an anterior MR jet. In this context, the observation of an anterior jet in the presence of SAM necessitates a thorough evaluation for primary mitral valve disease. The presence of a cleft influences the direction of the MR jet. In such cases, the direction of SAM-related MR, typically expected to be posterior or central, shifts to an anterior direction. However, in patients with a central jet, no significant correlation was found between the presence of a cleft and the direction of the MR jet. The situation differs in CLIs. No CLI was detected in HCM patients with an anterior MR jet. In patients with CLIs, there was no change in the direction of the MR jet. It can be inferred that mitral valve evaluation using 3D TEE may not provide additional clinical benefit in patients with posterior or central MR jets.

When compared to other echocardiographic findings, the vena contracta diameter was observed to be higher in the non-HCM group, likely due to the presence of eccentric jets in the HCM group. However, the EROA and regurgitant volume values, which reflect the severity of the MR jet, were higher in the HCM group. Another interesting finding in our study was that systolic anterior motion of the posterior mitral leaflet was present in 22% of cases, a higher rate than reported in previous publications. It is also important to emphasize that the MR jet in patients with SAM of the posterior mitral leaflet was central. This finding underscores the need for a detailed assessment of posterior mitral leaflet motion in HCM patients with a central jet.

Several limitations of our study should be noted. The relatively small number of patients is considered the most significant limitation; however, HCM with moderate or severe MR is uncommon in clinical practice. To prevent bias in the selection of the control group, patients from various etiologies were included. While the rates of clefts and cleft-like indentations are low in patients with rheumatic valve disease, they are observed at higher rates in those with MVP. Nonetheless, the lack of sequential patient recruitment represents another limitation. Another important shortcoming is the limited availability of related literature.

Conclusion

In conclusion, the frequency of clefts or CLIs in our study was 28% in patients with obstructive HCM, a rate higher than in the non-HCM-related MR population. While the presence of a cleft altered the direction of the MR jet, resulting in an anterior eccentric jet, this effect was not observed in CLIs. 3D mitral valve imaging is valuable for determining the etiology of anterior eccentric jets. However, 3D imaging specifically for the evaluation of CLIs does not provide additional benefits in the management of MR.

Ethics Committee Approval: Ethics committee approval was obtained from İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (Approval Number: 2022.03-16, Date: 15.03.2022).

Informed Consent: Informed consent was waived due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.Y.K., A.G., M.E., G.B.G.; Design – A.G., B.U., G.B.G.; Supervision – İ.H.T., M.E., G.B.G.; Resource – B.U., H.Z.A., S.T.K.; Materials – B.U., H.Z.A., S.T.K.; Data Collection and/or Processing – A.B., H.Z.A., S.T.K.; Analysis and/or Interpretation – İ.H.T., A.B., A.T.C.; Literature Review – A.B., S.T.K., A.T.C.; Writing – C.Y.K., A.G.; Critical Review – C.Y.K., A.T.C.

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