DISCUSSION

Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiomyopathy (prevalence of 1:500 in the general population) caused by mutations in genes encoding proteins of the cardiac sarcomere, is characterized by a generalized myopathic process affecting both ventricular and atrial myocardium.

The disease state characterized by unexplained LV hypertrophy associated with nondilated ventricular chambers in the absence of another cardiac or systemic disease that itself would be capable of producing the magnitude of hypertrophy evident in a given patient.

In patients with HCM, the enlargement of the LA has proved to be inconsistently related to LV diastolic dysfunction, mitral regurgitation degree, or LV dynamic outflow tract obstruction. Thus, the existence of an additional mechanism involved in atrial remodeling was postulated.

The assessment of LA function using traditional parameters such as atrial fraction or newer parameters derived from tissue Doppler or STE analysis brought new insights into the pathophysiologic mechanisms involved in atrial remodeling in HCM. The poorer LA function was indeed attributed to a possible atrial myopathic process.

Doppler tissue imaging has enhanced the noninvasive assessment of regional myocardial function. Strain and strain rate, derived from Doppler tissue imaging, examine myocardial deformation and rate of deformation, respectively, and are largely independent of the tethering effect of the myocardium compared to Doppler tissue imaging.

Although initially used for quantifying regional ventricular deformation, this technique has more recently been used to evaluate atrial function, in normal subjects and in conditions with atrial dysfunction.

The recognition of the upper limits of atrial size and function in HCM may be of clinical relevance by assisting in distinguishing cardiac remodeling and help with patients' risk stratification .

The study was done on 40 hypertrophic cardiomyopathy patients (20 hypertophic cardiomyopathy without left ventricular outflow obstruction, HCM; and 20 hypertophic cardiomyopathy with left ventricular outflow obstruction, HOCM) with normal sinus rhythm and normal LV systolic function (EF > 50%) and 20 healthy control of age and sex matched to the patients group.

The heart rate was significantly lower in HOCM group in comparison with the control, that was due to the drug effect as most of these patients were receiving beta blocker or calcium channel blocker.

Conventional transthoracic echocardiography:

Mitral regurgitation

In the present study, it was observed that patients with hypertrophic cardiomyopathy had more mitral regurgitation as comparing with the control group. Mitral regurgitation occurs in almost all patients with obstructive HCM as a consequence of SAM which induces abnormal mitral leaflet coaptation and may be an important cause of dyspnea. When additional mitral valve abnormalities other than SAM are not observed, a direct relation between the pressure gradient and the severity of MR is evident. The direction of the mitral regurgitation jet is useful in identifying patients with

independent mitral disease. In fact SAM induces a mitral regurgitation jet directed posteriorly, whereas in presence of a intrinsic mitral valve disease due to annular, papillary or leaflet disease, patients with obstruction and mitral regurgitation can show a systolic mitral anterior directed jet. **Kinoshita N et al** [249], studied 28 patients with hypertrophic cardiomyopathy, of the 28 patients, 14 patients had systolic anterior motion of the mitral echo, they studied by transthoracic echocardiography and heart catheterization, Mitral regurgitation is more frequent and more severe in the obstructive form than in the non-obstructive form. It is thought to be attributable to the distortion of the mitral orifice which may be inevitable in hypertrophic cardiomyopathy. The early part of the systolic murmur is generated mainly by mitral regurgitation but this also contributes to the mid and late systolic parts of the murmur, in contrast to our study there was no difference between the HCM and HOCM in the frequency of mitral regurgitation.

Aortic regurgitation

In the present study , it was observed that patients with HOCM had more aortic regurgitation as comparing with the control group, **Shiota et al**[250] studied 87 (out of 91in the start of the study) patient with hypertrophic cardiomyopathy In that study, colour Doppler echocardiography showed that aortic regurgitation was not uncommon in patients with hypertrophic cardiomyopathy. Signals of aortic regurgitation were limited to the left ventricular outflow tract, suggesting that the degree of the regurgitation was mild.

This is probably the reason why this association has rarely been detected by auscultation, phonocardiography, or conventional echocardiography. In 1987 ***Theard et al***[251] reported that conventional pulsed Doppler

echocardiography detected mild aortic regurgitation in nearly a third of patients with hypertrophic cardiomyopathy. Although the exact cause of aortic regurgitation is uncertain, the morphological abnormality of the aortic root was related to the regurgitation.

Left atrial diameters

in our study all left atrial diameters (antroposterior, mediolateral and infrosuperior) were significantly higher in HCM and HOCM groups in comparison with the control group, both mediolateral and infrosuperior diameters were significantly higher in HCM group than in HOCM group. In patients with HCM the enlargement of the LA has proved to be inconsistently related to LV diastolic dysfunction, mitral regurgitation degree, or LV dynamic outflow tract obstruction, LA dilation has proved to be a powerful determinant of exercise capacity and adverse outcome in this setting. Expansion of the LA in the AP dimension may be constrained by the thoracic cavity between the sternum and the spine. Predominant enlargement in the superior-inferior and medial-lateral dimensions will alter LA geometry such that the AP dimension may not be representative of LAsize, and it should be accompanied by LA volume determination in both clinical practice and research . In **Paraskevaidis IA et al** [252], the left atrial diameter did not differ significantly between HCM and HOCM, usually in practice only AP diameter is calculating which is not an accurate parameter.

Left atrial volumes

In our study left atrial maximum volume, minimum volume and left atrial volume index were significantly higher in HCM and HOCM groups in comparison with the control group, and all were significantly higher in HCM group than in HOCM group. Left atrial (LA) volume, measured by 2

dimensional echocardiography, is the most accurate measure of LA size because little variations in the linear dimension are often associated with large variation in volume as the result of asymmetric LA remodeling. In HCM, increased LA linear dimension is a strong predictor of poor outcome, moreover, increased LA volume predicts the development of AF and it is related to exercise capacity even in patients without obstruction at rest or during provocation. There is evidence of increased LA volume in patients with a history of cardiovascular morbidity. **Losi et al** [253] studied the prognostic effect of left atrium in 140 patients with HCM ; 87 men (mean age 40 _ 15 years, range 18–83 years), echocardiographic study was done initially and after follow up 5 _ 3 years, that study demonstrates that an enlarged left atrium or a fast dilating LA volume represent risk factors of unfavorable outcome in patients with HCM, patients with a normal LA volume at baseline and an increase in volume of at least 3 mL per year, prognosis was worse than in patients with stable LA volume throughout follow-up and similar to that of patients with dilated LAV index at baseline.

Transmitral Doppler flow velocities

In our study there was no significant difference between the three groups. In **Paraskevaidis IA, et al** [252] peak E velocity at lateral mitral annulus were similar in patients with HCM, patients with systemic hypertension and the control group and that was similar to our results. Peak A velocity, a traditional measure of atrial contractile function, reflects the atrioventricular pressure gradient and is age and load dependent. **Eshoo S et al**[254] demonstrated that peak A velocity was not sensitive enough to differentiate between HCM and patients with hypertension, like our study Peak A velocity was not differ significantly.

Mitral annulur tissue Doppler

In our study s^-, a^- waves showed no significant difference between the three groups but e^- wave was significantly higher in the control group than in patients with HCM and the e/e^- ratio was significantly lower in in the control group than patients with HCM. ***Nagueh et al*** [255] suggested that the ratio of early transmitral (E) to tissue Doppler early diastolic (e') velocities of the lateral mitral annulus accurately quantified LV pressures, in particular the LV pressure before atrial contraction, an E/e' ≥10 showed the best sensitivity and specificity for identifying LV pre-A pressure > 15 mmHg. However, that ratio shows only a modest correlation when related to mean left atrial (LA) pressure, and, moreover, the predictive accuracy of the E/e' ratio for estimation of mean LA pressure in an individual patient was modest. However, in some study this parameter identifies patients with low exercise capacity. **Kitaoka H. et al**[256] studied eighty-five HCM patients (52 males, 55.6+14.8 years.) belonging to the New York Heart Association (NYHA) functional class I or II with follow up of 4.5+1.7 years for cardiovascular events the study observed that Patients who experienced cardiovascular events showed lower septal s′, e′ and a′ velocities on TDI than those who did not, Consequently, the septal E/e′ value was larger in patients who experienced cardiovascular events than in those who did not , On the other hand, there was no significant difference in the lateral tissue Doppler index at the lateral corner between two groups evaluation of the LV diastolic dysfunction, a hallmark of the LV function in HCM, is important in the management of such patients, regardless of the patients' symptom status. On the other hand, the tissue Doppler index at the lateral corner was not related to combined endpoints. It is controversial whether the septal or the lateral E/e′ is more accurate in predicting the LV filling pressure or adverse events.

However, there is the possibility that the septal E/e′ is more useful than the lateral E/e′ in patients with HCM, because the myocardial hypertrophy at the septum (particularly basal septum of the LV) is often predominant compared with the lateral hypertrophy of the LV, the study recommended that measurement of the septal E/e′ value should be incorporated into the clinical management of HCM, and patients with a high septal E/e′ value should be regularly and repetitively examined.

Left atrial deformation imaging:

In our study we assessed the deformation of the left atrium (strain , peak strain rate, time to strain , time to strain rate and tissue velocities in four left atrial walls) using tissue dopper ; ***strain*** was significantly lower in patients with hypertrophic cardiomyopathy either with or without obstruction than in the control , and was significantly lower in HOCM group than in HCM group ***,strain rate*** was significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects, with no difference between patient with or without obstruction ***, time to strain*** was significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects, with no difference between patient with or without obstruction***, time to strain rate*** was significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects, with no difference between patient with or without obstruction***, tissue velocities of left atrium walls;*** all these parameters were significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects, with no difference between patient with or without obstruction except in the a wave of mid segment of left atrial anterior wall, it was significantly lower in patients without obstruction than patient with obstruction. LA longitudinal function is significantly reduced in patients with hypertrophic cardiomyopathy in comparison with other types of LV

hypertrophy . A decrease in LA reservoir function, as assessed by two dimensional atrial strain, with a cut-off value of 10.8%, had an added value in differentiating hypertrophic cardiomyopathy from other types of LV hypertrophy. The reduction in LA function, as assessed by two dimensional strain, has also been related to the presence of heart failure symptoms in hypertrophic cardiomyopathy. **IA Paraskevaidis, et al [(252)],** Studied 43 consecutive patients with familial HCM, aged 49 (SD 18) years, along with 21 patients with non-HCM left ventricular hypertrophy (LVH, aged 52 (12) years) and 27 healthy volunteers (aged 42 (13) years) , using both TDI and 2D left atrial strain during all three atrial phases , that study revealed that E wave velocity, E wave deceleration time and early diastolic wave (e^-) velocity at lateral mitral annulus were similar in the three groups, E/e^- ratio was significantly higher in HCM patients, regarding comparing HCM vs HOCM: Left atrial diameter did not differ significantly between those two subgroups but left atrial volume index was significantly higher in obstructive HCM TD atrial strain variables, with the exception of contractile strain, were significantly lower in obstructive HCM patients compared to non-obstructive HCM ones. In contrast, none of the 2D atrial strain measurements differed between obstructive and nonobstructive HCM, and regarding comparing HCM vs Non HCM LVH: Interventricular septal thickness, left atrial diameter, left atrial volume index and E/A and E/e^- ratios, none of those variables were independently significantly correlated with HCM; by TD strain only left ventricular systolic strain was significantly correlated with HCM ; by 2D strin only left atrial contractile strain was significantly related to HCM.

This study showed that left atrial longitudinal strain was reduced in HCM patients compared to patients with non-HCM left ventricular hypertrophy or healthy subjects. This finding was evident in all three atrial phases and in the overall longitudinal atrial function and was observed both by tissue Doppler and by 2D atrial strain imaging. In addition, 2D strain seemed to have an additive prognostic value in differentiating HCM from non-HCM left ventricular hypertrophy, when combined with conventional echocardiographic indices.

Eshoo S et al.[254], study left atrial (LA) phasic function evaluated by Doppler tissue imaging–derived strain and strain rate on thirty-seven patients with HC were compared to 44 patients with systemic hypertension (SH) and 65 normal controls ; revealed that Indexed maximal LA volume was increased in the HC group , Global S-Sr, E-Sr, and A-Sr were significantly reduced in the HC group lower compared to the normal group , There were no differences in strain and strain rate measures when the HC group was divided into subgroups with and without LA enlargement using a cut-off value of 30 ml/m2 additionally, A-Sr was reduced in the HC group compared to the SH group In contrast, only E-Sr was reduced in the SH group, with an increase in A-Sr compared to the HC group.

Both studies agree with us that left atrial deformation always significantly reduced in patients with HCM.

SUMMARY

Hypertrophic cardiomyopathy (HCM) is a primary cardiac disorder characterised by hypertrophy, usually of the left ventricle, in the absence of other loading conditions, such as aortic stenosis, hypertension or thyroid disease , it is caused by mutations in genes encoding proteins of the cardiac sarcomere . Although previously thought of as a rare disorder, recent population-based clinical studies suggest the prevalence of the condition to be as high as 0.2% (or 1 in 500) in the general population making HCM the commonest cardiovascular genetic disorder known.

It is thought to be a progressive disease that most often begins with left ventricular (LV) diastolic dysfunction and or structural remodeling of the atria , including chamber enlargement and interstitial fibrosis.

Noninvasive assessment of structure and function of the atria has been limited by a lack of suitable methods for making these measurements, tissue Doppler imaging (TDI) more directly estimates myocardial tissue velocities and thus is relatively load-independent.

LA strain and strain rate derived from tissue Doppler imaging, examine myocardial deformation and rate of deformation, emerge as a novel method to evaluate LA function.

The aim of this work was to evaluate the left atrial longitudinal myocardial function by strain and strain rate imaging in patients with hypertrophic cardiomyopathy.

The study included 20 patients with HCM , 20 patients with HOCM and 20 healthy individuals matched in age and sex.

All patients were subjected to:

1. Full history taking.
2. Complete physical examination.
3. 12-lead ECG.
4. Conventional transthoracic echocardiography; LV dimentions, LV-EF, LA diameters, LA volumes, LVOT gradient by continuous wave dopper and Trans-mitral flow using Pulsed wave doppler were measured.
5. Tissue Doppler Imaging (TDI) ;Pulsed wave tissue Doppler imaging at the mitral annulus, left atrial deformation study (strain , strain rate of left atrial lateral wall and segmental velocities of left atrial walls) were measured.

Results:

Mitral regurgitation was observed in patients with hypertrophic cardiomyopathy significantly more as comparing with the control group .

Aortic regurgitation was observed in patients with HOCM significantly more as comparing with the control group

All left atrial diameters (antroposterior , mediolateral and infrosuperior) were significantly higher in HCM and HOCM groups in comparison with the control group, and both mediolateral and infrosuperior diameters were significantly higher in HCM group than in HOCM group .

Left atrial maximum volume , minimum volume and left atrial volume index were significantly higher in HCM and HOCM groups in comparison with the control group, and all were significantly higher in HCM group than in HOCM group.

Trans-mitral Doppler flow velocities were not significantly differ among HCM, HOCM and the control groups

Tissue Doppler imaging at the lateral mitral annulus showed no significant difference in Peak ventricular systolic (S′) and late diastolic (A′) velocities between the three groups, but early diastolic velocity (E′) was significantly higher in the control group than in patients with HCM and the e/e′ ratio was significantly lower in the control group than patients with hypertrophic cardiomyopathy.

Peak longitudinal strain of the lateral left atrial wall was significantly lower in patients with hypertrophic cardiomyopathy either with or without obstruction than in the control , and was significantly lower in HOCM group than in HCM group.

Peak longitudinal strain rate of the lateral left atrial wall was significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects, with no difference between patient with or without obstruction.

Time to peak strain was significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects , with no difference between patient with or without obstruction.

Time to peak strain rate was significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects, with no difference between patient with or without obstruction.

Tissue velocities of left atrial walls were significantly lower in patients with hypertrophic cardiomyopathy than the normal subjects, with no difference between patient with or without obstruction except in the late diastolic velocity (a′ wave) of mid segment of left atrial anterior wall, it was significantly lower in patients without obstruction than patient with obstruction.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

1. Left atrial volume index is good volumetric parameter in detecting geometric change in the left atrium.

2. Left atrial deformation imaging (strain , strain rate and left atrial tissue velocities) is a new, powerful tool in assessment of left atrial function especially before geometric changes and before changes in other conventional diameters.

3. Left atrial deformation study always deceased in patients with HCM especially in symptomatic patients.