Ultrasonic myocardial tissue characterization by integrated backscatter (IB), extracted from unprocessed radiofrequency signals, has proven useful in the differentiation of various myopathies from normal myocardium.1–6 The analysis of IB indices provides information concerning pathological and physiological changes of the myocardium,7–9 and cyclic variation of IB (CVIB) is widely used for myocardial tissue characterization.

Previous clinical and experimental studies have shown that in normal hearts the subendocardial wall contributes more to total systolic wall thickening than does the subepicardial half.10–13 Hence, in ischemic heart disease patients14 and various myocardial manifestations,15 there is increasing interest in observing subendocardial and subepicardial myocardial function separately. In patients with a hypertrophied heart but with a normal left ventricular ejection fraction and fractional shortening, attenuated midwall fractional shortening has been reported;16,17 however, few studies have shown separate myocardial tissue characterization for the subendocardial and subepicardial myocardium.18,19

Backscattered Energy Temporal Analysis (BETA) is a newly developed system to evaluate the IB of myocardium using the power of tissue Doppler, and provides greater temporal and spatial resolution. This system is also able to separately acquire the IB values of the endocardial and epicardial halves in the region of interest (ROI).

In this study, we measured the IB values of the subendocardial and subepicardial halves in patients with hypertrophic cardiomyopathy (HCM) or pressure-overloaded hypertrophy (POH) using the BETA system. We evaluated whether the acoustic properties differed according to the etiology of left ventricular hypertrophy (LVH).

**Methods**

**Subjects**

The study population consisted of 41 patients with LVH [HCM (n=24; 7 women; age 31–75 years, mean, 62±13) and POH (n=17; 8 women; age 36–78 years, mean 66±11)] and 21 normal subjects (8 women; mean age, 52±13 years, range, 30–71). The diagnosis of HCM was established by echocardiographic demonstration of asymmetry of the ventricular septum (septal to free wall thickness ratio >1.3) and a non-dilated left ventricle, but without other cardiac or systemic disease that could cause LVH. Three of the 24 HCM patients were excluded because of either inadequate quality of the M-mode images (2) or atrial fibrillation (1). One of the 17 POH patients was excluded because of inadequate quality of M-mode images. Causes of overload were hypertension in 10 patients, aortic stenosis in 4 and both in 2 patients. All the control subjects had a normal cardiac history and physical examination, as well as normal cardiac size and function as assessed by conventional echocardiography.
was performed from the parasternal long-axis view with the subject in the left lateral decubitus position. After the BETA system was activated, M-mode IB images were obtained by directing the selected ultrasound beam across the ventricular septum and the left ventricular posterior wall (Fig 2). The gain controls had to be carefully adjusted to produce a uniform brightness of myocardium without saturation. IB images were frozen so that at least 2 cardiac cycles were included. The backscattered energy data from these images were digitized and stored on a 3.5 inch magnetic optical disk for further analysis.

**Data Analysis**

An analysis of IB in the myocardium was performed in the ROI that had been located in the ventricular septum and the posterior wall of the left ventricle. The size of the ROI was made as large as possible between the subendocardial and subepicardial borders, avoiding the subendocardial and subepicardial specular reflections. The size of the ROIs selected in this study ranged from 4 to 10 mm. After the ROI was moved with a trackball through the midpoint of the subendocardial and subepicardial borders in the ventricular septum or the posterior wall throughout the cardiac cycle, the curve of the myocardial IB values vs time in the ROI was displayed (Fig 2). The CVIB was determined as the difference between minimal and maximal peaks during one cardiac cycle. The ROI was then automatically divided into subendocardial and subepicardial halves of the myocardium and the CVIB of both ROIs was obtained.

**Reproducibility**

The IB images of 10 normal subjects (28–40 years of age) were obtained using the BETA system to investigate intraobserver variability. Interobserver variability of CVIB was assessed using 2 independent observers. A single observer, recorded on 2 separate occasions, assessed intraobserver variability. Mean absolute differences were 0.6±0.4 dB (intraobserver) and 0.4±0.3 dB (interobserver) in the ventricular septum and 1.2±1.0 dB (interobserver) and 0.7±0.6 dB (intraobserver) in the posterior wall.
Statistical Analysis

All data are presented as mean ± SD. One-way ANOVA followed by post hoc Scheffe’s F test was performed to test differences among control subjects and patients with hypertrophy. The relationship between CVIB and percent wall thickening was studied by means of linear regression analysis. A value of p<0.05 was considered to be statistically significant. In the variability study, observer variability was estimated by calculating the mean absolute differences between observers.22

Results

Conventional Echocardiographic Variables

In comparison with normal subjects, patients with HCM and POH had higher values for ventricular septum and posterior wall thickness. The percent wall thickening of the ventricular septum in patients with HCM and POH was reduced compared with normal subjects. The ventricular septum in patients with HCM was thicker than that of patients with POH, whereas the thickness of the posterior wall did not differ between these 2 groups. Left ventricular dimension, LVEF and percent wall thickening of the posterior wall were not different among the 3 groups (Table 1).

Measurements of IB

CVIB in the Entire ROI CVIB values in the entire ROI of the ventricular septum in patients with HCM and POH were significantly smaller than those in normal subjects; however, there was no significant difference between patients with each type of hypertrophy (Table 2). In the posterior wall, the CVIB values did not differ among the 3 groups.

CVIB in the Subendocardial and Subepicardial Halves of the ROI In both the left (subendocardial) and right (subepicardial) ventricular halves in the ventricular septum,
the CVIB values in patients with HCM and POH were less than in normal subjects; however, there was no significant difference between patients with each type of hypertrophy (Table 2). In each group, the CVIB values of both halves of the ventricular septum did not differ. In patients with POH, the CVIB was significantly less in the subendocardial half than in the subepicardial half of the posterior wall, and in the subendocardial half of normal subjects. In contrast with the subendocardial side, no differences were observed among the 3 groups in the values of CVIB in the subepicardial half of the posterior wall (Table 2).

Relation Between CVIB and LV Percent Wall Thickening. The relation between the magnitude of CVIB and percent wall thickening in the ventricular septum is plotted in Fig 3, and in the left ventricular posterior wall in Fig 4. In the ventricular septum, there was a significant correlation between CVIB of the entire ROI, CVIB of the endocardial half, and percent wall thickening (r=0.58, p<0.05 and r=0.45, p<0.05, respectively) in patients with POH. There was no correlation between CVIB of the endocardial half and percent wall thickening in patients with HCM or in normal subjects. In the posterior wall, there was no correlation between the CVIB of the entire ROI and percent wall thickening in all patients. However, the CVIB of the endocardial half in patients with POH weakly correlated with percent wall thickening (r=0.52, p<0.05).

Discussion

We analyzed the tissue characteristics of hypertrophied myocardium using the newly developed BETA system with which we were able to obtain the separate acoustic properties of the subendocardial and subepicardial halves with high spatial and temporal resolution. The CVIB of the ventricular septum decreased in patients with HCM compared with normal subjects, but in the posterior wall, there were no significant differences in CVIB among the 3 groups. However, in patients with POH, the CVIB in the endocardial side of the posterior wall was reduced compared with normal subjects. We hypothesized that the magnitude of the CVIB in the subendocardial half would be greater than in the subepicardial half in normal subjects, because the contractility of the myocardium is a major determinants of CVIB, and the percent wall thickening of the subendocardial half is usually greater than that of the epicardial half in normal subjects. However, we did not observe any difference in the CVIB values of the subendocardial and subepicardial halves, except in the posterior wall in patients with POH.

CVIB in the Hypertrophied Myocardium

Previous studies have shown that ultrasonic backscatter is strongly affected by the angle between the orientation of the myocardial fibers and the insonifying ultrasonic beam and directly related to sarcomere length and myocardial thickness. As previously described, the collagen content of the myocardium and myocardial fibrosis increase the value of IB. Furthermore, it has been shown that the CVIB is affected by myocardial contractile function, ischemia and fiber architecture, although the exact mechanisms responsible for CVIB are unclear.

In our study, the magnitude of the CVIB of the ventricular septum in the hypertrophied heart was lower than in normal subjects. In patients with LVH, the percent wall thickening in the ventricular septum, representing regional contractile performance, was smaller than in normal subjects; HCM, hypertrophic cardiomyopathy; POH, pressure-overloaded hypertrophy.
subjects. These findings are consistent with previous studies\textsuperscript{18,19} and are additional evidence that a decreased CVIB reflects reduced regional myocardial contractile performance in the hypertrophied heart.

In patients with HCM, all patients exhibited asymmetrical septal hypertrophy. Maron et al reported that cellular disorganization was common in the ventricular septum, and that pathological changes in the septum were greater than disorganization was common in the ventricular septum, and cal septal hypertrophy. Maron et al reported that cellular performance in the hypertrophied heart.

CVIB reflects reduced regional myocardial contractile of the muscle fibers changed from the endocardium to the subendocardium myocardium increased as heart weight increased, independent of the type of pressure overload\textsuperscript{36} Therefore, in patients with POH, increased subendocardial connective tissue may result in lower CVIB values in endocardial ROIs. Decreased midwall fractional shortening has been reported in patients with POH who have normal conventional measures of chamber function\textsuperscript{6,17} and is another possible cause of the reduced CVIB of the ventricular septum and subendocardium in the posterior wall in POH.

We measured the CVIB not only in the entire ROI but also in the subendocardial and subepicardial halves of the ROI. The CVIB in the entire ROI tended to be slightly less than in the endocardial or epicardial halves of the ROI. The timing of the maximal or minimal peaks of IB values in the endocardial and epicardial halves shifted slightly, which may be why the CVIB value for the entire ROI was not consistent with the mean value of the CVIB in the endocardial and epicardial halves.

Relation Between CVIB and Percent Wall Thickening

The CVIB in the entire ROI and in the left ventricular half of the ROI in the ventricular septum of patients with POH related to percent wall thickening, but not in the HCM patients or normal subjects. Although regional myocardial contractile function, represented by percent wall thickening, has been reported as a factor affecting the magnitude of CVIB, the relation between CVIB and percent wall thickening is not linear\textsuperscript{19} In the present study, the fiber disarray in patients with HCM may be a reason for the lack of a significant correlation between CVIB and percent wall thickening. In normal subjects, the range of CVIB and percent wall thickening may not be enough to derive a significant correlation between the 2 variables.

Reproducibility

There have been little previous data on the reproducibility of IB measurements. Stuhlmueller et al assessed the reproducibility of both acquisition and analysis process determination of CVIB and demonstrated a mean inter- and intra-observer variability of 2.8±1.7 dB and 1.6±1.4 dB, respectively\textsuperscript{22} In the present study, although we assessed the reproducibility for the analysis process only, the mean inter- and intra-observer variability was less than 1.2 dB and 0.7 dB, respectively. Masuyama et al also assessed reproducibility in the analysis process, and their mean inter- and intra-observer variability was less than 0.9 dB and 0.6 dB, respectively\textsuperscript{22} Thus, that CVIB values obtained by the system used in our study are as low as the variability values obtained by the earlier method.

Study Limitations

The ROI was defined along a tracing line that was drawn in the center of the myocardium throughout the cardiac cycle and we measured CVIB in subendocardial and subepicardial halves that had been automatically divided in the ROI. Therefore, in systole, part of the ‘subepicardial half ROI’ may have been involved in the subendocardial side of the ROI, and this may have led to the slight difference in CVIB values between the halves. Because we used M-mode based measurements, we had limited positions in which to place the ROIs; that is, septum and posterior wall. As previously mentioned, because ultrasonic backscatter is strongly affected by the angle between fiber orientation and the insinifying ultrasonic beam, it was not reliable to place the ROI in lateral positions.

Conclusions

Ultrasonic tissue characterization of the myocardium using the BETA system to obtain separate IB values in the subendocardial and subepicardial halves provided additional information that reflected pathological changes. This study showed the CVIB values in the subendocardium of the posterior wall of patients with POH were reduced, but not in patients with HCM. Although the present results are still insufficient to completely differentiate POH from HCM, the BETA system, with further improvement of the system of analysis, has potential for the ultrasonic tissue characterization of various heart diseases.

References

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