Dual-chamber pacing (DDD) is a therapeutic alternative to surgical septal myotomy–myectomy for patients with hypertrophic obstructive cardiomyopathy (HOCM). A reduction in the left ventricular (LV) outflow obstruction by DDD has been demonstrated in previous studies, and although pacing-induced paradoxical septal motion is the most conceivable mechanism, there are no data regarding the effects of DDD on regional wall deformation, particularly of the ventricular septum.

Myocardial deformation can be quantified by echocardiographic strain and strain rate (SR) imaging, techniques based on processing the velocity data from tissue velocity imaging. These methods are able to identify regional changes associated with a range of pathologies, and in particular, those associated with pacing. Recently, Breithardt et al reported that in heart failure patients, the peak strain and SR during systole were assessed in 8 segments in 4 left ventricular (LV) walls. With DDD turned on, peak strain and SR were significantly increased in the basal anteroseptal (strain –10.2±6.8 to –1.0±6.4, p<0.005; SR –0.76±0.46 to 0.05±0.58, p<0.001) and septal segments (strain –11.2±8.9 to –2.2±7.7, p<0.005; SR –0.85±0.54 to –0.19±0.75, p<0.05), but not in the basal posterior (strain –15.0±13.0 to –13.4±9.2, p=NS; SR –1.37±0.57 to –1.93±0.65, p=NS) and lateral segments (strain –18.1±10.2 to –15.7±5.6, p=NS; SR –1.33±0.68 to –0.84±0.88, p=NS). These findings were associated with a modest, but significant, change in the LV pressure gradient (24±12 mmHg to 14±7 mmHg, p<0.001).

In patients with HOCM, DDD appeared to produce myocardial lengthening in the basal septum during systole, which may have implications for the mechanism of reducing LV outflow obstruction during DDD. (Circ J 2006; 70: 63–68)

Key Words: Doppler ultrasound; Hypertrophic cardiomyopathy; Pacing

Effects of Dual-Chamber Pacing on Regional Myocardial Deformation in Patients With Hypertrophic Obstructive Cardiomyopathy

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Background This study examined the effects of dual-chamber pacing (DDD) on regional myocardial deformation, as determined by echocardiographic strain and strain rate (SR) imaging, in patients with hypertrophic obstructive cardiomyopathy (HOCM).

Methods and Results Fourteen patients (11 men, 3 women; mean age 55±16 years) who had been on long-term DDD (mean period 7.4±2.1 years) underwent strain and SR imaging. Before and after DDD, the peak strain (%) and SR (s⁻¹) during systole were assessed in 8 segments in 4 left ventricular (LV) walls. With DDD turned on, peak strain and SR were significantly increased in the basal anteroseptal (strain –10.2±6.8 to –1.0±6.4, p<0.005; SR –0.76±0.46 to 0.05±0.58, p<0.001) and septal segments (strain –11.2±8.9 to –2.2±7.7, p<0.005; SR –0.85±0.54 to –0.19±0.75, p<0.05), but not in the basal posterior (strain –15.0±13.0 to –13.4±9.2, p=NS; SR –1.37±0.57 to –1.93±0.65, p=NS) and lateral segments (strain –18.1±10.2 to –15.7±5.6, p=NS; SR –1.33±0.68 to –0.84±0.88, p=NS). These findings were associated with a modest, but significant, change in the LV pressure gradient (24±12 mmHg to 14±7 mmHg, p<0.001).

Conclusions In patients with HOCM, DDD appeared to produce myocardial lengthening in the basal septum during systole, which may have implications for the mechanism of reducing LV outflow obstruction during DDD. (Circ J 2006; 70: 63–68)

Methods

Patients Between December 1994 and April 2001, 18 patients with HOCM underwent pacemaker implantation (DDD) at Osaka Medical College for persistently high LV pressure gradient (LVPG). Of these, 2 patients died from sudden cardiac death during follow-up and of the remaining 16 patients, 14 accepted the study protocol and were enrolled. Each patient had been stable in clinical condition (functional class I or II) on the basis of long-term DDD. Exclusion criteria included chronic atrial fibrillation, dilated phase of disease process, and prior septal myotomy–myectomy operation. Atrioventricular delay was optimized in individual patients to achieve the lowest LVPG at their last visit to the outpatient department. Each patient gave informed consent before the echocardiographic examination.

Two-Dimensional and Doppler Echocardiography

All patients underwent 2-dimensional Doppler, and tissue velocity imaging during DDD and immediately after the DDD was turned off. We used a commercially available echocardiographic apparatus (Vivid 7 echocardiographic (GE-Vingmed Ultrasound, Horten, Norway)) with a 2.5-MHz transducer. Changes in LV volume were assessed by modified Simpson’s rule (apical 4-chamber view). Parameters of LV diastolic function were also assessed by pulsed Doppler echocardiography: early and atrial filling velocity at the mitral valve and their ratio, and the deceleration...
there is myocardial shortening (negative value), and
separated by a distance (L). When the 2 locations are getting
dial Doppler velocities (V1 and V2) measured at 2 locations
y data. SR reflects how fast regional myocardial shorten-
ments were assessed in total: basal- and mid-anteroseptal
sample volume did not deviate for each LV wall. Eight seg-
gional myocardial velocity curves were reconstituted off-
ration, and sector size and depth were optimized for the
pacing. At least 3 consecutive beats of these were digitally
the apical long-axis and 4-chamber views with and without
or color Doppler myocardial images, were recorded from
graphic apparatus and transducer. Tissue velocity images,
Image Acquisition
Ultrasound data were acquired with the same echocardio-
apparatus and transducer. Tissue velocity images, or color Doppler myocardial images, were recorded from the apical long-axis and 4-chamber views with and without pacing. At least 3 consecutive beats of these were digitally stored for post-processing. Gain settings, filters, and pulse repetition frequency were adjusted to optimize color saturation, and sector size and depth were optimized for the highest possible frame rate (>140 frames per second). Regional myocardial velocity curves were reconstituted offline from a sample volume of 8x4mm. We used a semi-automatic tracking technique for all measurements so that the sample volume did not deviate for each LV wall. Eight segments were assessed in total: basal- and mid-anteroseptal segments, basal- and mid-posterior segments, basal- and mid-septum, and the basal- and mid-lateral segments.

Strain and SR data were processed from the tissue velocity data. SR reflects how fast regional myocardial shortening or lengthening occurs. SR is calculated from myocardial Doppler velocities (V1 and V2) measured at 2 locations separated by a distance (L). When the 2 locations are getting closer, there is myocardial shortening (negative value), and

when they are moving apart, there is lengthening (positive value). Accordingly, SR is calculated as the instantaneous spatial velocity gradient and has units of s⁻¹; SR=(V2− V1)/L. In the present study, L was set at 10mm. Strain is calculated as the time integral of SR and has units of %, with a reference used at end-diastole.

Image Analysis
Tissue velocity data were all analyzed with the software program provided with the echocardiography machine. Strain and SR measurements were obtained for the 8 myocardial segments and peak systolic strain and SR were determined. As noted, peak strain and SR can have either positive or negative value, so if an inflection point is above the zero-line and upward during systole, the actual value is “positive”, whereas if an inflection point is under the zero-line and downward during systole, the actual value is “negative”. In addition, we counted the myocardial segments showing positive or negative strain/SR for the total segments analyzed (112 segments for 14 patients) with and without DDD. If the strain/SR curve was above the zero-line, even after opening of the aortic valve, this indicated that myocardial lengthening had occurred instantaneously and the resultant strain/SR value was “positive”. Conversely, if the a strain/SR curve was under the zero-line, this was read as “negative”. Data from pulsed Doppler recordings at the aortic and mitral valves were incorporated to identify the exact timing of mitral and aortic valve opening. Strain and SR data were all averaged for 3 consecutive beats.

Observer Variability
Interobserver variability for the peak strain and SR during systole was assessed from 5 randomly selected patients (80 segments in total). Using Bland-Altman analysis²⁰ the mean difference for each was 0.2±4.4% and 0.1±0.39s⁻¹,
respectively. The coefficient of the correlation (r) for the peak strain and SR was 0.90 (p<0.0001), and 0.84 (p<0.0001), respectively. The agreement in determining inflection points (positive or negative) was assessed by kappa (κ) statistics. The κ coefficient for strain and SR was 0.82 (p<0.0001, 95% confidence interval (CI) 0.62–1.02) and 0.54 (p<0.0001, 95% CI 0.24–0.84), respectively.

Statistics
Paired t-test was used to evaluate changes in echocardiographic variables, McNemar's test was performed to assess the changes in categorical variables, and all data are expressed as mean±SD. A value of p<0.05 was considered statistically significant.

Results

Patient Characteristics (Table 1)
There were 11 men and 3 women, with a mean age of 55 years. Twelve patients had been receiving concomitant...
-blocker therapy and none of the patients had been treated with disopyramide or cibenzoline. There was no significant change in heart rate with DDD, but the QRS duration was significantly prolonged.

Changes in 2-Dimensional and Doppler Echocardiographic Parameters (Table 2)

LV end-systolic volume tended to be increased with DDD but no significant change was observed in LV ejection fraction. For diastolic function, the early to atrial filling velocity ratio was increased and the deceleration time was shortened with DDD, indicating that the LV inflow profile became more restrictive. There was a modest, but significant reduction of LVPG.

Changes in Strain- and SR-Derived Parameters (Table 3)

During DDD, peak strain and SR increased in all the segments except for the mid-lateral and mid-posterior segments; however, significant increases in these were observed only in the anteroseptal and septal wall segments. Fig 1 shows how the inflection points changed with DDD. Without DDD, 1 of 56 (1.8%) segments in the anteroseptal/septal wall showed positive strain and SR. During DDD, the number of segments with positive strain and SR markedly increased to 14 segments for strain (25%) (p<0.001) and 16 segments for SR (28.6%) (p<0.001). For the posterior/lateral wall, 2 segments showed positive strain and none showed positive SR without DDD, whereas no segments exhibited positive strain (p=NS) or SR (p=NS) during DDD. Representative analyses of strain and SR imaging are shown in Figs 2 and 3.

Relationship to Decline in the LVPG

A possible relationship between changes in the inflection point and LVPG was examined. Patients who developed positive strain in at least 1 basal anteroseptal/septal segment during DDD (n=8) showed a greater decline of LVPG than those who did not (n=6) (14±6 mmHg vs 4±3 mmHg, p<0.005). Likewise, in patients who had positive SR during DDD (n=9), LVPG was decreased to a greater extent than in those who did not (n=5) (13±6 mmHg vs 3±3 mmHg, p<0.01).

Discussion

Main Findings

The present study demonstrated that in patients with HOCM, DDD led to myocardial lengthening, especially at the basal septum, as expressed by the increase in peak strain and SR during DDD. These changes appeared to be related to the degree of LVPG decline.
Pacing and Regional Wall Deformation

Very few data are available of the effects of pacing on regional wall deformation. Breithardt et al investigated such effects in heart failure patients undergoing cardiac resynchronization therapy and observed that this treatment modality significantly induced reverse septal–lateral strain/SR relationship, with septal strain/SR increased relative to lateral strain/SR, which they suggested was related to better energy-efficient contraction and more homogeneous wall stress distribution induced by the therapy. On the other hand, the present patients exhibited relative decreases in septal strain/SR during DDD, indicating that there was more energy-wasteful and heterogeneous inter-segmental contraction.

Strain and SR Imaging

As mentioned before, strain reflects the extent of myocardial fiber shortening and lengthening, whereas SR reflects the velocity of the shortening or lengthening. Therefore, these 2 methods reflect somewhat different aspects of myocardial function, but may provide complementary information. In the present study, both strain and SR imaging were used to assess regional myocardial deformation, with the goal of providing detailed information about regional LV function with and without DDD. We found that the number of segments showing a positive or negative value did not always match in the strain and SR analyses (Fig 1). The reason is unclear, but may be attributed to the mathematical integration algorithm. Also, 2 segments in the posterior and lateral walls exhibited “positive” strain without pacing, which became “negative” with pacing. Pacing might modify preexisting disorganized contraction in the relevant segments, but further investigation is necessary to elucidate the pathophysiological basis of this finding.

Implications for the Mechanism of Responsiveness to DDD

The mechanisms of the reduced LVPG during DDD are considered to be 2-fold: a negative inotropic effect and modification of the septal contraction pattern. However, these 2 factors may be associated during DDD because pacing-induced asynchronous septal contraction is automatically accompanied by decreased LV synchrony and contractility. From a fundamental point of view, there are several anatomical and functional explanations for the development of LV outflow obstruction, including Venturi or drag forces, septal bulge, elongation of the mitral leaflets, and anterior displacement of the papillary muscles. Of these, septal bulge is considered essential in narrowing the LV outflow tract and setting the stage for systolic anterior motion of the mitral leaflets via Venturi force. The present study showed that DDD caused the ventricular septum to lengthen longitudinally during systole, indicating that DDD may generate opposite force against “systolic septal bulging” and hamper the aforementioned mechanical sequence. Such local derangement of myocardial contraction could affect global LV contractility, which may also accelerate lowering of the LVPG.

In the present study, changes in peak strain and SR during systole were greater in the basal septal segments relative to the mid septal segments (Table 3), indicating that myocardial lengthening was more likely to occur in segments remote to the pacing site. The precise mechanism of this finding is unclear, but may explain the observation that pacing from the right ventricular apex reduces LVPG to a greater extent than pacing from the high septum. On the other hand, no significant changes in strain and SR were observed for the posterior and lateral wall segments in the present study. In the LV free wall, such pacing-induced inter-segmental interaction may be not strong enough to be reflected in strain or SR measurements.

Study Limitations

The present study included chronically stable patients on the basis of long-term DDD, and therefore the cardiac...
memory effect may have influenced the results.\textsuperscript{25} Data accumulation from an acute hemodynamic study for de novo patients would be desirable (Fig 4), although induction of DDD for HOCM patients is currently less common, and instead there has been increasing use of percutaneous septal ablation.\textsuperscript{26,27} Strain and SR measurements are angle-dependent because they are based on Doppler techniques, so there is the possibility that our data only reflected changes in the Doppler beam direction. However, we selected the basal and mid myocardial segments in order to keep the Doppler beam less than 20 degrees against the longitudinal LV walls. In addition, peak strain and SR were quite different between the basal and mid myocardial segments within the same LV wall, indicative of pacing-induced myocardial deformation. Finally, interobserver variability for the peak strain and SR was not slight, which seems an important limitation inherent to currently available techniques, although determination of the inflection points offered fairly good agreement.

Conclusions

We performed strain and SR imaging to examine the effects of DDD on regional myocardial deformation in patients with HOCM. DDD increased longitudinal strain and SR in the ventricular septum, which was associated with a reduction of LVPG. Further studies are needed to confirm a direct relationship between changes in myocardial deformation and LV outflow obstruction.

References