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Short Report

Systolic Heterogeneity of Transmural Myocardial Function in Normal Subjects: Physiological Functional Heterogeneity

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Koiwa, Y., Kamada, H., Inose, M., Shirato, K., Hasegawa, H. and Kanai, H. *Systolic Heterogeneity of Transmural Myocardial Function in Normal Subjects: Physiological Functional Heterogeneity*. Tohoku J. Exp. Med., 2002, **197** (3), 183-187 —— Because of the lack of a clinical method for assessing the transmural myocardial function, few studies on the heterogeneity during the myocardial contraction/relaxation sequence inside the human ventricular wall have been reported, despite the fact that the importance of the pathophysiology in the transmural heterogeneity has been stressed in previous experimental studies. We studied the transmyocardial functional heterogeneity of the basal anteroseptal segment in normal subjects ($n=8$, 40.0 ± 12.8 year, male), adopting the novel high resolution Doppler measurement "Phased Tracking Method". Each transmural layer of 0.75 mm thickness showed functional heterogeneity (physiological transmural functional heterogeneity), namely larger thickening occurred in the left ventricular endocardial side (right side 1/3: $26.1\pm5.2\%$ of the total wall thickness, middle 1/3: $31.9\pm2.7\%$, left side 1/3: $42.1\pm6.4\%$) and the peak thickening shifted smoothly in time from the middle layers to the left subendocardial side during the contraction period. We concluded that transmural functional heterogeneity does exist in normal subjects as well as in the experimental animals of previous reports. Smooth and coordinate myocardial layer contraction across the ventricular wall (physiological transmural functional heterogeneity) is fundamental to maintain the normal ventricular function. ———— echocardiography; transmural myocardial function; Phased Tracking Method; transmyocardial systolic heterogeneity

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Transmural heterogeneity of the coronary vascular vasodilator capacity, myocardial blood flow and myocardial metabolism across the ventricular wall have been considered as dominant factors in many pathological conditions such as subendocardial myocardial ischemia, subendocardial infarction, and hypertensive heart. Functional differences between the inner and outer layers of the left ventricular wall have already been demonstrated in experimental models, namely the systolic thickening at the inner half of the ventricular wall accounts for approximately 70% of the entire systolic wall thickness in normal heart (Gallagher et al. 1985; Myers et al. 1986). In these experimental studies, however, the detailed spatial transmural distribution and the temporal sequence of the myocardial layer contraction have not been clarified.

Recently, we have developed the novel high resolution (micron-order) Doppler measurement "Phased Tacking Method" for clinical use (Kanai et al. 1997; Kanai and Koiwa 2001). From histology examinations using doxorubicin injected rabbits, the transmural systolic function by this method has been confirmed to relate closely to the magnitude of myocardial damage (Koiwa et al. 1999). In this clinical study, we aimed to clarify whether the dominant functional role is localized at the human left ventricular inner side as suggested in experimental studies, and how it is coordinated during systole by adopting the Phased Tracking Method to describe the transmural functional distribution of myocardial layers of 0.75 mm-thickness.

Methods

We examined 8 normal healthy subjects (40.0 ± 12.8 year, male). They had no abnormalities in the annual medical examination.

The principles of the "Phased Tracking Method" including the theoretical, in-vitro and in-vivo evaluations of the myocardial layer thickening rate have been detailed elsewhere (Kanai et al. 1997) and the firm relation to the myocardial histology has also been demonstrated (Koiwa et al. 1998). In brief, the following ideas provide the framework of this Phased Tracking Method.

Step 1 established the principle for the precise measurement of the local micron-order vibration velocities preset at the intramyocardial wall, (velocities at each transmyocardial preset point: v(xi; t) in the figure) which was superposed on the large amplitude pulsation of the beating ventricle (Kanai et al. 1994).

Step 2 describes the loci of the vertical transition of the points in the ventricular wall along the cardiac cycle by the time integration of the high resolution velocity signal and by adopting the restricted auto-correlation, phased tracking technique. Here, the initial point of the tracking was at the R wave of ECG in M-mode of the echocardiography. This locus is the vertical positional change of a preset point during the cardiac cycle.

Step 3 evaluated the thickening and thinning of each layer between two preset points at incremental depths in the wall by calculation of the difference of two vertical tracking loci throughout the cardiac cycle. Multiple points were preset vertically across the wall, and changing views of the thickening of every myocardial layer were determined.

In practice, we measured the transmural function at the basal septum in the longitudinal view of the ultrasonic B-mode image. The system adopted in this measurement employed a 3.0 MHz Doppler frequency, 9 kHz Repetition frequency and 1 MHz sampling frequency of AD conversion. In this system, the lower limit of the thickness is 0.1 mm and the changing rate of thickness change is 0.1 mm/sec as demonstrated in the report (Kanai et al. 1997).

The transmural myocardial function of each 0.75 mm-thickness layer was evaluated by the maximum longitudinal velocity at each preset point (peakV), the maximum %thickening (tkn) (=systolic thickness/thickness at R

wave) of the layer (max%tkn), the maximum rate of %thickening of the layer (Vmax%tkn), the interval from the R wave in ECG to the point of Vmax%tkn (t-Vmax%tkn). The contribution of each 1/3 across the wall to the total systolic wall thickness was also evaluated by the maximum %thickening of each 1/3 across the wall (max%tkn[1/3]).

Results

The typical systolic thickening of each transmural myocardial layer of the septum is shown in the left (a) of Fig. 1. Here, the thickening velocity in each myocardial layer was color-coded in 21 levels as in the inset at the bottom. The open circle shows the point of Vmax%tkn in each layer. The middle top figure (b) is the peakV at each preset point and

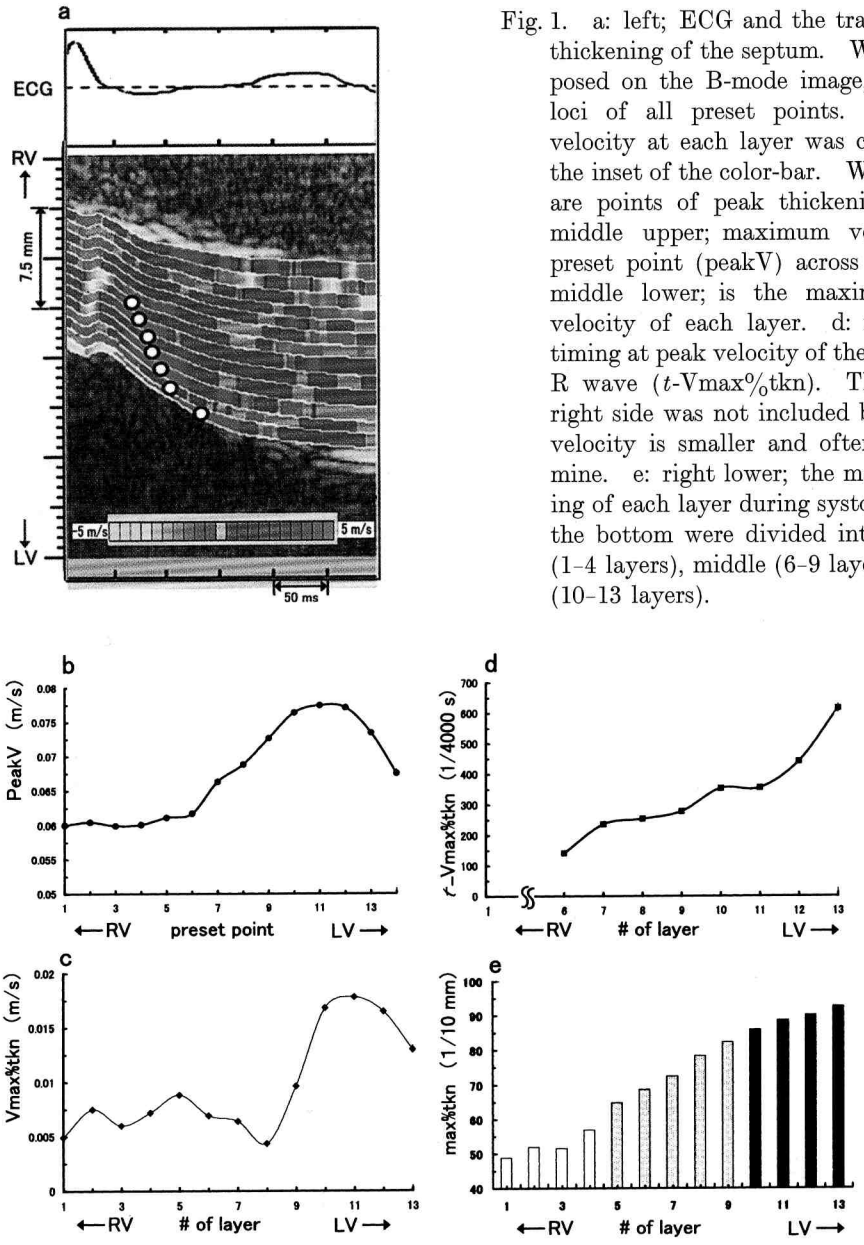

Fig. 1. a: left; ECG and the transmural systolic thickening of the septum. White lines superposed on the B-mode image, lower, indicate loci of all preset points. The thickening velocity at each layer was color-coded as in the inset of the color-bar. White open circles are points of peak thickening velocity. b: middle upper; maximum velocity at each preset point (peakV) across the septum. c: middle lower; is the maximum thickening velocity of each layer. d: right upper; the timing at peak velocity of the thickening from R wave (t-Vmax%tkn). The value at the right side was not included because the peak velocity is smaller and often hard to determine. e: right lower; the maximum thickening of each layer during systole. The bars at the bottom were divided into three as right (1–4 layers), middle (6–9 layers) and left side (10–13 layers).

the lower one (c) is Vmax%tkn during systole. Both peakV and Vmax%tkn are larger on the left side. The right side of the figure shows t-Vmax%tkn at each layer in the middle to the left side of the septum (top). In this figure, t-Vmax%tkn at the right side of the septum was not displayed because of the smaller Vmax%tkn value. The t-Vmax%tkn gradually and smoothly increased at the left side. In the right lower side, the max%tkn at each layer is shown. The middle and left side layers were shaded as in Fig. 1. Here, the larger systolic function was obvious at the left side of the septum.

When the ventricular wall was divided into thirds across the wall, the functional heterogeneity was obvious in the human ventricular wall as a major part of the systolic thickening was due to the contribution of the mid and left side of the ventricular wall. That is, max% tkn(1/3) at each 1/3 of the septum from the right to left ventricular side was $26.1\pm5.2\%$, $31.9\pm2.7\%$, and $42.1\pm6.4\%$. The larger physiological importance of the mid- to left side of the septum during systole was consistent with the experimental reports. The gradual increase in t-Vmax%tkn is also common in normal subjects as the slope of the transmission time across layer was 0.03 ± 0.01 (mean$\pm$S.D.) sec per mm in trans-myocardium of these left side.

Discussion and Conclusion

In the light of the potential impact of the intramyocardial heterogeneity on the clinical outcome, the importance of the Phased Tracking Method for explaining the change in ventricular contractility within the context of this almost totally unexplored field of cardiac pathophysiology is obvious. This is the first report that demonstrates the transmural heterogeneity of the systolic function "the physiological functional heterogeneity" in normal subjects. These functional characteristics result in larger oxygen demand at the left ventricular endocardial side, and they constitute the background of many pathological states together with other heterogeneities in metabolism and/or in the coronary vascular structure. In our study of normal subjects, the point of the maximum thickening moved smoothly across the wall as shown by open circles in the left figure, indicating the transmural contribution across the wall is a time-dependent phenomenon. The sensitive transition from the physiological heterogeneity during exercise test and how the magnitude of distortion in the physiological heterogeneity relates the clinical severity in coronary artery disease and adoriamycin cardiotoxicity are now being examined in our laboratory.

In clinical measurement, we should keep in mind that the Phased Tracking Method measures only the vertical transition of each intramural preset point and can not demonstrate the rotational and horizontal temporal movement, even though the significant change might occur in 3-D movement during the clinical course of the heart disease.

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