Computational Assessment of Spatio-Temporal Heterogeneity of Human Left Ventricular Contractions in Normal and Ischemic Heart

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Abstract

Two-dimensional echocardiographic images of left ventricle are analyzed to characterize quantitatively spatio-temporal heterogeneity of regional wall motion in norm and ischemic heart disease. A negative correlation between the regional heterogeneity and the global ejection fraction is revealed. Regional heterogeneity is shown to increase significantly in patients with ischemic heart disease compared to normal subjects. A special contribution of the apex is identified, and a diagnostic index of regional wall motion abnormality is suggested.

1. Introduction

While there is much evidence on myocardial heterogeneity at different levels of organization (from cell to organ), the physiological and pathophysiological roles of myocardial heterogeneity are still poorly understood. In many studies, regional left ventricle (LV) wall motion was assessed in normal or diseased heart using one to three dimensional echocardiography, radiography, or MRI [1 - 3], but there has been little focus on heterogeneity pattern identification and quantitative measures for correlation with LV function. Accordingly, the goals of this study are: (i) to quantitatively characterize regional LV wall motion, (ii) to propose indices of spatio-temporal heterogeneity of LV motion, and (iii) to assess the role of heterogeneity in LV pump function in normal and ischemic human heart.

2. Methods

To characterize spatio-temporal heterogeneity of LV regional wall motion, we developed a computer program for frame-by-frame analysis of two-dimensional (2D) echocardiographic LV images in apical four-chamber and two-chamber views.

Ventricular ejection fraction was derived as a global parameter from 2D end-diastolic and end-systolic images, using a modified Simpson's rule approach. The difference (ΔS) between end-diastolic and end-systolic image areas (EDS and ESS, respectively) provided a 2D estimate of the ejection fraction:

$$\Delta S(\%) = (EDS - ESS) / EDS \,. \quad (1)$$

Analysis of regional LV wall motion was based on the assessment of regional contributions to ejection fraction, using a radial method (Fig. 1; [2]). Each LV endocardial contour, obtained throughout the cardiac cycle, was superimposed on the end-diastolic contour by aligning their centre of mass. Total EDS was divided into 20 radial sectors, either of equal angle or of equal area. This number of sectors fulfilled the convergence criterion, i.e. provided stability of results and calculation accuracy. Regional wall motion was calculated on a frame-by-frame basis throughout the cardiac cycle as the fractional area change for each sector. The maximal fractional area change (ΔS_j) in j-th region was defined as the "regional ejection fraction", and used to assess the regional LV wall contribution to global ejection fraction.

$$\Delta S_j(\%) = (EDS_j - ESS_j) / EDS_j \,, \quad (2)$$

where EDS_j is the diastolic segmental area and ESS_j is the minimal area attained by the j-th region during ejection (local end-systole).

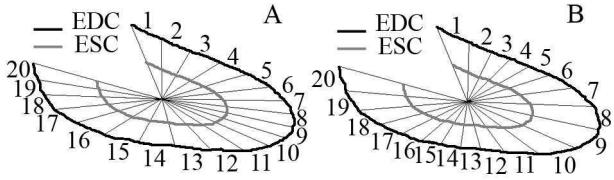

Figure 1. Radial method of regional LV wall motion evaluation with equiareal (A) and equiangular (B) segmentation of LV images, numbered clockwise. EDC / ESC: end-diastolic / end-systolic contours, respectively.

It is worth mentioning that the timing of local end-systole may not coincide with that of the whole LV. This mismatch reflects regional asynchronism of LV wall

motion during contraction. To characterize this asynchronism, we used the ratio (τ_j) of the completion time of local systole ($t(ESS_j)$) to that of global end-systole ($t(ESS)$):

$$\tau_j(\%) = t(ESS_j) / t(ESS) . \quad (3)$$

Note, that calculation of the above characteristics ΔS_j and τ_j of regional wall motion is based on the analysis of LV images throughout the entire cardiac cycle, while routinely only end-diastolic and end-systolic LV contours are accounted for [1, 3].

Two modalities of the radial sub-division of end-diastolic LV area were considered (Fig. 1) with either (i) equiangular sectors (which is conventionally used [2]) or (ii) equiareal sectors (suggested here). Equiangular end-diastolic sectors yield different areas (due to the lack of rotational symmetry of LV geometry), which may hamper comparison of regional contributions to global ejection fraction. This can be avoided by the equiareal segmentation method, which provides a framework for direct comparison between the various regional ΔS_j, and between every ΔS_j and global ΔS (where $\Delta S = \Sigma \Delta S_j$ / 20 in the equiareal modality).

The normal reference group included 22 healthy subjects (20 men, age 31 ± 9 years, ejection fraction 71 ± 10%, heart rate 68 ± 9 beats/min; all data in this paragraph presented as mean ± SD). The group of 52 patients with ischemic heart disease (45 men, age 50 ± 9 years) was selected from patients who were referred for surgical revascularization and had preserved global ejection fraction (mean ejection fraction 65 ± 12% at heart rate 69 ± 14 beats/min). In a part of the patients (n = 25), echocardiography was performed both before and about 3 month after revascularization.

Individual characteristics of LV global and regional function were calculated for each subject using all 4 combinations of LV imaging data (2- or 4-chamber view) and segmentation methods (equiangular or equiareal). Individual data were collected in two groups (normal and patients). In- and inter-group data were compared using ANOVA and Student's t-tests, where appropriate, within *Statistics (SoftGraph*) package. The data below (presented as mean ± SEM, if not differently specified) is focused on the combination of 4-chamber LV view and equiareal segmentation method. Qualitative differences with other combinations are discussed, where applicable.

3. Results

3.1. Heterogeneity of regional LV wall motion in the normal heart

The reference group of healthy volunteers (Fig. 2, black solid line) showed a spatially heterogeneous distribution of regional ejection fractions (numbered clock-wise along the LV contour as shown in Fig 1). This provides a reference pattern of dependence of mean regional ΔS_j (see formula (2)) on spatial position of *j*-th segment within the LV. Different LV wall regions vary considerably in their apparent mean contribution to global ejection fraction; this variation is nonlinear but regular. There are two peaks of mean ΔS_j in regions of the mid antero-lateral wall and the mid septum (60 ± 2% and 63 ± 2% in regions #5 and #17, respectively), with a minimum of mean ΔS_j in the apical area (48 ± 2% in region #10). The curve pattern was similar in all 4 combinations of LV view and radial analysis methodology.

We found significant differences ($p < 0.05$) between the two ΔS_j maxima and the ΔS_j minimum, as well as between each of the ΔS_j extremes with mean 2D global ejection fraction ΔS (see formula (1), mean ΔS = 51 ± 2%), confirming significant spatial heterogeneity in the regional LV wall motion (as assessed here), suggestive of different regional contributions to global ejection fraction.

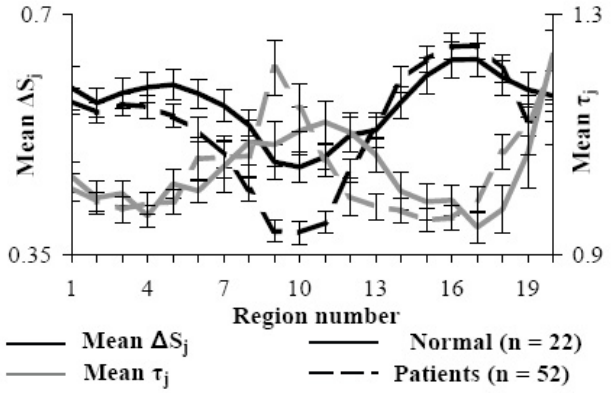

Figure 2. Spatio-temporal heterogeneity of regional LV wall motion. Mean ΔS_j (black lines) are on the left vertical axis. Mean τ_j (grey lines) are on the right vertical axis. Region numbers on horizontal axis are as in Fig. 1. Vertical bars denote SEM. Solid lines indicate data from the normal volunteers; dashed lines are patient data.

Analyzing time dependent regional wall motion, we assessed temporal heterogeneity of LV contractions. We used measure τ_j (see formula (3)) to quantify asynchronism of local end-systole versus global end-systole. Similarly to regional area changes, ANOVA revealed a significant difference in τ_j means, where $\tau_j < 1$ denotes regions that reach minimal segmental area prior to global end-systole, while $\tau_j > 1$ are for regions completing local inward motion later (Fig. 2, grey lines). The dependence of mean τ_j on segment position is nearly opposite to that of ΔS_j, with minima in the mid wall regions, and a maximum in the apical area. Accordingly,

we found a significant negative correlation (r = –0.6, p = 0.005) between means of τ_j and ΔS_j in the normal group (solid lines in Fig. 2). This suggests that LV wall regions that reach local end-systole earlier also deform faster and/or contract more strongly, thus making a greater contribution to ejection fraction as assessed here.

We suggest that the coefficient of variation in individual regional ejection fraction ΔS_j [4], and the coefficient of variation in regional asynchronism τ_j, may characterize spatial and temporal heterogeneity in subject LV wall motion. In the normal group, the mean coefficient of variation in ΔS_j was 15 ± 1%, and in τ_j it was 14 ± 1%. We found a negative correlation (r = –0.56, p = 0.007) between the coefficient of variation in ΔS_j and the global ejection fraction (Fig. 3). Similarly, a negative correlation between the coefficient of variation in τ_j and global ejection fraction was found in the normal group, but this was significant only for 2-chamber LV view (p < 0.05).

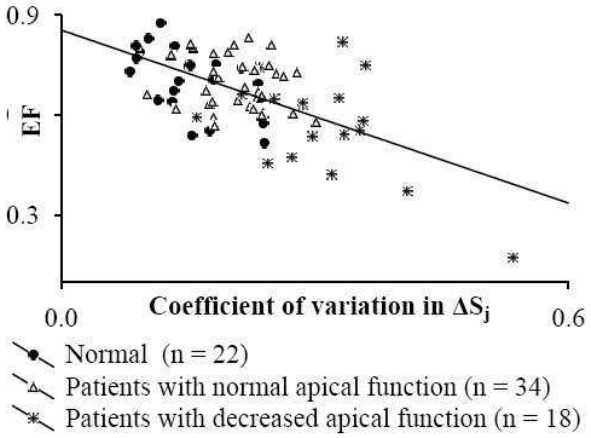

Figure 3. Relation between heterogeneity of individual regional wall motion (assessed by variability in regional area change) and ejection fraction. The coefficient of variation (CV) in individual ΔS_j is on the horizontal axis. Global ejection fraction (EF) is on the vertical axis. Line shows linear regression (r = –0.59; p < 0.0001; EF = 0.85 – 0.86 * CV) for the pooled data from normal volunteers and patients.

These results allowed us to hypothesize a possible relation between LV pump function and the degree of spatial and temporal heterogeneity of wall motion, where increased heterogeneity and decreased LV ejection fraction coincide.

3.2. Heterogeneity of regional LV wall motion in ischemic heart disease

Among patients with ischemic heart disease, the patterns of segmental distribution of both the ΔS_j and τ_j were qualitatively similar to that in the normal group (Fig. 2, dashed lines). However, t-tests found significant differences between the normal group and patients in ΔS_j means of several regions. The most marked decrease in mean ΔS_j was seen in the apical regions (38 ± 2% in patients *vs*. 48 ± 2% in normal volunteers for segment #10, p = 0.002), but this decrease was significant only in the 4-chamber LV view.

Both mean coefficients of variation in ΔS_j and in τ_j were significantly higher in the patient group (variability of ΔS_j 24 ± 2% in patients *vs*. 15 ± 1% in normal volunteers, p < 0.0001; variability of τ_j 18 ± 1% vs 14 ± 1%, p = 0.025). These results indicate a pronounced increase in spatio-temporal heterogeneity of LV wall motion in patients with ischemic heart disease. Analysis of linear regression between the coefficient of variation in ΔS_j and global ejection fraction did not separate patients from normal volunteers (Fig. 3), although patients showed a decreased global ejection fraction, along with an increase in the variability of individual ΔS_j.

We identified a sub-population of patients (n = 18) whose individual regional ejection fractions in the apical area (segments #8 to #10) was particularly low (Fig. 4a). Mean apical ejection fractions in this sub-population were significantly below the means of both the whole patient group and normal volunteers (Fig. 4b, section #10: mean regional ejection fraction 27 ± 2% in the sub-population (n = 18) *vs*. 38 ± 1% in whole patient group (n = 52), and 48 ± 2% in normal volunteers (n = 22), p < 0.001). Interestingly, mean ΔS_j in several other regions of this sub-group were also significantly reduced compared to normal (Fig. 4b, marked by *). As a result, the mean 2D estimate ΔS of global ejection fraction in this sub-group was significantly below the means of both whole patient group and normal reference (38 ± 3% (n = 18) *vs*. 45 ± 2% (n = 52) and 51 ± 2% (n = 22), p < 0.007, respectively). Global ejection fraction was also significantly reduced in the sub-group (57 ± 4% *vs*. 65 ± 2% and 71 ± 2%, p < 0.027, respectively). This data suggest that abnormalities in apical motion may be of diagnostic value for LV overall mechanical dysfunctions. Sensitivity and specificity (30% and 95%, respectively) of a decrease in apical function for patients with ischemic heart disease was high enough to suggest clinical significance of apical function evaluation during patient examination.

3.3. Heterogeneity of regional LV wall motion after revascularization

We analyzed post-revascularization data obtained from echocardiography in a sub-group of patients, re-evaluated

about 3 months after the operation. Mean global ejection fraction in this sub-group was in the normal range both before (65 ± 1%) and after (68 ± 1%) the operation. The whole set of average characteristics of LV regional motion after the operation did not differ significantly from that before the operation. However, considerable changes in LV function were found in those patients (n = 7 of 25), who had decreased apical function before the intervention. In more than half (in 4 of 7) of these, apical function recovered after operation, and global ejection fraction increased (72% after revascularization *vs.* 65% before, n = 4). The increase was correlated with a decrease in the coefficient of variation in ΔS_j (though the latter was not statistically confirmed). Because the post-revascularization data were obtained in a rather small sample of patients, more subjects will be examined for solid conclusions.

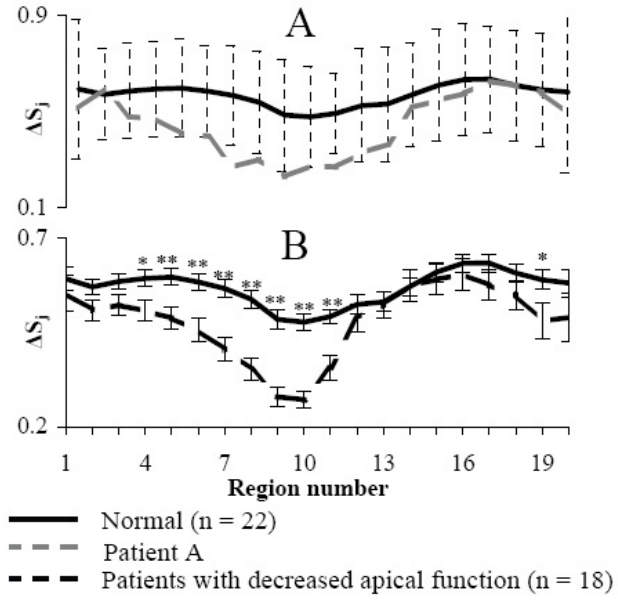

Figure 4. Test for decreased apical function in patients. A: dashed line is an illustration of individual regional LV motion below the normal range in apical regions #9 – #11 (solid line is the normal mean ΔS_j ± 2 SD). B: the mean ΔS_j ± SEM in patients with decreased apical function (dashed line) is shown against normal (solid line). Asterisks show regions with significantly decreased ejection fractions (* – $p < 0.05$, ** – $p < 0.01$).

4. Conclusions

The data on regional LV wall motion (Fig. 1), derived from 2D ultrasound LV images, show that regional LV motion is spatially and temporally heterogeneous in normal heart (Fig. 2). The magnitudes of local movement differ significantly among regions, suggesting different contribution of LV wall segments to the global ejection fraction as assessed by fractional area change. Regional LV wall contractions are significantly asynchronous, with a strong negative correlation between duration and magnitude of regional inward motion during global systole. These data suggest close interrelations between spatial and temporal heterogeneity of contractile activity in myocardial regions.

The degree of individual heterogeneity of regional LV wall motion varies among normal subjects, but shows a strong negative correlation with global ejection fraction. A significant increase in regional heterogeneity is observed in patients with ischemic heart disease. This corresponds to a decrease in ejection fraction, and suggests that myocardial heterogeneity may be a key factor contributing to the reduction in LV function in the diseased heart.

In 30% of studied patients with ischemic heart disease, function of the apical regions was significantly below the normal range, and this correlated with a decreased global ejection fraction. Apical function recovered after revascularization in more than half of re-evaluated patients. This suggests that apical function deserves further evaluation as an indicator of LV functional status.

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