Quantification of transmural differences in myocardial function with MRI tagging.

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Abstract-**Many cardiac diseases cause transmural differences in myofiber function. With the Magnetic Resonance Imaging Tagging technique a grid of magnetic tags was attached to the heart. Using a model of cardiac mechanics the motion of these tags was analyzed to deduct the transmural gradient of myofiber shortening. In normal, young healthy subjects (n=9), the transmural difference in myofiber shortening varies little, about ±4% (sd) of mean shortening. In patients with aortic stenosis subendocardial function is at risk. In a group of such patients (n=5) fiber shortening in the subendocardial layers was found to be decreased by 23±20% relative to the subepicardial layers. This finding indicates that a model of cardiac mechanics can be used as a tool to convert MRI-tagging motion data to clinically useful information on a transmural gradient in contractile function. Presently, no other methods are available to detect such transmural gradient non-invasively.**

INTRODUCTION

In patients with heart failure assessment of contractile function of the heart is common. Currently, two-dimensional echocardiography (2DE) is the most important tool for non-invasive diagnostics of contractile function. With this imaging technique, the measurement of ejection fraction provides an indication of whole heart function. Regional non-uniformities in function can also be detected. Wall thinning during the ejection phase is used as a marker of regional dysfunction.

Many cardiac diseases involving coronary flow insufficiency cause transmural gradients in contractile function. Currently, no techniques are available to detect such transmural gradients. For instance, 2DE is an excellent tool for detection of the motion of contours, but tissue motion in more than one dimension can hardly be quantified. Because transmural gradients in function generally do not generate abnormalities in cardiac shape, 2DE cannot detect them.

Recently, Magnetic Resonance Imaging (MRI) tagging is a technique entering the field of clinical application [5, 7]. With MRI-tagging, at the beginning of a cardiac cycle, a grid of magnetic tags is applied non-invasively to the heart. These tags are visualized during part of the cardiac cycle. The tags move with the tissue so that tissue deformation can be assessed. One of the main problems in MRI-tagging is that the analysis of the sequence of images is complicated and time consuming.

In the present study we show that by the use of MRI-tagging a transmural difference in contractile function can be detected by proper image analysis. The presence of a transmural gradient in contractile myofiber function affects ejection somewhat, but has a profound effect on the amount of torsion occurring in the heart during the ejection phase. Torsion is defined as rotation of the apex with respect to the base around the long axis of the left ventricle. We propose to measure rotation of two short axis sections around the equator, separated by a known distance. The amount of contraction can be determined from the decrease of cavity area. Torsion is reflected by a difference in rotation of both short axis sections.

In the normal heart we do not expect large transmural differences in myofiber strain [1, 2]. To evaluate the feasibility of the method, we will apply our analysis to aortic stenosis patients. We selected this group of patients because it is known that severe aortic stenosis eventually leads to subendocardial ischemia and/or infarction. Milder forms of aortic stenosis are likely to cause underperfusion of the subendocardial layers. The high level of systolic left ventricular pressure, which squeezes the coronary blood from the subendocardial coronary vasculature, causes this underperfusion. Furthermore an aggrieving factor is the high metabolic need due to the high pressure load. Thus we expect some degree of subendocardial dysfunction in this group of patients.

METHOD OF ANALYSIS

An equatorial section of the wall of the left ventricle has been modeled as a cylinder containing myofibers. During the ejection phase the myofibers shorten. Normally myofiber shortening is about the same everywhere in the wall [3, 8]. This characteristic may be explained as follows. In the wall of the left ventricle, myofibers at midwall are oriented circumferentially. Near the epicardium, the myofibers follow a left handed helix parallel to the wall. Near the endocardium, the helix is similar, but right handed. When cavity volume decreases, the inner circumference shortens more than the outer circumference. As a result, the subendocardial myofibers will contract more than the subepicardial ones. Now assume pure torsion occurs. With this motion at constant cavity volume the basal plane rotates counterclockwise with respect to the apical plane, when observing the left ventricle from atop of the base. Then the subepicardial myofibers shorten while the subendocardial ones lengthen. Given a certain amount of volume decrease, an amount of torsion can be selected so that the transmural difference in myofiber shortening is zero. In the normal healthy heart this condition is satisfied accurately [1], as

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Abstract

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shown by a fixed ratio of torsion and the relative decrease in cross-sectional area of the cavity.

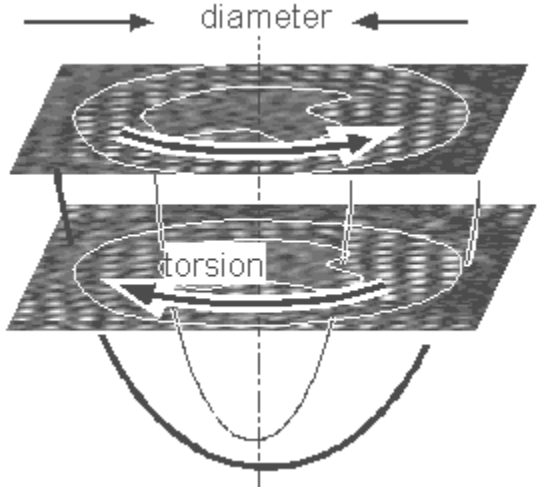

Fig. 1: The basal (top) and apical (bottom) short axis cross-sections of the left ventricle are visualized with MRI-tagging. Torsion and the relative area decrease (shortening of diameter) are indicated. The ratio of torsion to shortening is an important indicator of the transmural course of fiber shortening.

In the present analysis we have quantified torsion as the axial gradient of rotation during the ejection phase, multiplied by the epicardial radius (Fig. 1), averaged over the state at the beginning and end of ejection. Shortening is quantified as the change in the logarithm of the cavity cross-section during the ejection phase. Numerical estimates of Torsion and Shortening are derived from the rotation angles α_b and α_a of the basal and apical slices, respectively, and the areas of cavity and wall (A_{cav} and A_{wall}) in the basal and apical cross-section (indices b and a). The torsion to shortening ratio TSR is calculated from the measured data by:

$$\mathrm{TSR} = \mathrm{Torsion}/\mathrm{Shortening} = \mathrm{T}/\mathrm{S} \quad \text{with}$$

$$\mathrm{T} = \frac{(\alpha_b - \alpha_a)\,R_o}{d}\ ;\ \mathrm{S} = \Delta \ln\left(\frac{A_{cav,a} + A_{cav,b}}{A_{wall,a} + A_{wall,b}}\right) \qquad (1)$$

$$R_o = \sqrt{\left(A_{cav,a} + A_{wall,a} + A_{cav,b} + A_{wall,b}\right)/(2\pi)}$$

The variable d indicates the base to apex distance between the slices. In the group of controls, the transmural course of myofiber shortening is close to zero [1, 2]. Using the cylindrical model of cardiac mechanics with known myofiber direction in the wall, the transmural difference $\Delta e_{f,(epi\text{-}endo)}$ of myofiber shortening, relative to mean myofiber shortening $e_{f,mean}$ was calculated as a function of TSR. For the normalized transmural myofiber shortening difference ΔEF it was found by a linear approximation:

$$\Delta EF = \frac{\Delta e_{f,(epi-endo)}}{e_{f,mean}} \approx 0.35\left(\frac{TSR}{TSR_{control}} - 1\right) \qquad (2)$$

We assume that for TSR= mean($TSR_{control}$) it holds ΔEF=0. For TSR=0, according to the model of cardiac mechanics we calculated the subendocardial myofibers to shorten about 35% more than the subepicardial ones. Generally, with subendocardial dysfunction, $TSR > TSR_{control}$.

METHODS

Magnetic Resonance experiments were performed on a group of healthy volunteers (n=9) and a group of patients with aortic stenosis (n=5), using a 0.5 T MR imaging system (Philips Gyroscan T5 II, Philips Medical Systems, Best, The Netherlands). Images were obtained in two 8 mm thick short axis slices of the left ventricle. The slices were located symmetrically around the equator at a mutual distance of 20 mm. The ECG was used to trigger image acquisition over about 200 cardiac beats for each run. Contours of inner and outer left ventricular geometry were obtained from a non-tagged image about halfway the ejection phase. For the same slice 20 ms after peak ECG, a 5 mm square grid of tags was applied by spatial modulation of magnetization (SPAMM, [4]). Images were obtained each 20 ms thereafter with a resolution of 256x256 pixels and with a pixel size of 0.82x0.82 mm.

In an off-line analysis, motion of the tags in the images was determined by applying a cross-correlation technique between subsequent images. This technique has been applied previously in ultrasound doppler imaging [6]. The cross-sectional areas are determined from manual contouring in an image analysis program. In the analysis papillary muscles were considered part of the cavity. The TSR is determined using Eq. 1. Next the transmural difference has been quantified by ΔEF (Eq.2).

RESULTS

During the ejection phase, motion of the apical and basal short axis cross-section was measured. For the group of normals, the average of basal and apical wall area decreased from 31.0±6.0 cm^2 (mean±sd) to 28.7±6.0 cm^2. Cavity area decreased from 24.8±3.3 to 15.5±1.4 cm^2. The change in the logarithm of the ratio of cavity area to wall area was 0.44±0.08. Torsion was 0.11±0.03 according to Eq. 1. TSR was 0.23±0.03. Using Eq. 2 the difference between myofiber shortening near the epicardium and near the endocardium varied by ±4% (sd) of average myofiber shortening.

For the group of patients, the average of basal and apical wall area decreased from 41.5±5.0 cm^2 (mean±sd) to 40.6±5.1 cm^2. Cavity area decreased from 21.0±4.6 to 13.2±3.4 cm^2. The change in the logarithm of the ratio of cavity area to wall area was 0.43±0.08. Torsion was 0.16±0.04. TSR was 0.38±0.14. Using Eq. 2 in these patients myofiber shortening near the endocardium was 23±20% less than near the epicardium.

DISCUSSION

In normals the transmural difference of myofiber shortening (ΔEF) was found to vary very little, indicating that the group of normals is homogeneous with respect to this parameter. In the group of patients with aortic stenosis shortening of the myofibers near the endocardium was always less than near the epicardium, but spread was so large that there is an overlap with the normal group. This overlap may be explained by the inherent non-uniformity of patient groups. Patients with a mild aortic stenosis develop a mild increase of left ventricular pressure. This pressure will tend to narrow the subendocardial coronary vessels. Apparently, in mild cases, coronary dilatory reserve is sufficient to prevent underperfusion and dysfunction of the subendocardial layers. The more severe stenosis will result in coronary underperfusion, and will develop clear signs of subendocardial contractile dysfunction.

The method to determine transmural differences in myofiber shortening appears to be sensitive. The average of the patient group is about 6 standard deviations different from normal. Thus on the basis of single individual measurements abnormalities can be detected with a high degree of certainty. This property makes the method promising as a diagnostic tool in the clinic.

Numerical models of cardiac mechanics have helped us to relate mean myofiber shortening to a change in cavity volume. Torsion appears to be a main determinant of the distribution of myofiber shortening over the wall. Combining the measurement of torsion and cavity area as a function of time enabled us to estimate the transmural difference in myofiber shortening. Earlier circumferential shortening was proposed as the basis for determining transmural differences in myocardial function. According to our models, this parameter is very sensitive to regional dysfunction, i.e. infarction, but not sensitive to transmural differences in dysfunction. Without the insights obtained with models, we would not be aware of the possibilities to analyze the complicated motion data successfully.

Metabolic needs of cardiac muscle are determined more by development of stress than of strain. This property may suggest that for quantification of function the measurement of stress is more appropriate. According to our model studies this is not the case. Within the heart, the distribution of stress is mainly determined by the distribution of myofiber orientations. Because the myofibers follow pathways, along such pathway, stress tends to be homogeneous. If somewhere along this pathway the cardiac tissue is dysfunctioning, the stress load is not very different. Given this load, the myofiber has to shorten to what it can do. The malfunctioning parts will thus shorten less. As a result, non-uniformities in myofiber function within the heart can be determined better by analysis of non-uniformities in myofiber strain than in myofiber stress.

CONCLUSIONS

With the MRI-tagging technique, regional motion within the heart was measured. Using a model of left ventricular mechanics, from these motion data the transmural gradient in myofiber shortening during the ejection phase was quantified. In normal, young healthy subjects (n=9), the transmural difference in myofiber shortening varies by about ±4% (sd) of mean shortening. In patients with aortic stenosis subendocardial function is at risk. In a group of such patients (n=5) myofiber shortening in the subendocardial layers was found to be decreased by 23±20% relative to the subepicardial layers. This finding indicates the importance of a model of cardiac mechanics as a tool to convert MRI-tagging motion data to clinically useful information on a transmural gradient in contractile function. Presently, in the clinic no other methods are available to detect such transmural gradient.

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