Tissue Structure and Ventricular Wall Mechanics

James W. Covell, MD

Considering that the left ventricle is a thick-walled body that maintains its volume while reducing intracavitary volume by two thirds, it should come as no surprise that the ventricular wall thickens during systole and that there is a transmural gradient in wall thickening. Wall thickening on the inner wall may exceed values of 40% measured by a variety of techniques. These values far exceed the 8% diameter increase estimated by simple conservation of volume in an individual myocyte shortening by 15%. Physiologists have long understood that changes in the macrostructure of the wall (cellular rearrangement) must account for the difference between wall thickening and estimates of cell thickening. Reorientation of laminae or sheets of muscle cells has been proposed to account for this change in macrostructure. The dichotomy between wall thickening and estimated change in myocyte diameter has been elegantly framed by Cheng et al in this issue of Circulation, which shows nearly identical transmural fiber shortening at 2 ventricular sites, with very different wall thickening in the ovine ventricle. Similar data have been shown for other species. However, the data presented by Cheng et al provide strong evidence that the cellular rearrangements are different at the 2 sites. Cheng et al used a method developed by Costa et al in which regional histological measurements of muscle fiber and sheet orientations were used to resolve 3-dimensional transmural strain distributions obtained from implanted arrays of radiopaque markers into components. These components were defined by local axes that are parallel to the fibers, transverse to the fibers in the sheet plane, and transverse to the sheets. Wall thickening then can be resolved into components of sheet motion. Costa et al and Takayama et al reported that the interlaminar shear-strain term (Esn) and the sheet extension term (Ess) were chiefly responsible for the additional wall thickening not explained by myofiber shortening, and that this result was similar at 2 sites within the dog left ventricle. Cheng et al have shown that Esn is similar at 2 sites but provide evidence for very different roles for Ess and the sheet-thickening term (Enn) at the 2 sites in the ovine heart. Cheng et al found that on the subendocardium, where most wall thickening is generated, the most significant differences between the 2 regions was in sheet thickening (Enn) and shearing within the sheet planes rather than across them (Efs), and a loss of sheet extension (Ess). However, in the dog heart, Ess is a major component of wall thickening at both sites measured. These data, taken with the differences in the role of sheet thickening and sheet extension and compared with studies in the dog, further support the concept proposed by Cheng et al that there are large regional and species-specific differences in the mechanism by which fiber shortening is amplified to produce wall thickening. As pointed out by Cheng et al, these differences may be important in the response of the ventricular wall to disease. For example, fibrosis that primarily affects connections between myocytes might be expected to preferentially affect deformation within myocardial laminae (Efs, Ess, Enn).

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The structure of the ventricular wall is complex. Myofibers course in the epicardial tangent plane with only a small imbrication angle. Fiber direction changes approximately 100° transmurally, and fiber direction over the whole left ventricle forms a helical wrap. The work of LeGrice et al shows that fibers are arranged in branching sheets 4 to 6 cells thick, and Spotnitz et al demonstrated that acute changes in this laminar structure occur as diastolic volume is expanded. However, directly relating local deformation to the underlying structure is difficult and requires assumptions at several levels. Transmural deformation in these studies has been measured by biplane radiography of markers placed transmurally or tagged magnetic resonance images. The former method determines deformation at several transmural levels in an approximately 25 mm² area that is assumed to homogeneous in the epicardial tangent plane. Histological measurements usually examine <1 mm² of tissue. Thus the spatial scale associated with the deformation calculation is an order of magnitude greater than the area of tissue usually sampled histologically, and both the structure and deformation are assumed to be uniform over the area of tissue in which deformation is measured. As pointed out by Cheng et al, the histological approach to determining the configuration of myocardial laminae is also important. Gerneke et al have used plastic imbedding of tissue blocks with detailed confocal imaging that allows 3-dimensional reconstruction of the laminar architecture as well as the associated collagen matrix. Although it has clear advantages, this approach is currently too labor intensive for studies on the relationship between deformation and structure, and as discussed below, there are no current methods for relating structure to function at this level of resolution. Costa et al used an approach termed indirect by Harrington et al that reconstructed sheet-angle measurements from 3 sections. This approach has the advantage that it can be used on small hearts and it gives similar results to the direct approach for obtaining predominant angle. However, it has several disadvantages. First,
sheets are often hard to detect if the section is parallel to the sheet direction, and perhaps more importantly, one must assume a single predominant sheet angle in each section to reconstruct the sheet angle from the 3 sections. This eliminates the possibility of examining sheet-angle variance. Several years ago, John Criscione devised an approach in which sections perpendicular to the fiber direction were taken from 1-mm-thick transmural blocks. Harrington et al., Cheng et al., and Ashikaga et al. used frozen sections that dry somewhat on the slide, exposing cleavage planes. Zimmelman et al. used plastic embedding that produces less distortion. The Figure (left) shows 2 regions of interest of an area approximately 0.5 to 1 mm² that were obtained from frozen sections of 1-mm-thick blocks of dog myocardium using the Criscione method. Angle measurements were made using the automated method of Karlon et al. The Figure (right) shows the distributions of sheet angle determined from 2 to 4 regions of interest in several sections in each 1-mm-thick tissue block. Published sections obtained with this technique, such as the ones in the Figure, appear to demonstrate substantial variance. Variance is greater near the endocardium, and in this example, there are 2 separate endocardial distributions. To date, investigators have not included the effects that this variance in structure may have on transmural function. Computational models can be used to integrate the contributions of different sheets to the overall tissue stress and deformation. These basic models suggest that the mean sheet angle may be a good approximation to the distribution in areas of 1 sheet population; however, the models predict that the mean or predominant angle is a poor approximation when 2 sheet populations exist.

There is accumulating evidence that muscle-fiber direction does not change with cardiac hypertrophy or infarction; thus, it is tempting to speculate that pathological changes in macrostructure of the ventricular wall may influence sheet motion and, therefore, wall thickening.
Fibrosis, myocyte loss, and dilation characterize the end-stage failing heart, and it is likely that changes in the laminar structure or other elements of the wall occur. Although small temporal changes in sheet angle were observed in the dilated volume-overload heart by Ashikaga et al, Zimmermann et al and Helm et al showed 10° to 15° changes in the border zone surrounding an infarct and in the dysynchronous failing heart, respectively. Even small changes in the initial sheet angle may have large effects on wall thickening. Significant changes in sheet motion that affect wall thickening can occur without changes in initial angle. Moreover, it seems likely that such factors as sheet-angle dispersion, the length and thickness of sheets, as well as factors such as nature and location of collagen that may affect motion between sheets are likely to change with disease.

In summary, the study by Cheng et al clearly illustrates the importance of the regional structure of the ventricular wall in amplifying fiber shortening to produce wall thickening. Although this approach has the potential to provide insight into the role of pathological changes in tissue structure on regional function of the ventricular wall, advances in techniques to determine the 3-dimensional structure of the wall as well as new approaches to determine their deformation likely will be necessary before these interesting insights can be applied to the understanding of diseases that affect the ventricular wall.

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Disclosures

None.

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