

BRIEF REVIEWS

Ventricular Wall Stress

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SUMMARY Quantification of ventricular wall stress is necessary for an understanding of both normal and pathological ventricular mechanics. At present there are no reliable means to measure, directly, wall stresses in the intact ventricle. Thus, we must rely on mathematical models to predict these stresses, knowing that the predictions cannot be validated directly. Since each model employs certain simplifying assumptions, one must be aware of the limitations of stress predictions derived from that model. All of the models currently used to calculate wall stresses were reviewed and the following major conclusions were reached: (1) For most applications, detailed knowledge of the stress distribution across the wall is not essential and cannot be verified by current means. The midwall or stress averaged across the wall is adequate. Hence, the Falsetti et al. (1970) thin-walled or the Mirksy (1969, 1979) thick-walled ellipsoidal formulas derived from a generalized Laplace's law are probably the best compromise in terms of ease of computation, and incorporation of realistic albeit greatly oversimplified geometry. Use of thin- or thick-walled spherical formulas underestimate circumferential stresses by about 20-40% and overestimate longitudinal stresses by about 10-20%, respectively. (2) The wide qualitative and quantitative differences predicted by the various analytical thick-walled formulas make it difficult to judge which gives the most realistic representation of the actual stress distribution across the wall and are, thus, of little practical utility. (3) The finite-element method offers an extremely powerful method for analyzing regional variations in stress. This method can account for variations in material properties, complex geometry, anisotropy, and variations in fiber angle from region to region. However, until faster and better methods of accurate three-dimensional reconstruction of the heart are available and until more data on the multiaxial constitutive properties of myocardium are obtained, this method cannot be utilized to its full capabilities. In addition, the effort and expense involved in using the finite-element method are considerable and will limit its widespread application. (4) Until accurate and reliable methods to measure wall stresses are developed and the predictions of the models are validated, our quantitative knowledge of ventricular wall stress will be incomplete. *Circ Res* 49: 829-842, 1981

CARDIOLOGISTS, physiologists, and engineers have long been intensely interested in quantification of the forces or stresses acting in the wall of the heart. The extent of this interest is evident in the voluminous literature containing references to ventricular wall stress since Woods' publication late in the last century (Woods, 1892). There are many reasons for this interest in wall stress: (1) Myocardial wall stress is one of the primary determinants of myocardial oxygen consumption (Sarnoff et al., 1958). (2) In diseases characterized by abnormal

loading of the heart, normalization of wall stress is thought to be the feedback signal that governs the rate and extent of ventricular hypertrophy (Alpert, 1971). Cardiac decompensation is thought to result when this feedback loop dysfunctions. (3) Insight into the fundamental principles underlying ventricular mechanics requires knowledge of the relationship between the stresses and deformations acting on the muscle comprising the wall. Our understanding of ventricular muscle mechanics is, to a large extent, based on studies of the stress or force-length-time relationships of isolated cardiac muscle. Assuming that extrapolation of these concepts to the intact heart is valid, these ventricular stress or force-velocity-length relationships form one of the cornerstones in our understanding of overall ventricular mechanics (Levine and Britman, 1964; Sonnenblick et al., 1969).

Because of the complex structure of the ventric-

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ular wall, its highly nonlinear material properties, the large deformations involved, the complex geometry of the ventricle, and the inherent difficulty in accurately measuring most of these parameters, a completely satisfactory approach to quantification of wall stress still eludes us. The approaches that have been used to determine wall stress can be grouped into three major categories. In the first category, a simplified geometric shape, which can be described in terms of a few parameters, such as a sphere, spheroid, or ellipsoid, is used to approximate the shape of the ventricle. Assuming that the cavity pressure represents the loading acting on the wall and assuming certain factors about the material properties of the wall, one can then derive an expression for wall stress in terms of the geometric parameters and intracavitary pressure (Sandler and Dodge, 1963; Wong and Rautaharju, 1968; Ghista and Sandler, 1969; Falsetti et al., 1970; Walker et al., 1971; Mirsky, 1969, 1970, 1973, 1979; Moriarity, 1980). Obviously, the information that can be obtained from such an approach is limited because of the simplifying assumptions used. Nevertheless, because of the relative ease of performing the calculations, these approaches are useful in providing some important insight into ventricular mechanics.

Second, direct measurement of wall force in the intact heart using various types of strain gauge transducers coupled directed to the myocardium has been attempted over the years (Hefner et al., 1962; Feigl et al., 1967; Burns et al., 1971; Lewartowski et al., 1972; McHale and Greenfield, 1973; Robie and Newman, 1974; Huisman et al., 1980a). Recently, some of the limitations and problems associated with these direct measurement techniques have been clearly reviewed (Huisman et al., 1980a). They demonstrated that much of the uncertainty in the measured values of wall stress related to the degree of coupling between the transducer and the muscle wall. This study concluded that current techniques do not allow reliable direct quantification of wall stresses.

With the advent of high-speed digital computers, numerical approximation schemes such as the finite-element method of structural analysis (Zienkiewicz, 1977) evolved in the late 1950's as the need for structural analysis of complex structures in the aerospace industry arose. Models using this method comprise the third category for assessing ventricular wall stresses. This method is a numerical approximation scheme in which a continuous structure is conceived as being comprised of a finite number of subunits or elements such that regional variations in geometry, loading, and material properties can be taken into account. Each element interacts with neighboring elements only at certain points called nodes, so that forces and displacements are transmitted only at the nodes. Basically, a set of algebraic equations describing the relationship between the forces and displacements within

each element is derived by applying principles of mechanics. Solving this set of equations subject to the loading and boundary conditions acting on the structure allows calculation of the stresses and strains throughout the structure. This method of structural analysis has, to a large degree, enabled the aerospace and many other industries to perform structural analysis on complex structures which would otherwise have been impossible (Zienkiewicz, 1977).

This powerful method is probably the best approach for obtaining a realistic quantitative assessment of regional variations in ventricular wall stress. Before such a detailed analysis can be accomplished, however, we need to be able to define accurately the regional geometry, structure, and material properties of the intact heart. To date, there are no studies that have systematically examined regional variations in the material properties of the myocardium even in the passive state, let alone during contraction. Attempts are being made to improve our ability to measure accurately the three-dimensional geometry of the ventricle (Sandler and Alderman, 1974; Rankin et al., 1976; Vinson, 1977; Ritman et al., 1980), but realization of this difficult goal in an easily implemented manner is still not possible. Hence, we are faced with the dilemma of possessing the necessary tools for accurately predicting regional stress variations but are unable to utilize these tools fully because of lack of sufficient data. Furthermore, once these data become available, it remains to validate the predicted wall stress with direct measurements.

The present review will focus primarily on categories 1 and 3. The specific assumptions, limitations, and usefulness of each of the models in category 1, beginning with the simplest and proceeding to the more complex, will be briefly discussed. The models in category 3 will be examined in roughly chronological order. Since an extensive discussion of the finite-element models has not been presented, this portion will examine in some detail the new insights available from, as well as the drawbacks associated with, using this theoretically promising but as yet unvalidated method. This review will summarize the available methods for calculating ventricular wall stress and provide the reader with enough information to allow evaluation of the trade-off between accuracy and detail of information desired vs. computational effort needed. Predictions of wall stress in association with various clinical states will not be emphasized.

Definitions

Before proceeding, some of the nomenclature that will be used will be defined.

Axisymmetric means symmetric about an axis. Geometric axisymmetry is obtained when the structure has been generated by revolving a curve about an axis of revolution. Material axisymmetry per-

tains to the condition in which there is no variation of properties about the axis.

Bending moment is a force resultant that produces a rotation rather than an extension of a portion of the structure.

Circumferential refers to the direction around the axis of revolution (see Fig. 1).

Constitutive relation is the quantitative relationship between the stresses and strains in a material. If the relationship between stress and strain is linear, the slope of the stress-strain is called the Young's modulus of the material. Another commonly used term for the slope of the stress-strain relation is stiffness, and the term compliance is used for the inverse of the slope. Most biological tissues, however, exhibit a nonlinear relation between stress and strain that is concave toward the stress axis so that the stiffness is not a single-valued parameter but varies according to the position on the stress-strain curve. In many biological tissues, this relationship is exponential (Fung, 1968).

Isotropy refers to the condition in which the constitutive relation is the same in all directions. Conversely, a material whose constitutive relations depend upon direction is called anisotropic. A material in which the constitutive relations are the same in one plane and differ in the direction perpendicular to the plane is transversely isotropic. A material in which the properties are the same in three mutually perpendicular directions is called orthotropic.

Large deformation theory refers to the case when strains are not small. Large strains can be described only by retaining the higher order terms of the displacement field resulting in nonlinear strain-displacement relationships.

Meridional refers to the direction along the axis of a solid of revolution, i.e., in the longitudinal direction. Meridional stresses are also called longitudinal stresses.

Radial refers to the direction across the wall thickness along the radius of curvature. This direction is mutually perpendicular to the meridional

and circumferential directions and is often referred to as the transverse direction.

Small deformation theory in the engineering sense pertains to deformations that are very small with respect to the undeformed size of the body. Typically, strains of less than 1.0% are considered small. The importance of small deformation theory lies in the fact that the strains in this condition are linear functions of the displacements.

Stress is defined as the force acting on a surface divided by the cross-sectional area over which the force acts. Usually the stress has many components, some of which act perpendicular to a surface (normal stresses) and others parallel to the surface (shear stresses). An example of the stress components in a spherical coordinate system is shown in Figure 1. The units of stress are thus dyne/cm², lbs/in², etc.

Strain is a nondimensional quantity that is a measure of the deformation of a structure under a particular load. Like stress, strain has many components, some of which act along the direction of the applied force representing elongation or shortening and others which represent angle changes. Strains are normalized by dividing by a reference length or angle. There are many ways to quantify strain, but the details of these are not critical to our present discussion.

Tension is defined as a force per unit of length perpendicular to the direction of force and is analogous to the stress in a structure which has no thickness.

Transverse refers to the direction across the thickness of a structure. Stresses and strains in this direction are often termed transverse or radial stresses and strains.

Thin-Walled Ventricular Models

The basic assumption of thin-walled models is that the wall is thin relative to the diameter. Typically the thickness-to-radius ratio should be less than 1:10 in order for this approximation to be valid. Assuming a thin wall implicitly assumes that

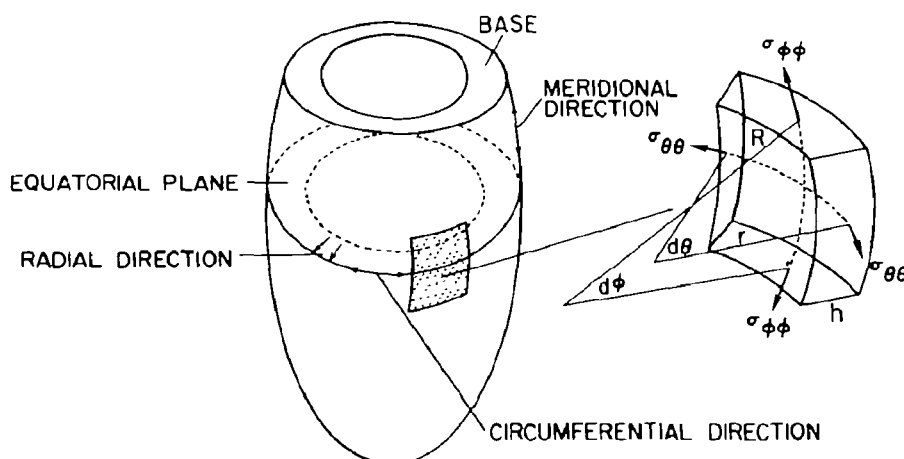


FIGURE 1 Illustration of the principal directions and corresponding normal stress components in a spherical coordinate system. R is the meridional radius of curvature and r is the circumferential radius of curvature.

there are stress components acting only in the plane of the surface and that these act in the meridional or circumferential direction. That is, there are no radial or transverse shear components so that there are also no bending stresses. Another result of this assumption is that there is no variation of the in-plane stresses through the wall—that is, the stress is uniform across the wall thickness.

LaPlace (1806) derived the relationship relating the pressure inside a membrane to the radii of curvature and wall tension (in this case the normalized force is expressed as tension rather than stress since there is no cross-sectional area):

$$P = \frac{T_1}{R_1} + \frac{T_2}{R_2} \quad (1)$$

where R_1 and R_2 are the two principal radii of curvature and T_1 and T_2 are the principal wall tensions.

Woods (1892) assumed that the heart could be modeled by a sphere and calculated the wall tension as a function of the radius and internal pressure. For a sphere $T_1 = T_2$ and $R_1 = R_2$ thus

$$P = \frac{2T}{R} \quad (2)$$

Assuming a sphere adds the additional implicit assumptions that the ventricular wall is isotropic and homogeneous. Obviously, the left ventricle does not fulfill any of the assumptions used in deriving Equation 2. Even so, this simplest of all models provides some insight into ventricular mechanics. Based on Equation 2, Woods postulated that one of the functions of the papillary muscles was to help eject blood by pulling along a chord of the sphere which would be more effective than depending solely on tension developed in the wall to eject blood. This would be most beneficial at the onset of systole since the heart is largest and developed pressure is lowest at that time. Because tension is directly proportional to radius, he also postulated that the trabeculae carneae reduced the tension on each fiber in the wall since the local radius of the trabeculae is small relative to the chamber radius. It is remarkable that the insight originally demonstrated by Woods still pervades our thinking in terms of the relationship between size, pressure, and wall force in assessing ventricular wall mechanics.

Sandler and Dodge (1963) assumed that the left ventricle could be approximated by a thin-walled ellipsoid and derived a modified form of Equation 1 in the form

$$\frac{P}{h} = \frac{\sigma_1}{R_1} + \frac{\sigma_2}{R_2} \quad (3)$$

where σ_2 and σ_1 are the circumferential and meridional stresses, R_2 and R_1 are the respective radii of curvature, and h is the wall thickness. Using this

equation they then derived two formulas for the meridional and circumferential wall stresses at the equator based on the following assumptions: (1) that the ventricle is isotropic and homogeneous, (2) that the stress across the wall is constant (a constant stress across the wall implies that there are no shear forces and bending moments), and (3) most important, that the wall stresses act only at the inner surface. Their formulas for the stresses at the equator are

$$\sigma_1 = \frac{PR_2^2}{h(2R_2 + h)} \quad (4)$$

$$\sigma_2 = \frac{Pb}{h} \left[1 - \frac{b^3}{a^2(2b + h)} \right] \quad (5)$$

where a is the major semi-axis and b is the minor semi-axis. Equation 5 is erroneous, since σ_1 should equal σ_2 for the limiting case of a sphere ($a = b$), and such is not the case except in the limiting case where $h \ll b$. The reason for the error relates to the fact that their third assumption is valid only if the wall is negligibly thin. That is, h is so small relative to b that it can be ignored. Otherwise, since the uniform wall forces act all across the wall and not just at the inner surface, equilibrium conditions must be enforced all across the wall. The correct derivation of the circumferential stress formulas using these assumptions was presented by Falsetti et al. (1970) and later by Walker et al. (1971) and is

$$\sigma_2 = \frac{Pb}{h} \frac{(2a^2 - b^2)}{2a^2 + bh} \quad (6)$$

where a and b are the endocardial major and minor semi-axes, respectively.

Even with the rather restrictive assumptions of the thin-walled models, they have been applied widely and do indicate several important points: (1) Wall stress increases markedly with LV dilation unless wall thickness also increases. (2) Peak wall stress may occur at a different time than peak pressure, depending on the instantaneous geometry.

Thick-Walled Ventricular Models

The Lamé (1866) derivation for wall stress in a pressurized uniform thick-walled sphere was a landmark in the field of solid mechanics because for the first time it predicted radial variation of stresses. Since the left ventricle is also a thick-walled structure, there must also be a variation of stress across its wall. The desire to gain insight into the nature of this stress variation is the primary motivation behind the many thick-walled ventricular models.

Wong and Rautaharju (1968) derived formulas for the stress distribution in a thick-walled ellipsoid using the following major assumptions: (1) the two minor semi-axes were equal; (2) the myocardium was isotropic, linearly elastic, homogeneous, and in equilibrium; (3) distortion occurred only in the ra-

dial direction, thus bending moments and transverse shear stresses were ignored; (4) the meridional radius of curvature equaled the inner radius of curvature plus the wall thickness; and (5) the only load on the ventricle was an internal pressure. They derived closed form solutions for the circumferential, meridional, and radial stress components at any point in the wall. Numerical calculations based on angiographic data revealed several interesting facets of the stress distribution: (1) at both the apex and equator, all three stress components decrease monotonically from endocardium to epicardium; (2) the hoop stresses at the equator were more than twice the meridional stress, and the pattern of stress did not change with either dilation or increased pressure load, although both conditions increased the absolute level of stress (pressure more so than dilation); (3) increasing wall thickness decreased all of the stress components needed to maintain the same cavity pressure.

Ghista and Sandler (1969) used a different approach from that of Wong and Rautaharju (1968) to derive the stress distribution in an approximately ellipsoid thick-walled model of the ventricle. Their major assumptions were: (1) there were only normal stresses and no shear stresses at the inner and outer boundaries; (2) the material was isotropic, incompressible, homogeneous, and linearly elastic; and (3) the only loading was an internal pressure. Their model could account for shear stresses in the wall, but this was obtained at the expense of a slight inexactness in geometry such that the model was not mathematically an exact ellipsoid. Their results demonstrated roughly the same pattern of stress distribution as found by Wong and Rautaharju except that the circumferential stress at the equator exceeded meridional stress by only 60%. One interesting result of their analysis was that the stress distribution turned out to be independent of the elastic properties of the wall so that the model would apply also to a viscoelastic material.

Mirsky (1969) used a still different approach to calculate the stress distribution in a prolate spheroid. He also assumed isotropy, incompressibility, homogeneity, and linear elasticity. The solution was obtained by using a displacement field that was linear in the meridional and quadratic in the radial direction and substituting this displacement field into the appropriate equilibrium equations. The resulting differential equations were solved by numerical integration for a thick-walled shell of revolution. A simplified set of formulas for the stress distributions at the equator was obtained by retaining terms only up to second order in an asymptotic expansion approach to the solution. His results differed from the two preceding analyses in that the meridional stress at the equator increased rather than decreased from endocardium to epicardium. Otherwise the results were qualitatively similar.

Using the same basic assumptions and differen-

tial equations, Mirsky (1979) presented simplified formulas for the stresses at the equator of an ellipsoid in the form

$$\sigma_{\phi} = (Pb/2h) (1 - h/2b)^2 \quad (7)$$

and

$$\sigma_{\theta} = (Pb/h) (1 - b^2/2a^2 - h/2b + h^2/8a^2) \quad (8)$$

where σ_{ϕ} and σ_{θ} are, respectively, the meridional and circumferential stresses, p is cavity pressure, h is wall thickness, and a and b are, respectively, the midwall semimajor and semiminor axes.

Mirsky (1970) investigated the influence of anisotropy and inhomogeneity on left ventricular stress. The basic analysis was similar to that used by Wong and Rautaharju (1968) and assumed the heart to be an incompressible prolate spheroid whose wall thickness remained constant throughout the cardiac cycle. Axisymmetric deformation was also assumed so that bending moments and shear forces were ignored. The material was assumed to be linearly elastic and orthotropic. Inhomogeneity was taken into account by assuming a parabolic distribution for the circumferential elastic modulus. This particular choice of inhomogeneity was chosen to mimic the effect of inhomogeneity based upon a study (Streeter et al., 1969) indicating a roughly parabolic variation of fiber angles across the wall. Numerical results indicated that inhomogeneity had a greater effect than anisotropy upon stress variations. In fact, for a parabolic variation of elastic modulus, the circumferential stress distribution was also parabolic, being maximum near the mid-wall.

Mirsky (1973) investigated the specific effect of large deformations on stresses in the left ventricle which, for this analysis, was approximated by a thick-walled sphere composed of isotropic, homogeneous, and incompressible material. The stresses at a given pressure level were calculated from a strain energy density function. Using data from dog studies, he evaluated this function at the midwall, based on strains and cavity and wall volumes at that particular cavity pressure. The nonlinear relation between stress and strain was assumed to be of exponential form. The major finding of this study was that inclusion of nonlinear stress-strain properties predicted a very high stress concentration at the endocardium which was almost 10 times higher than predicted by linear theory. This stress concentration increased markedly as the cavity pressure was increased.

Moriarty (1980) also used a thick-walled spherical model of the ventricle to investigate the effect of nonlinear constitutive relations on wall stress. He assumed that the wall was isotropic and incompressible. Two different types of materials with nonlinear constitutive relations were investigated: a Valanis-Landel type and Rivlin-Saunders type. For calculation of stress distribution across the wall, he

first assumed that the material was homogeneous across the wall. A uniaxial constitutive relation was derived for each material type in the form

$$S = C(\lambda^a - 1/\lambda^{a/2}) \quad (9)$$

and

$$S = C_1 (\lambda^2 - 1/\lambda) + C_2 (\lambda - 1/\lambda^2) (2\lambda + 1/\lambda^2 - 3)^2, \quad (10)$$

respectively, for the Valanis-Landel and Rivlin-Saunders material where S is stress, and λ is stretch ratio. His results were similar to Mirsky's in that the predicted wall stress distribution for a diastolic pressure of 24 g/cm² showed a concentration near the endocardium that was nearly six times as high as that predicted by the exact solution for a thick-walled sphere composed of a linearly elastic material. At the epicardium, the nonlinear material predicted a stress that was slightly lower than that

predicted by the linear material. The Valanis-Landel type material predicted stresses that were about 10% higher than the Rivlin-Saunders material at pressures higher than 3 g/cm². Another finding of this study was that the pressure-volume relationships predicted by each of the models differed considerably, despite being based on the same geometrical and material property data. One reason for this disparity may relate to the fact that a uniaxial constitutive relation does not uniquely define the material properties of the tissue.

Huisman et al. (1980b) recently published an informative review comparing the stresses predicted from several of the previously described models when the same angiographic data obtained in a number of disease states were used as input to each model. In each case, the material was assumed to be isotropic, homogeneous, and incompressible. Their findings are summarized in Figure 2 and are as follows: (1) The absolute magnitude of the cal-

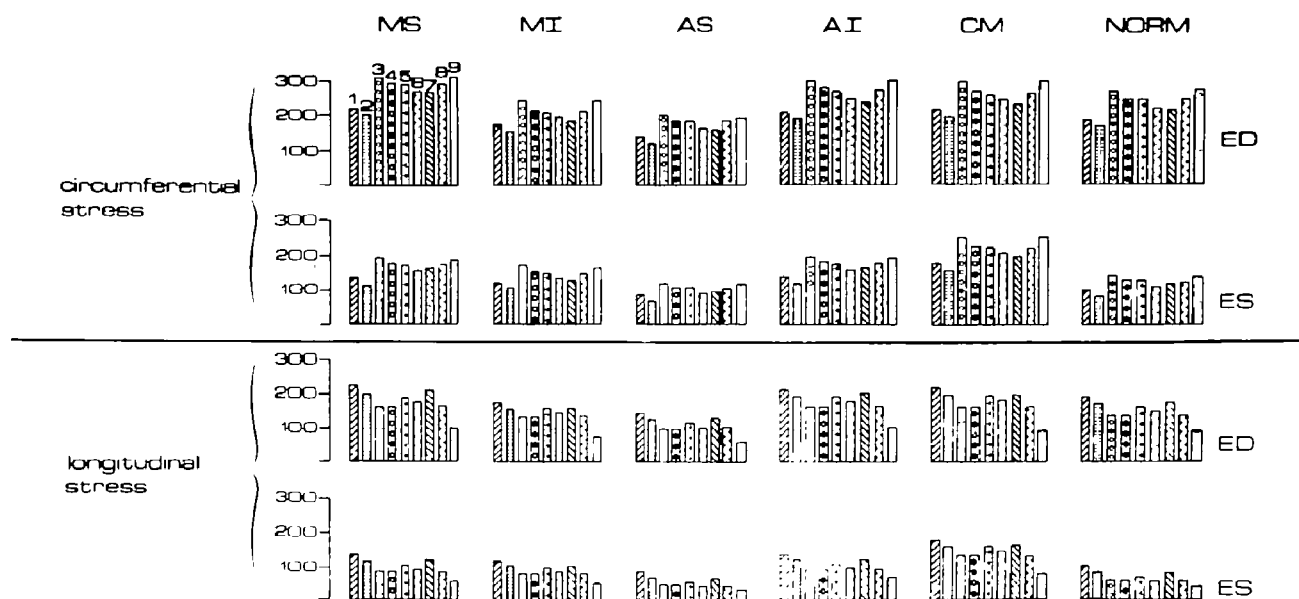


Fig. 2 Mean stress values (relative to pressure) for the studied models under several conditions

m.s. = mitral stenosis
m.i. = mitral insufficiency
a.s. = aortic stenosis
a.i. = aortic insufficiency
c.m. = cardiomyopathy
norm = normal human heart
e.d. = end-diastolic
e.s. = end-systolic

The stress values are represented by columns:

Column

- 1 thin-walled sphere
- 2 thick-walled sphere
- 3 Sandler and Dodge model
- 4 Falsetti model
- 5 Wong model
- 6 WONCO model
- 7 Ghista model
- 8 Mirsky model
- 9 Streeter model

(further see text)

FIGURE 2 Comparison of end-systolic and end-diastolic wall stresses predicted by various analytical models for several disease states. [Reproduced from Huisman et al. (1980b) Comparison of models used to calculate left ventricular wall force. *Med Biol Eng Comput* 18, by permission of Peter Peregrinus, Ltd.].

culated wall stress differed depending on the model used. The difference in mean stress predicted by a thin compared to a thick-walled sphere was about 12% at end-diastole and 20% at end-systole. (2) Although the models differed quantitatively from one another, the relative differences among models remained relatively constant regardless of the disease process.

They also calculated the stress distribution across the wall for the various models (Fig. 3). These thick-walled models yielded both quantitatively and qualitatively different results. The circumferential stress gradients predicted by all models decreased from endocardium to epicardium but by differing amounts. The longitudinal stress gradients increased by 36% for the Mirsky (1969, 1979) model but decreased by 26% for the Ghista and Sandler (1969) model and showed no overlap. At the midwall, however, the Mirsky (1969, 1979) model and the Huisman et al. (1980b) modification to the Wong and Rautaharju (1968) formula yielded the same result despite directionally opposite gradients at points away from the midwall. Without experimental verification, the discrepancy between the thick-walled models makes it difficult to know which one is most accurate. Thus, at present we cannot state with certainty what the stress distribution across the wall of the ventricle is. This being the case, it seems that using an averaged wall stress

or a midwall stress would be most appropriate for applications in which the interest is in a global estimate of stress. Thus, the simplified midwall stress formulas of Mirsky (1969), Equations 7 and 8, or the mean stress formulas of Falsetti et al., (1970), Equations 4 and 6 for midwall stress, should suffice for most clinical applications.

Finite Element Models

All of the models discussed thus far approximate the ventricular geometry by a simple axisymmetric geometric figure that is everywhere concave toward the cavity. To take complicated geometry into account, particularly when complex changes in curvature occur, as is the case with the actual ventricular geometry, an approximate and more complex method must be used. This, plus the ability to introduce inhomogeneity, anisotropy, and nonlinear material properties, is the rationale for use of the finite-element models of the left ventricle.

Gould et al. (1972) applied the finite-element method for stress analysis of the left ventricle. Geometric data were obtained from single plane ventriculograms with the ventricular shape approximated by using the long silhouette of the angiogram and revolving one half of the angiogram about the long axis. The model was comprised of 13 elements, each of which was a ring with the meridian of each element being represented by a 4th order

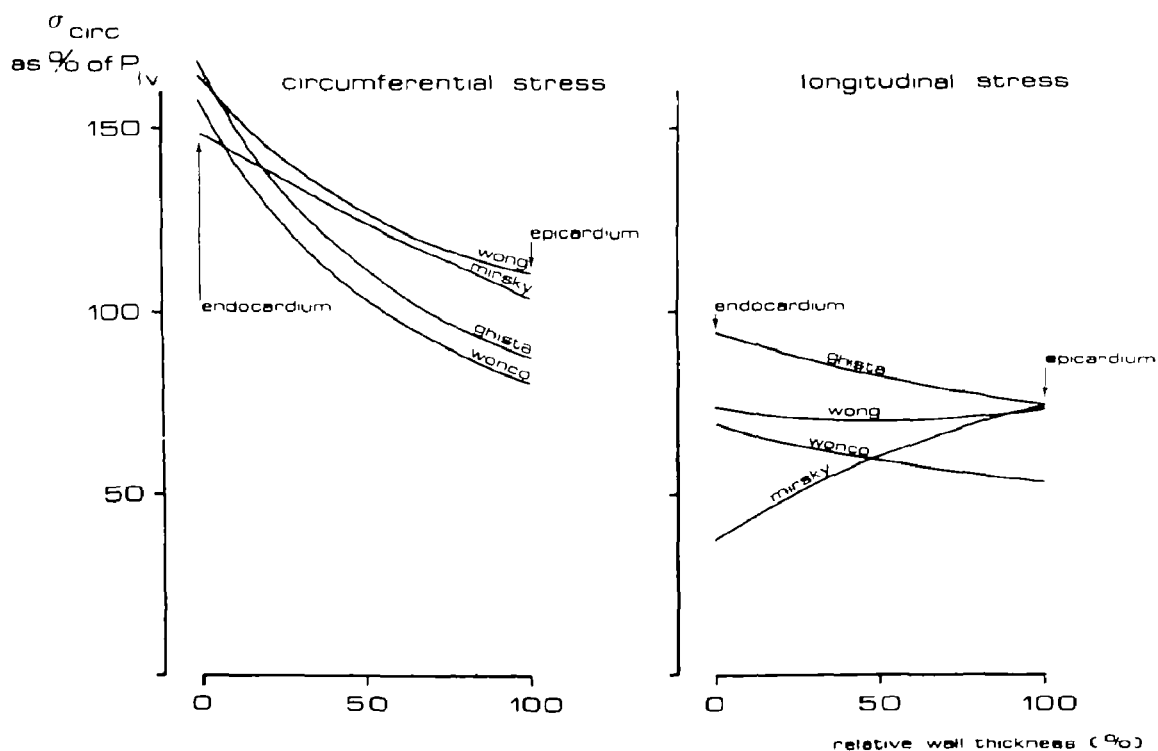


FIGURE 3 Comparison of the stress distribution across the wall for the thick-walled ellipsoid models demonstrating marked quantitative and qualitative differences between the models. The WONCO model is a modification of the model of Wong and Rautaharju (1968) with transverse shear taken into account. [Reproduced from Huisman et al. (1980b) Comparison of models used to calculate left ventricular wall force. *Med Biol Eng Comput* 18, by permission of Peter Peregrinus, Ltd.].

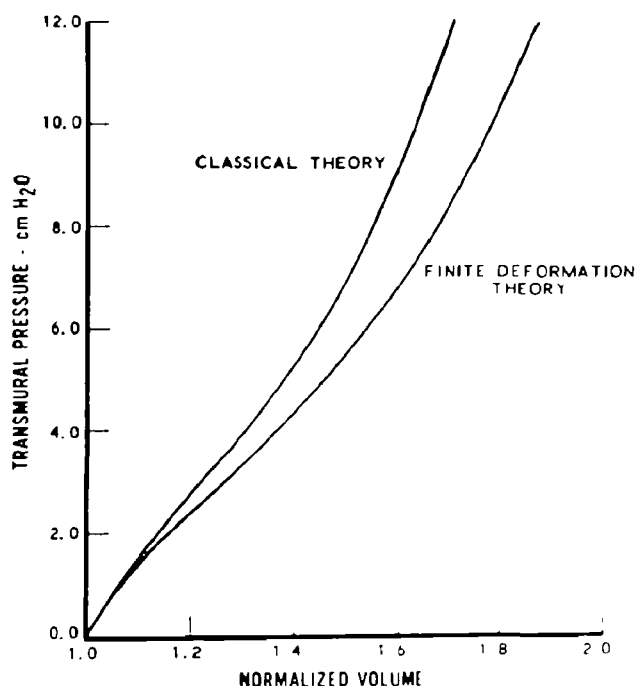


FIGURE 4 Comparison of the diastolic left ventricular pressure-volume curves obtained when large vs. small deformation theory was employed in a finite element model of the heart. [Reprinted with permission from *J Biomech* 7, RF Janz, BR Kubert, and TF Moriarity (1974) *Deformation of the diastolic left ventricle. II. Nonlinear geometric effects*, Pergamon Press, Ltd.]

polynomial so that bending and transverse shear could be taken into account. Each axisymmetric element was assumed to be of uniform thickness, no external loads were present on the elements so that the effects of lung and right ventricle were ignored, and the material was assumed to be linearly elastic. The major finding of that study was that the linear stress distribution across the wall thickness reversed when the curvature of the wall changed signs. That is, instead of an endocardial-to-epicardial stress gradient in regions where the ventricle was concave inward, the opposite obtained where the wall was concave outward. Thus, use of the finite-element method produced a result which otherwise could never have been predicted by the simple geometric models. Although we don't know the real stress distribution, the possible existence of a reverse stress gradient across the wall could have major implications for our understanding of regional myocardial mechanics. Both the meridional and circumferential stresses exhibited the same behavior. In addition, the circumferential stress at the apex predicted by this model was considerably higher than that predicted by the analytical solutions of Mirsky (1969) and Ghista and Sandler (1969). Furthermore, the maximum meridional stress was found to be at the equatorial endocar-

dium, whereas the two analytical models found the maximum stress to be at the apex.

Also beginning in 1972 Janz and his colleagues published a series of studies using the finite-element method for structural analysis of the left ventricle with progressive complexities taken into account. The initial model (Janz and Grimm, 1972) employed linear elastic theory but allowed for heterogeneity of wall structure. The material at the base was assumed to be isotropic with properties comparable to that of collagen. The remainder of the ventricle was assumed to be composed of two layers: one that was transversely isotropic with constitutive properties like muscle, and the other that was isotropic with the properties of muscle. The finite-elements were quadrilateral cross-section rings of revolution. Use of 198 elements produced a close approximation to the actual state of deformation in rat hearts arrested in diastole at pressures up to 12 cm H₂O. At 24 cm H₂O, the predicted deformation significantly exceeded that observed. They postulated that this discrepancy was due to not incorporating nonlinear stress-strain relationships into the model. Further analysis with this model revealed that inhomogeneity and anisotropy of the wall had only a small effect on predicted deformations with an isotropic model predicting deformations at the equator that were 8% less than the heterogeneous model. Despite the close agreement in deformations, the stresses predicted by the isotropic model differed by factors of 2 to 3 from those predicted by the heterogeneous model.

Janz and Grimm (1973) expanded the analysis to take into account nonlinear stress-strain properties. They proposed a triaxial constitutive relation for rat myocardium that could be reduced to closely approximate previously observed uniaxial stress-strain relationships. The model was still axisymmetric and assumed isotropic material but allowed for heterogeneity as in their previous model. An incremental loading approach was used to approximate the nonlinearity in material properties. Use of nonlinear rather than linear material properties still produced markedly different pressure-strain curves despite similar pressure-volume curves. Their study demonstrated the insensitivity of the pressure-volume curve to marked variations of wall properties. Although they did not calculate the regional wall stresses, it is clear that stresses predicted from using the model with nonlinear constitutive properties would differ considerably from those obtained using only linear properties.

Janz et al. (1974) analyzed another aspect of nonlinearity by extending their previous analyses to include large deformation theory by retaining the nonlinear terms in the strain-displacement relations. This model was axisymmetric, heterogeneous, and nonlinearly elastic. The effect of including large deformation effects compared to using small deformation theory is shown in Figures 4 and

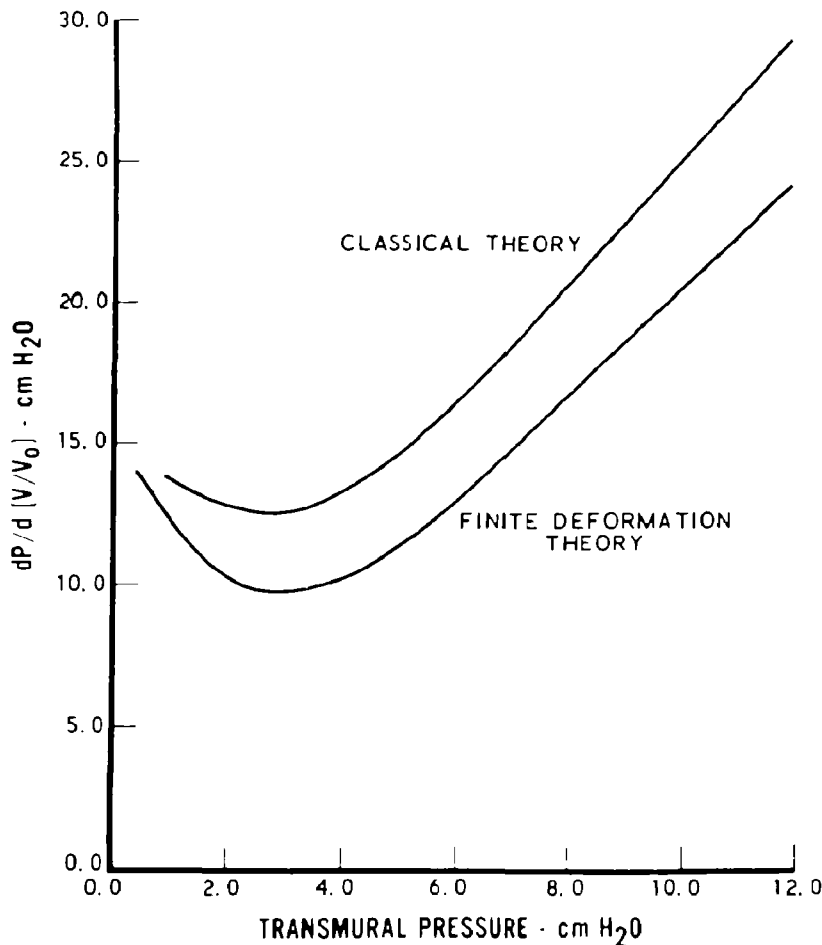


FIGURE 5 Comparison of diastolic stiffness-pressure curves of the left ventricle when large vs. small deformation theory was employed in a finite-element model of the heart. [Reprinted with permission from *J Biomech* 7, RF Janz, BR Kubert, and TF Moriarity (1974) *Deformation of the diastolic left ventricle. II. Nonlinear geometric effects*, Pergamon Press, Ltd.).

5. Incorporation of these nonlinear geometric effects produced a lower chamber stiffness than when linear theory was used. As with the previous study, there were small differences in the pressure-volume curve with as much as 100% difference in strain at the apex at a pressure of 12 cm H₂O. They attributed these results to rotational effects near the apex that were not accounted for in the linear theory.

Recently, Janz and Waldron (1978) used the finite-element method to specifically examine the effects of apical aneurysms on ventricular deformations and on the ventricular pressure-volume curve. In this model, they used axisymmetric elements and assumed that the wall was regionally homogeneous, but did allow for nonlinear stress-strain properties and large deformations. The properties of aneurysmal tissue were assumed to be those obtained from an earlier study by Parmley et al. (1973) who performed uniaxial length-tension tests on human aneurysmal tissue of muscular, mixed fibromuscular, and fibrous composition. Their major finding was that a fibrous or fibromuscular aneurysm tethered both scar and normal tissue in the region near the scar (Fig. 6). All of these findings occurred at low diastolic pressures of 12 mm Hg. At higher diastolic pressures, the tethering

effect was still present near the aneurysm, but in regions far from the aneurysm there was even more elongation than in the normal ventricle. Regional stresses produced by the presence of the aneurysm would be highly dependent on the constitutive properties of the aneurysm as well as its size, but detailed stress analysis was not performed in this study. They examined the pressure-volume (P-V) relationships due to apical aneurysms and found that, as expected, the P-V curves shifted toward the left with increasing size of the aneurysm. However, when the P-V curves were quantified by an exponential relationship of the form

$$\frac{dP}{d\left(\frac{V}{V_0}\right)} = \alpha P + \gamma,$$

the parameter, α , was found to depend on both aneurysm size and stiffness. Thus they felt that the utility of α as an index of aneurysm properties was limited.

Pao et al. (1974) employed triangular cross-section ring elements in their finite-element model of the left ventricle. The ventricular geometry was obtained from orthogonal angiograms in an isolated,

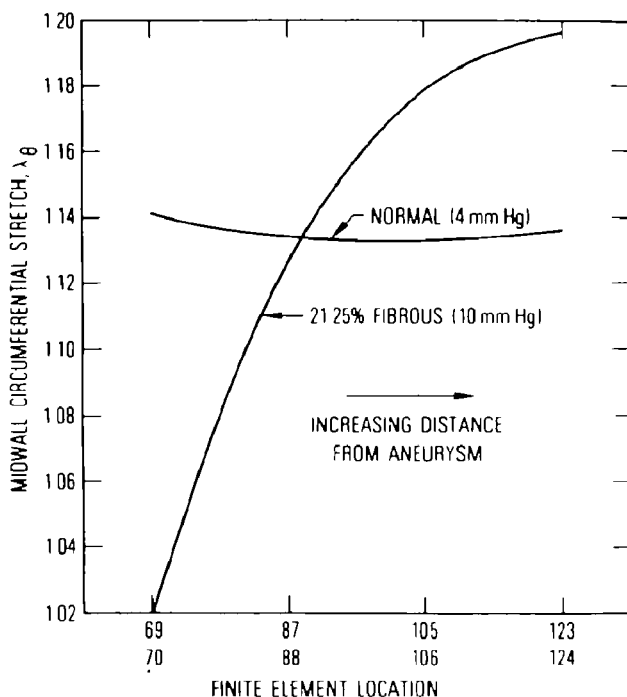


FIGURE 6 Predicted effect of a fibrous apical aneurysm comprising 21% of the left ventricular wall on regional stretch at various distances from the aneurysm compared to the stretch in a ventricle without an aneurysm. The tethering effect near the aneurysm as well as the compensatory effects at portions remote from the aneurysm are demonstrated. [Reproduced from RF Janz and RJ Waldron (1978) Predicted effect of chronic apical aneurysms on the passive stiffness of the human left ventricle. *Circ Res* 42, by permission of the American Heart Association, Inc.].

supported dog heart. Using the approach of Gould et al. (1972), they created a solid of revolution by rotating one half of the angiogram about the long axis. Thus, the ventricle was assumed to be free of any restraints imposed by the right ventricle or lungs. Small deformation theory was implicitly utilized. Results qualitatively similar to the previously discussed nonlinear, thick-walled geometric models were found with both meridional and hoop stresses varying nonlinearly across the wall. Maximum circumferential stress was found to be 5.5 times intracavitary pressure and to occur at the endocardium near the base of the heart.

Heethaar et al. (1976) used up to 7000 tetrahedral elements to study the stress distribution in both a single left ventricle and in a combined right and left ventricle model. This model was much more realistic than all previous models, since each chamber was not restricted to being axisymmetric and since the effect of the right ventricle was included. The geometric data for left ventricular studies were obtained from multiple x-ray views of an isolated working dog heart in which the heart pumped fluid containing a radiopaque compound. Geometric data

for the combined right and left ventricle model were obtained from a dead heart filled with the contrast fluid which was placed in the x-ray field. The myocardium was assumed to be isotropic, homogeneous, and linearly elastic. The diastolic left ventricle was shown to have highest stresses at the endocardial surface. The combined ventricle model also demonstrated largest stresses at the endocardium with a large stress concentration at the septal-right ventricular junction. Compressive stresses were found in the septum which was a result which had not previously been predicted.

Pao et al. (1976) used a plane-strain approximation to examine in more detail the stress distribution at a cross-section of a left ventricle not connected to a right ventricle. The plane-strain assumption implies that the left ventricle is a long irregular cylinder whose configuration at any cross-section is the same as that used in the analysis. Again multiplanar x-rays were used to obtain the geometric data from an isolated dog heart. Three hundred and eight triangular elements were employed with the material assumed to be isotropic, homogeneous, and linearly elastic. The results demonstrated that maximum stresses occurred at the endocardial surface only in the anterior and posterior regions of the cross-section. In the septum and free wall, the maximum circumferential stress occurred at the epicardial surface. Again compressive stresses were found to occur in these regions where the curvature became convex inward. Thus, like the study of Gould et al (1972), this study demonstrated that regions of small curvatures or curvature reversal may be associated with dramatic alterations in the wall stress patterns.

Panda and Natarajan (1977) modeled the human left ventricle as a thick-walled layered shell of revolution in a study designed to assess the effects of fiber orientation on wall stress. They assumed that the fiber directions in the inner, middle, and outer wall were 40° , -5° , and -50° , respectively, from the horizontal. They assumed that the material properties along the fiber direction were orthotropic and that the transverse properties were a certain fraction of those in the fiber direction. For the isotropic case, their results demonstrated circumferential stress values that were higher than those predicted by the solutions of Ghista and Sandler (1969) and Mirsky (1969). The meridional stresses were found to be higher than the previous studies, with a high stress concentration at the apex. For the layered model, they found that the maximum circumferential endocardial and epicardial stresses diminished and midwall stress increased as the ratio of the longitudinal to transverse stiffness increased. However, the meridional stress increased in both the inner and outer layers and diminished in the middle layer with increasing relative stiffness.

Vinson et al. (1979) used a left ventricular model composed of 36 brick-type elements composed of six layers each. The geometry of the ventricle was

obtained by reconstruction from biplane ventriculograms. The effects of the pericardium and right ventricle were not considered. Anisotropy was allowed by assuming the wall to be twice as stiff in both the circumferential and radial directions as in the meridional direction in one case and by assuming a transverse stiffness to be one-half of the tangential stiffness in another case. Inhomogeneity was accounted for by allowing the elements near the base and apex to have variable material properties. Results demonstrated maximum stress concentrations at the right anterior and left posterior regions of the endocardium which were of the same order as those found by Hamid and Ghista (1974). In addition, they found that the most important determinants of the diastolic deformation were the ratio of circumferential to meridional stiffness, the variation of fiber angle, the variation of shear modulus, and the relative stiffness of the base compared to the remainder of the heart.

These examples demonstrate the power of the finite-element method when applied to ventricular structural analysis. The studies provide some theoretical insight into the effects of nonlinear material properties, heterogeneity of the wall, and large deformations. Without experimental validation of these predictions, however, the results must be viewed as preliminary. Our ability to optimally utilize this powerful method of analysis is also currently limited by our inability to define very accurately the moment-to-moment three-dimensional geometry of the ventricle and our lack of data relative to the regional constitutive relations of myocardial tissue. Unfortunately, until all of these problems are resolved satisfactorily, this powerful tool, which has the potential for providing otherwise unobtainable insight into regional myocardial mechanics, remains of qualitative use and is of limited utility for clinical applications.

Myocardial Constitutive Relations

Wall stress data can be obtained either from use of a model to predict the stress or from direct measurement of the wall stresses. Since current techniques for direct stress measurement are unreliable (Huisman et al., 1980a) one must resort to predicting wall stress from one of the models discussed in the previous sections. A requisite for stress prediction is a knowledge of the constitutive relations of myocardial tissue. In actuality, very little is known about myocardial constitutive relations. The need for more data has been emphasized in the last section as well as in many recent publications: (Bergel and Hunter, 1979; Janz, 1980; Huisman et al., 1980b).

Two basic approaches have been used to quantify myocardial constitutive relations: (1) direct measurement from excised tissue and (2) prediction of global material properties from measured loading (pressure) and deformations (volume or strains). Thus far, the direct measurement of material prop-

erties has been limited to uniaxial tests conducted on papillary muscles or strips of trabeculae carnae. In these tests the specimen is pulled longitudinally while either its overall length or a segmental length is measured while the force developed at the ends is recorded. Many such studies (Hill, 1950; Sonnenblick, 1964; Pinto and Fung, 1973; Mirsky and Pasipoularides, 1980) have been performed and the results are in general agreement that the passive uniaxial stress-strain relationship can be accurately described by an exponential function of the form

$$\sigma = Ae^{B\lambda} + C$$

where λ is a strain quantity and A, B, and C are numerical coefficients. The numerical values of the coefficients vary somewhat from study to study partly due to different methods of normalizing the strain parameter. The values of the coefficients are altered by certain interventions including hypertrophy (Mirsky, 1976; Mirsky and Pasipoularides, 1980), infarction (Parmley, et al., 1973), and aging (Janz et al., 1976; Spurgeon et al., 1977). A recent summary (Mirsky, 1976) presents an excellent review of the myocardial properties in the passive state and the reader is referred to this work.

Recently, several studies have examined the constitutive relations during activation of these muscle strips (Templeton et al., 1973; Loeffler and Sagawa, 1975; Spurgeon et al., 1977) and have found that the relationship between stress and strain remains exponential during muscle activation. The values of the coefficients change from the resting to the active state so that the muscle becomes stiffer during activation and viscous effects become more prominent. Yin et al. (1980) recently demonstrated, for example, that with aging there was no change in the passive constitutive relation but that the active aged muscle was stiffer than the young muscle. A portion of this increase in active stiffness was attributable to age alone but a portion was accounted for by the underlying cardiac hypertrophy with aging.

Whereas these uniaxial studies have provided some insight into the pathogenesis of various disease processes, the quantitative extrapolation of these data to the entire ventricle is subject to question because the tissue in the ventricular wall is not subject to uniaxial stresses. A strain energy function is a requisite for the general formulation of the constitutive relations of tissue undergoing large deformations such as occur in the heart. From a theoretical standpoint uniaxial stress-strain data cannot be extrapolated to yield a strain energy function which is valid for multiaxial states (Fung, 1973; Abe et al., 1978; Moriarity, 1980). Even when the ventricle is assumed to be a simple structure such as a thick-walled sphere, extrapolation from uniaxial stress-strain data to the entire ventricle produces spurious results. Moriarity (1980) demonstrated that a single uniaxial stress-strain curve produced multiple pressure-volume relationships.

Conversely, Abe et al. (1978) utilized a single pressure-volume relationship and demonstrated that non-unique uniaxial stress-strain curves were obtained, depending on one's choice of the form of the strain energy function, whereas a unique biaxial stress-strain curve was obtained that was independent of the choice of the form of the strain-energy function. Thus, for us to be able to utilize the analytical power of a method such as the finite-element method, we need data on the constitutive relations of myocardial tissue under multiaxial states of loading. These data are currently not available. In addition, we strongly suspect that anisotropy and inhomogeneity are present in heart tissue. However, we do not know precisely how inhomogeneous the myocardium is from region to region or across the wall. Neither do we know how anisotropic the heart tissue is in either the passive or active states. Clearly these areas of investigation need to be pursued if further progress is to be made in ventricular stress analysis.

When one considers the properties of the heart wall during contraction, even less data are available and more complications arise. The demonstration by Streeter et al. (1969) of the variation of fiber orientation across the wall has led to numerous attempts to calculate stresses along the fiber directions at various times in the cardiac cycle (Voukydis, 1972; Streeter et al., 1970). However, these theoretical studies all are predicated on the assumption that stresses both at rest and during contraction occur only along the fiber direction and not in the transverse direction. This assumption seems attractive because the forces produced by contraction in a single muscle fiber should be directed predominantly along the fiber axis. However, interfiber connections could produce significant transverse or shear stresses both at rest and during contraction and the magnitude of these is as yet unknown. Thus, until experimental data are available regarding the anisotropy of heart muscle during activation, the conclusions of these studies must be considered as preliminary. When these data become available and one wishes to utilize, for example, the finite-element method to analyze stresses during contraction, it is clear that the fiber orientation and its changes during the cardiac cycle also need to be measured at every location in the heart. The problem becomes much more complex than that for the passive state. Given our current inability to measure accurately even the geometry of the intact passive heart, the challenge of measuring fiber orientation on a moment-to-moment basis in a heart during contraction is a formidable one.

Recently, there have been studies published (Nikravesh, 1976; Ghista et al., 1980) in which the authors employ the finite-element method, not for stress analysis, but for predicting the constitutive relations of the tissue. Basically the idea is based on the principle that the finite-element solution will

converge to the real solution if the proper loading conditions, boundary conditions, deformations, and constitutive relations are employed and equilibrium and compatibility are enforced. The approach is to measure the loading, boundary conditions, and deformations and use an iterative approach to successively approximate the constitutive relation of the tissue. When the predicted and measured deformations are "close enough," the constitutive relation giving the predicted deformation is considered to represent that of the tissue.

Although the approach is theoretically sound, in practicality it still presents considerable problems. First of all, one needs to assume that the constitutive relations can be expressed in some form that is amenable to iteration. That is, it must be expressible in terms of a few coefficients. Since the constitutive relation is probably nonlinear, even a simple relationship like an exponential makes attempts to iterate to this curve very difficult and could lead to numerical instabilities in addition to the tremendous computer expense involved in such iterative schemes. Second, for the method to work for predicting regional properties, one must have knowledge of the constitutive relation of the normal portions of the tissue (as pointed out earlier, even these data are not currently available). If one is interested only in predicting averaged global material properties, there is no reason to use a method of analysis that is so expensive and detailed. Use of one of the simpler models would probably suffice. Third and most important is the fact that one must validate the predicted material properties with directly measured values in order to make a convincing argument that the iterative scheme works. Ideally, this should be done in the same heart in which the loading and deformations were used to make the prediction. This, obviously, is an extremely difficult proposition because of our current inability to accurately measure the exact three-dimensional geometry of the heart wall. Neither angiography nor 2-D echocardiography seem to be able to yield the high resolution necessary for such precise measurements. Computerized tomography (Ritman et al., 1980) or direct visualization of the heart borders with multiple markers (Shoukas et al., 1980) offers possible solutions to this problem in the future, but the development of each is still in very preliminary stages. Practical application of these methods may be some time away from realization.

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