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The Morphogenesis of Left Ventricular Hypertrophy of Heart as Correlated with the Muscle Fiber Orientation

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Muscle fiber orientation in the left ventricular wall was histometrically estimated on tissue slides of normal, concentric- and eccentric-hypertrophied human hearts. The angle of inclination of muscle bundles from the transverse section of the ventricle showed continuous transmural change from the outer to inner layer in all the hearts and significant difference in the inner layer among the hearts. The inclination here was depressed remarkably in eccentric hypertrophy, while it was elevated in concentric hypertrophy. This result suggests that concentric and eccentric hypertrophy represents entirely different adaptation to different kinds of increased load with the configuration of the ventricle diametrically opposite to that of the normal ventricle.

INTRODUCTION

When the left ventricle of human hearts is persistently overloaded, the quantity of its muscle tissue is increased as an adaptation process for the overload. This is referred to as left ventricular hypertrophy and generally classified into two types of hypertrophy, concentric and eccentric (Spotnitz and Sonnenblick 1976; Olsen 1980; Tezuka 1982). The former is usually caused in pressure overload as in systemic hypertension and defined by thickening of the ventricular wall without corresponding increase in ventricular capacity (Fig. 1-A). The latter develops in volume overload as in hearts with valvular regurgitation and is characterized by ventricular dilatation predominating over thickening of the ventricular wall (Fig. 1-B) (Tezuka 1982). In spite of the conspicuous contrast in the ventricular configuration, there is no difference in the morphological characters of muscle fibers between the two types of hypertrophy. The length and thickness of individual muscle fibers are enlarged in hypertrophied left ventricles exactly in the same proportion to those of normal hearts (Arai et al. 1968). The total number of muscle fibers in the left ventricular wall is kept constant in the course of postnatal development and even in cardiac hypertrophy. These observations lead to the assumption that muscle fibers of hypertrophied ventricles grossly retain their geometry similar

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to those of normal ventricles, regardless of the types of hypertrophy. Consequently, different macroscopic configuration of the ventricle must result from some difference in the structural principle of the ventricular wall with the same constituent muscle fibers. In view of this conclusion, the muscle fiber orientation in hypertrophied hearts deserves in this paper special attention.

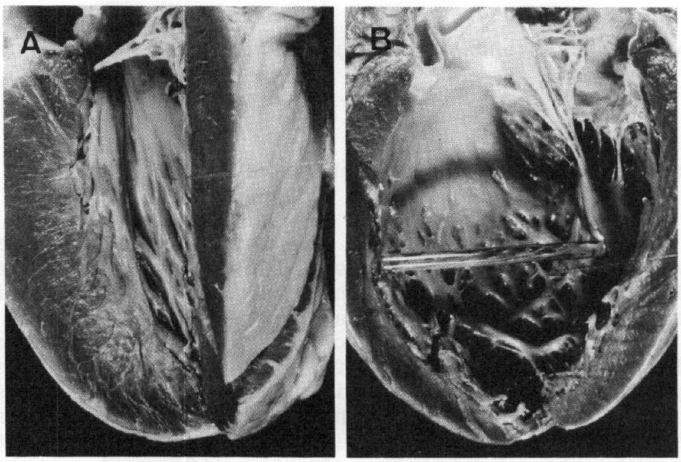

Fig. 1 Two types of left ventricular hypertrophy; (A) concentric and (B) eccentric.

On the regular muscle fiber arrangement in the ventricular wall there have been a number of investigation (Benninghoff 1931; Hort 1960; Streeter et al. 1969; Tezuka 1975; Tezuka 1982). Little is known, however, about the muscle fiber orientation of hypertrophied ventricles of human hearts. One of the reasons of this retarded analysis is sought in the conventional technique of serial histologic sections, because it is extremely laborious and time-consuming. Its application can hardly be extended beyond a very limited number of cases. In the present study, the difficulty is evaded by introducing a histometrical method, which makes it possible to estimate the muscle fiber orientation of the ventricular wall on a single tissue slide.

PRINCIPLE OF HISTOMETRICAL METHOD

Suppose a straight circular cylinder (='bundle') of b in radius filled with smaller, parallel straight circular cylinders (='fibers'). If this bindle is oriented in the XYZ-space with the angle of inclination, θ , from the YZ-plane and cut by the xy-plane, and ellipse is generated on this plane. When the length of the major and minor axes of this ellipse is 2a and 2b respectively, θ is immediately obtained from

$$\cos\theta = \frac{b}{a} \tag{1}$$

This ratio is equivalent to the ratio between the reciprocals of the counts of intersection of the fibers obtained with test lines of equal length in the direction of the minor and major axes of the ellipse. The ellipse can be determined mathematically by counting intersected fibers on the XY-plane.

The equation of an ellipse is expressed on a polar coordinate system on the XY-plane as

$$r^2 = \frac{b^2}{1-e^2 \cos^2(\varphi-a)},$$

where r is the radius, φ the angle of rotation of the radius from the X-axis of the coordinate system, α the angle of rotation of the major axis from the X-axis and e the eccentricity.

Determination of α , or the angle of rotation of the major axis of an ellipse: The sum A of squares of the perpendiculars from every point on the circumference of the ellipse to a diameter takes its minimumvalue, when the diameter coincides with the major axis. The radius r corresponds to the reciprocal of the count of intersected fibers which can be obtained with the test line of equal length in any direction. If radial test lines of equal length from a center dividing 2π into 24 equal angles of $\pi/12$ (Fig. 2) are superposed on the

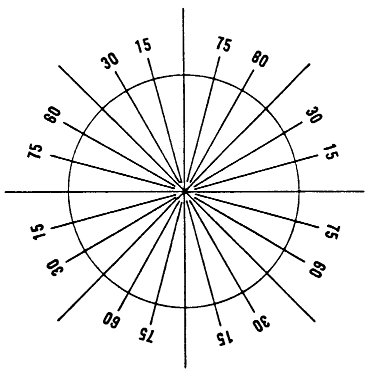

Fig. 2 The design of the eyepiece with radial test lines of equal length from a center dividing 2π into 24 equal angles of $\pi/12$.

XY-plane, A is defined by

$$A = \sum_{i=0}^{23} r_i^2 \sin^2(\varphi_i - a),$$

where φ_i is the angle of rotation ot the i-th test line from the X-axis, r_i the radius corresponding to the reciprocal of the count of intersected fibers in the i-th test line, and α the angle of rotation of a given diameter. Upon differentiation in reference to α , one obtains

$$\frac{dA}{da} = (\Sigma r_i^2 \sin 2\varphi_i) \cos 2a - (\Sigma r_i^2 \cos 2\varphi_i) \sin 2a \tag{2}$$

and

$$\frac{d^2A}{da^2} = -\frac{2 \cos 2a}{\Sigma r_i^2 \cos 2\varphi_i} \left[(\Sigma r_i^2 \sin 2\varphi_i)^2 + (\Sigma r_i^2 \cos 2\varphi_i)^2\right]. \tag{3}$$

In order that A may take its minimum value,

$$\frac{dA}{d\alpha} = 0,$$

and, on account of (2), α is obtained from

$$\tan 2\alpha = \frac{\Sigma r_i^2 \sin 2\varphi_i}{\Sigma r_i^2 \cos 2\varphi_i} \qquad (4)$$

under the restriction from (3) of

$$\frac{d^2A}{d\alpha^2} > 0. \qquad (5)$$

Determination of b/a, or the ratio of the minor to major axes of an ellipse: The angles of rotation of the major and monor axes, α and $\alpha+\pi/2$, being determined with (4) and (5), a and b can be given by the reciprocals of the counts of intersected fibers in the two mutually perpendicular direction . Finally, the angle θ of inclination of the bundle from the YZ-plane can be calculated using (1).

APPLICATION OF THE PRINCIPLE TO THE MUSCLE FIBER ORIENTATION OF LEFT VENTRICULAR WALL

Material: Normal and hypertrophied left ventricles of 31 autopsy human hearts were submitted to the present study. The hypertrophied ventricles included both types of hypertrophy, concentric and eccentric. The group of concentric hypertrophy consisted of 11 hearts weighing over 400g and showing no distinct dilatation of the chamber of the left ventricle. The group of eccentric hypertrophy, on the other hand, consisted of 10 hearts with remarkable dilatation of the left ventricle. As the control, normal hearts were selected from the cases without any disease which could influence heart weight.

Method: In each case, the left ventricle was fixed en-bloc in formalin and the positional setting was made as follows. The longitudinal axis of the left ventricle was firstly set from its apex to the middle point between aortic and mitral ostia, and then the transverse plane of the ventricle was set at its equator of largest ventriclular diameter and perpendicular to its longitudinal axis. A tissue slide was excised from the anterior wall of the left ventricle including its whole wall thickness from the outer to inner surface along its longitudinal axis perpendicular to its transverse plane. In these settings the longitudinal axis of the ventricle corresponds to the X-axis, the transverse plane of the ventricle to the YZ-plane and the excised tissue slide to the XY-plane. On the tissue slide, a number of reference lines were drawn perpendicularly transverse across the ventricular wall. The wall thickness was subdivided into 10 sublayers from the outer to inner surface along these reference lines. In each sublayer, the eyepiece as demonstrated in Fig. 2 was superposed and the intersection of test lines with muscle fibers were counted (Fig. 3). From the reciprocals of the counts of intersection, the angle of rotation of the major axis of the ellipse was first calculated using (4) and (5), and then the angle θ of inclination of muscle fibers using (1) with the reciprocals of the counts in the directions of major and minor axes. These procedures were repeated from sublayer to sublayer to obtain the transition of the angle of inclination of muscle bundles across the ventricular wall in each case.

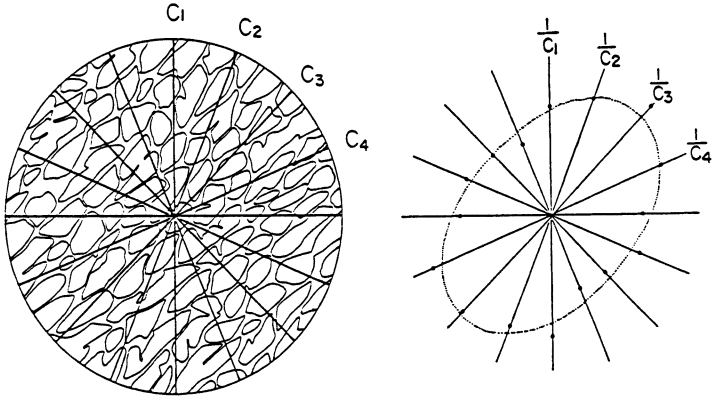

Fig. 3 Radial test lines of equal length are superposed on a histologic slide. The reciprocals of the counts of intersection are plotted in each direction to produce an ellipse.

RESULT AND DISCUSSION

The mean of the angle of inclination of muscle bundles is demonstrated in Fig. 4 according to the sublayers in each of the

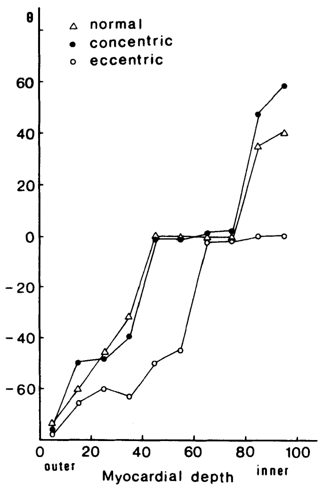

Fig. 4 The angle of inclination of muscle bundles. "Myocardial depth" gives the distance from the outer toward the inner myocardial (=ventricular) surface in percentage of the whole ventricular wall thickness.

three groups of normal, concentric- and eccentric-hypertrophied left ventricles. As for the former two groups, the principle of the fiber orientation was essentially the same, where the angle was largest both in the innermost and outermost sublayers and became progressively smaller toward the middle sublayer. However, there was some difference in the inner sublayer and the acuter inclination was observerd in concentric-hypertrophied ventricles than in normal ones. One the other hand, the fiber orientation was basically different in the group of eccentric hypertrophy from the groups of normal and concentric hypertrophy, in which the muscle fibers of both the middle and the inner sublayers diminished their inclination to approach to a circular orientation.

The result indicates that the change in the angle of muscle fiber orientation, especially in the inner layer, plays a very important role in determining the ventricular configuration. The narrow ventricle in concentric hypertrophy is really induced with acute inclination of the muscle fibers which take a spiral course surrounding the ventricle, while the pronounced dilatation of the ventricle in eccentric hypertrophy is generated with rearrangement of the muscle fibers losing their inclination.

The left ventricle responds to overload not only by hypertrophy of indivdual muscle fibers but also by structural rearrangement of muscle fibers. The arrangement of muscle fibers reflects an adaptation for achieving the optimal effectiveness of converseion of the energy of contraction into the blood of the ventricle. The longitudinal or acutely spiral-oriented fibers could permit the maximal efficiency for complete ejection of the blood into the aorta in pressure overload. The circular-oriented fibers would need the least energy to ensure the most effective contractile force against volume overload.

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