Myocardial Structure of Hypertrophied Hearts

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Behavior of Heart Muscle Fibers

The first detailed histomorphological study was performed by Linzbach (1947) on the behavior of heart muscle fibers in cardiac hypertrophy. The results can be summarized as follows: In the course of normal heart growth after birth heart muscle fibers are simply enlarged without increasing their number. This pattern of growth is also observed in cardiac hypertrophy, until the total heart weight attains a critical weight of 500 g. If cardiac hypertrophy advances beyond that limit, the number of heart muscle fibers increases through progressive cleaving at anastomoses. The thickness of individual fibers does not then increase to such a grade as would be expected from heart weight.

The concept of the number of heart muscle fibers, however, is in reality difficult to define, since the myocardial layer consists of a complicated network of heart muscle fibers. In the analysis of such a structure the "number" of fibers does not seem to be an adequate parameter. Quantitative changes of heart muscle fibers would be better characterized by the mean thickness $D$ of individual heart muscle fibers and their total length $L_m$. The latter parameter expresses the length of a hypothetical thread-like structure produced by attaching all the anastomoses and aligning end-to-end all the muscle fiber segments.

On a logarithmic co-ordinate system, $D$ exhibits a roughly linear regression against $W_m$, the net muscular weight of the left ventricle, as demonstrated in Fig. 1. Except in a special case, which will be further described in the proper place, there is no difference in the behavior of $D$ through normal cardiac growth and cardiac hypertrophy. The type of hypertrophy, whether concentric or eccentric, does not exert any influence. Nor is there any general tendency toward a declining $D$, even if $W_m$ exceeds 200 g, which approximately correspond to a total heart weight of 500 g. The regression coefficient is very close to $1/3$, which means that the heart muscle fiber grows in an essentially isometric manner, or the breadth and length of individual

\[ D (\mu) \]

\[ \begin{align*}
10 & \quad 50 \quad 100 \quad 400 \quad W_m (g) \\
\text{o} & \quad \text{b} = 0.34
\end{align*} \]

Fig. 1: Mean thickness $D$ of heart muscle fibers versus net muscular weight $W_m$ of the left ventricle on a logarithmic co-ordinate system.

- $\bullet$ = hearts of normal postnatal growth and concentric hypertrophy, $\circ$ = dilatation hypertrophy, $\ast$ = exceptional case, $b$ = regression coefficient. For explanation see the text.

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fibers are enlarged practically in the same proportion. However, $D$ is remarkably lower in the above-mentioned special case than the value expected from the heart weight.

The result suggests immediately that $Lm$ will also exhibit a linear regression on a logarithmic co-ordinate system, if the special case is excluded, and the regression coefficient will be practically equal to $1/3$. This assumption is really substantiated by histometry as demonstrated in Fig. 2. No difference in the regression of $Lm$ is observed between concentric and dilatation hypertrophy. Only in the above-mentioned special case $Lm$ is evidently larger than that of the other hearts.

The present histometrical study reveals that the growth of heart muscle fibers is essentially isometric in the great majority of hypertrophied hearts, regardless of the difference in the ventricular capacity. It does not demonstrate that as a rule, the increase in $D$ is decelerated or that of $Lm$ is accelerated in excessive hypertrophy.

In this connection, the exceptional case which showed a small $D$ and large $Lm$ in Figs. 1 and 2 deserves further notice. It is a case of dilatation hypertrophy due to congenital malformation of the aortic valve. The valve was made of two leaflets and wide passages were left between them. The defect seems to cause inevitably significant regurgitation. On the histological section, heart muscle fibers are relatively slender and not so thick as expected from the heart weight. The nuclei are rather small and oval in shape and do not show the well-known bizarre pattern characteristic of remarkable cardiac hypertrophy. Histometrical analysis on the nuclear level reveals further some properties specific to this heart. The total number of muscle fiber nuclei of the left ventricle is distinctly increased in this case, while it is usually constant through normal postnatal growth and even in excessive hypertrophy (Fig. 3). The nuclear length remains unchanged in the course of normal growth, but increases with the progress of hypertrophy, except in this particular case in which it keeps the level of the normal heart, in spite of remarkable hypertrophy.

The results of the present quantitative analysis can be summarized as follows: As the general rule heart muscle cells undergo isometric enlargement in cardiac hypertrophy as well as in the normal postnatal growth. The number of heart muscle cells remains constant throughout the postnatal life even in remarkable cardiac hypertrophy. Different ventricular capacity of hypertrophied hearts does not seem to exert a significant influence upon the behavior of heart muscle cells. Only in an exceptional case, proliferation of heart muscle cells plays an important role in producing hypertrophy.

Cardiac hypertrophy is usually classified into concentric and dilatation hypertrophy, according
Muscle volume 150ml
Rest blood volume 50ml
Stroke volume 50ml

External layer 1:0.89
Internal layer 1:0.71
Thickness 1:1.76

Fig. 4. The model of transverse ventricular sections corresponding to diastole (left) and systole (right) of a normal heart. In the upper part the conditions of the model are presented. In the lower part, relative reduction of external and internal parameters of the ventricular wall and relative increase in the thickness of the ventricular wall in systole are calculated. Note larger change of internal perimeter than that of external perimeter.

Fig. 5. The number \( N_f \) of muscle fiber layers of the compact layer of the left ventricle versus the ratio \( V_L/W_L \), the ratio of ventricular capacity to ventricular weight. \( N_f \) gives the number of intersections of a transmural test line with muscle fibers on histological sections. Histological specimens are taken from the portion of the largest thickness of the ventricular wall. In normal hearts \( V_L/W_L \) is approximately 0.1. The ratio is smaller in concentric hypertrophy and larger in dilatation hypertrophy.

to the difference in the ventricular capacity. The difference should be mainly attributed to a different arrangement of heart muscle fibers in the myocardial layer, because the behavior of individual heart muscle cells is essentially independent of ventricular capacity. If cardiac hypertrophy develops through isometric growth of individual heart muscle cells without changing muscle fiber orientation, the ventricular capacity will increase exactly in proportion to the weight of the left-ventricular myocardial layer. This condition may be called isometric hypertrophy.

The hearts of concentric or dilatation hypertrophy will then respectively correspond to the state of contraction or dilatation of isometrically hypertrophied hearts. The only difference is that the muscle fiber thickness should remain invariable in contrast to normal cardiac activity. Consequently, the analysis of changing muscle fiber orientation in normal cardiac contraction and dilatation is effective for understanding the architecture of the myocardial layer in different types of cardiac hypertrophy.

Contraction and Dilatation of Normal Hearts

It is assumed at first that the total myocardial volume is not influenced by systole and diastole. Two important conditions must be then satisfied in this cardiac activity. One of them is that the number of muscle fiber layers constituting the ventricular wall should be reduced in cardiac dilatation, because the attenuation of individual fibers cannot compensate that of the ventricular wall. The other is that relative enlargement of internal ventricular surface should be larger than that of external one. This is incompatible with uniform elongation and shortening of individual fibers, if fiber orientation should remain unchanged. The situation is diagrammatically visualized in Fig. 4.

The former condition requires a transformation of the muscle fiber arrangement into such a pattern, as if the ventricular wall were compressed by transmural force. The distance of every two adjacent fibers is shortened in the transmural direction and elongated in the other directions. The expected number of intersections of a transmural test line with heart muscle fibers will then be reduced.

For alleviating the latter condition the following mechanism seems to be effective: The heart muscle fibers of the myocardial layer have a series of different inclination against the transverse sectional plane across the left ventricle. The angle of inclination is largest in the innermost myocardial layer, becomes smaller toward the middle layer, where it takes its minimum value, and resumes gradually higher values toward the

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external layer. Due to this particular configuration the heart muscle fibers can reduced their inclination more strongly in the internal layer than in outer layer, which contributes to augmenting the dilatation of the internal ventricular surface.

**Fig. 6.** Histological patterns of left ventricular walls. A: normal heart. B: concentric hypertrophy. C: dilatation hypertrophy. Note the angles of bifurcation of connective tissue septa.

Myocardial Structure of Hypertrophied Hearts

Histological and histometrical studies can really demonstrate characteristic myocardial structural changes of hypertrophied hearts which are essentially equivalent to those expected from the theoretical analysis of systole and diastole of the normal heart. The number of intersections of a transmural test line with heart muscle fibers of the compact myocardial layer is reduced with the progress of ventricular dilatation (Fig. 5). The angles of inclination of heart muscle fibers in the internal myocardial layer are rather enlarged in pronounced concentric hypertrophy but distinctly lowered in dilatation hypertrophy. A further mechanism influencing myocardial thickness is immediately recognized from Fig. 6. Distortion of heart muscle fiber orientation is clearly indicated by the configuration of connective tissue septa separating heart muscle bundles. On the histological sections the angles of bifurcation of connective tissue septa is smaller in con-
centric hypertrophy and larger in dilatation hypertrophy than that of the normal heart. The distortion is diagrammatically presented in Fig. 7.

At the same time another important structural change is observed in Fig. 6. In concentric hypertrophy the trabecular portion of the myocardial layer is partly incorporated into the compact layer. In dilatation hypertrophy, on the contrary, the internal part of the compact layer is dissolved into trabecular formation. The mutual transformation of the trabecular portion and internal compact layer is more clearly visible on the tracings of the transverse ventricular sec-

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Fig. 9. Radius $r_f$ of the coronary trunk versus total heart weight $W$ on a logarithmic co-
ordinate system. The regression coefficient is 0.38.

Fig. 10. Total capillary length $L_c/W_m$ per unit muscular weight versus net muscular weight $W_m$ of the left ventricle. ● and ○ are equivalent to those of Figs. 1 and 2.

Fig. 11. Total capillary length $L_c/S_m$ per unit surface area of muscle fibers versus $W_m$.

• and ○ are equivalent to those of Figs. 1 and 2.

The transformation is obviously brought about by the following mechanism: Distortion of heart muscle bundles and changing muscle fiber inclination cannot completely compensate the large difference in relative contraction and dilatation between the internal and external surfaces of the ventricular wall. The internal compact layer can neither adapt to ventricular dilatation in pronounced dilatation hypertrophy nor to excessive diminution of ventricular cavity in concentric hypertrophy. As a result, the internal compact layer is extracted into the ventricular cavity in dilatation hypertrophy and transformed into the trabecular portion. In concentric hypertrophy the trabecular portion is compressed against the compact layer and partly incorporated into the layer.

Myocardial Blood Circulation in Hypertrophied Hearts

It is generally accepted that hypertrophied hearts are susceptible to coronary insufficiency. Apart from the stenotic effect of coronary sclerosis which may frequently complicate cardiac hypertrophy, the reason is usually sought either in retarded growth of large coronary arteries or in reduced capillarization of myocar-
dial layer.

The blood flow $Q$ of an arterial branch of radius $r$ in
radius is given by $Q = qr^{2.7}$, where $q$ is a con-
stant. The value 2.7 of the exponent is common
to all arterial systems. If the growth of coronary
arteries in cardiac hypertrophy proceeds in such
a way that the radius of the coronary trunk is
proportional to $W^{1/2.7}$, $W$ being the total cardiac
weight, the assumption of retarded development
of coronary arteries is not sustained. In Fig. 9,
the radius of the coronary trunk is plotted against
the total cardiac weight on a logarithmic co-
ordinate system. The regression coefficient is
0.38 or very close to 1/2.7. The result does not
support the view that retarded growth of coro-
mary arteries plays an important role in precipi-
tating coronary insufficiency of hypertrophied
hearts.

The capillarization of the myocardial layer is
defined histometrically by the total length of
capillaries per unit volume of heart muscle. It
is demonstrated in Fig. 10 that myocardial
capillarization is distinctly reduced with the
progress of hypertrophy. The only exception
is the case of increased muscle cells, in which the
mean thickness of heart muscle fibers is much
smaller than that of other hearts of equivalent
weight. The capillarization is maintained practi-
cally at the level of a normal heart in this particu-
lar case.

It deserves attention that the total capillary
length per unit surface area of heart muscle fibers
in Fig. 11 does not show a tendency toward
decrease even in excessive hypertrophy. No
particular behavior is observed in the special case
of heart muscle cell proliferation. It seems very
likely that myocardial capillaries are always
uniformly distributed on the surface of heart
muscle fibers through normal postnatal growth
and hypertrophy. The results of the present
study suggest the importance of diffusion insuf-
ficiency, because the mean distance from the
surface of individual heart muscle fibers to their
innermost parts is much increased in hypertro-
phied hearts. Degenerative changes accentuated
in the central part of heart muscle fibers, which
are often observed histologically in pronounced
hypertrophy, may be interpreted from this
mechanism.