Arterioles of Kidney and Pancreas in Cases of Cardiac Hypertrophy of Undetermined Causation

By Harold A. Ferris, Jr., M.D.

The arterioles in the kidneys and pancreas in 50 consecutive necropsy cases of cardiac hypertrophy of undetermined cause and in 50 control cases were measured and studied histopathologically in an effort to determine the cause of the cardiac hypertrophy. The weight of the heart, the ventricle affected by hypertrophy and the age of the patient also were recorded in each case and correlated with the changes in the ratio of the wall to lumen in the arterioles. This study revealed that in about 40 per cent of cases the cardiac hypertrophy was probably due to antecedent hypertension.

Cardiac hypertrophy with recordings of normal arterial blood pressure is commonly considered to be the result of arterial hypertension at periods other than when the blood pressure recordings were made. The work of Kernohan, Anderson, and Keith, Morlock, Cain, and Pilcher and Schwab has shown diffuse arteriolar disease in cases of arterial hypertension, and it would seem advisable to study the arterioles in representative organs in cases of cardiac hypertrophy of undetermined cause to record any hypertensive changes that may be present.

Accordingly, 50 consecutive cases of cardiac hypertrophy of undetermined cause were chosen from the necropsy records at the Mayo Clinic. The ages of the patients at the time of death ranged from 30 to 85 years and the hearts weighed at least 50 Gm. more than the maximal normal weight, according to H. L. Smith’s formula, and were based on protocols of the clinic from 1931 to 1946. The actual heart weights are tabulated in Table 1. The blood pressure was neither more than 150 mm. of mercury systolic nor more than 90 mm. diastolic in these cases. The usual causes of myocardial hypertrophy were excluded, such as hypertension, cardiac valvular disease, chronic cor pulmonale, thyrotoxicosis, and congenital defects. Fifty control cases in which the ages of patients ranged from 21 to 78 years were studied during the same period. In these cases heart weight and blood pressure were normal; cardiac, renal or systemic diseases were not found.

<table>
<thead>
<tr>
<th>Weight range</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>301-350</td>
<td>2</td>
</tr>
<tr>
<td>351-400</td>
<td>5</td>
</tr>
<tr>
<td>401-450</td>
<td>14</td>
</tr>
<tr>
<td>451-500</td>
<td>12</td>
</tr>
<tr>
<td>501-550</td>
<td>10</td>
</tr>
<tr>
<td>551-600</td>
<td>5</td>
</tr>
<tr>
<td>601-650</td>
<td>1</td>
</tr>
<tr>
<td>651-700</td>
<td>0</td>
</tr>
<tr>
<td>701-750</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
</tr>
</tbody>
</table>

**Method**

Four sections were made from the kidneys and four from the pancreas in each case. These were fixed in 10 per cent solution of formalin, blocked in paraffin, and stained. The sections were stained by the hematoxylin and eosin, the van Giesen, Mallory-Heidenhain, or the Elastin H. method, and measurements were made of the arterioles. To prevent bias, I arranged the work so that I would not know to which group the particular section in question belonged, while these measurements and computations were being made. Using the method of Kernohan, wall-to-lumen ratios were computed on arterioles varying in outside diameter from 25 microns to 100 microns. Six arterioles were measured in each section, making a total of 24 arterioles from the kidneys and 21 arterioles from the pancreas in each case. A Bausch and Lomb micrometer eyepiece.
piece was used over a high power objective, obtaining a magnification of 450. The wall of each vessel was measured in areas which appeared to be cut at right angles to its course as in figure 1, that is ab, cd, ef and gh, and the lumen in two diameters, that is, be and fg. Then the average width of the wall and lumen of each vessel was computed. Finally, the wall-to-lumen ratio was determined for each vessel; then the average wall-to-lumen ratio for each kidney and pancreas was computed. Since sections from the control cases and from cases of cardiac hypertrophy were subjected to similar methods and since vessels are shown in figure 2. In general, vessels in which the wall-to-lumen ratio was less than 1:2 show evidence of intimal proliferation, thickening of the media by hypertrophy of smooth muscle or by hyaline replacement of the media.

The distribution curve of wall-to-lumen ratio according to age of patients in decades in cases of cardiac hypertrophy and in controls

\[ \begin{array}{c|c|c|c|c} 
\text{Ratio of} & \text{Kidney} & & \text{Pancreas} \\
\text{wall-to-lumen} & \text{Cardiac} & \text{Controls} & \text{Cardiac} & \text{Controls} \\
1:1.2 & 3 & 1 & 1 & 1 \\
1:1.3 & 4 & 2 & 1 & 1 \\
1:1.4 & 7 & 2 & 4 & 4 \\
1:1.5 & 3 & 4 & 1 & 1 \\
1:1.6 & 8 & 1 & 4 & 4 \\
1:1.7 & 6 & 2 & 4 & 4 \\
1:1.8 & 4 & 5 & 1 & 1 \\
1:1.9 & 8 & 4 & 4 & 6 \\
1:2.0 & 2 & 5 & 3 & 7 \\
1:2.1 & 2 & 6 & 2 & 5 \\
1:2.2 & 2 & 11 & 5 & 3 \\
1:2.3 & 4 & 4 & 5 & 5 \\
1:2.4 & 8 & 4 & 3 & 3 \\
1:2.5 & 2 & 2 & 4 & 4 \\
1:2.6 & 2 & 2 & 2 & 2 \\
1:2.7 & 1 & 2 & 6 & 6 \\
1:2.8 & 1 & 2 & 1 & 1 \\
1:2.9 & 2 & 1 & 1 & 1 \\
1:3.0 & 1 & 2 & 1 & 1 \\
1:3.1 & 1 & 2 & 1 & 1 \\
1:3.2 & 1 & 1 & 1 & 1 \\
1:3.3 & 1 & 1 & 1 & 1 \\
1:3.4 & 1 & 1 & 1 & 1 \\
1:3.5 & 1 & 1 & 1 & 1 \\
\end{array} \]

in kidney and pancreas are given in figures 3 and 4. There appears to be no relationship between wall-to-lumen ratio and age.

The number of cases of cardiac hypertrophy of unknown etiology in which thickness of the left ventricle only, the right ventricle only, or both left and right ventricles was increased was determined. The upper limits of normal for the thickness of the left ventricle is considered to be 1.5 cm. and for the right ventricle 0.4 cm. The average arteriolar wall-to-lumen ratio for kidney and pancreas was correlated

Cross section of small artery or arteriole

Fig. 1. Method of measuring an arteriole.

In this a comparative study, it does not seem likely that laboratory methods will enter as an important source of error.

**Results**

The distribution of wall-to-lumen ratios for kidney and pancreas in cases of cardiac hypertrophy of undetermined origin and in control cases is given in table 2. It will be noted that for the kidney in only 3 (6 per cent) of the control cases was the wall-to-lumen ratio less than the normal ratio of 1:2, whereas in 35 (70 per cent) of the cases of cardiac hypertrophy it was below 1:2. The wall-to-lumen ratio in arterioles in the pancreas was less than 1:2 in only 4 (8 per cent) of the control cases and in 23 (46 per cent) of the cases of cardiac hypertrophy. In 20 (40 per cent) of the cases of cardiac hypertrophy the wall-to-lumen ratio of the arterioles was less than the normal ratio of 1:2 in both kidney and pancreas.

The histopathologic findings of the vessels studied varied from essentially normal to those characteristic of hypertension. Several of these...
with these groups. The results are shown in table 3.

It is noted incidentally that 29 (58 per cent) of the patients showed coronary sclerosis of grade 2 or more, using grade 0 as meaning no sclerosis and grade 4 as meaning complete closure of the vessel. Eleven of these patients (38 per cent) presented wall-to-lumen ratios below 1:2 in both kidney and pancreas. Sixteen (32 per cent) of the patients showed evidence of chronic myocardial infarction. Among this

sclerosis was found, 18 or 60 per cent had coronary sclerosis of grade 2 or more, 4 or 13 per cent had congestive heart failure, and 7 or 23 per cent had mild anemia.

Ten of the 50 cases of undetermined cardiac hypertrophy had only one blood pressure re-

FIG. 2. A. Small artery in kidney, showing moderate intimal proliferation (hematoxylin and eosin, X235). B. Arteriole in pancreas of another case showing marked medial hypertrophy (hematoxylin and eosin, X205). C. Arteriole in pancreas showing hyaline replacement of media (hematoxylin and eosin, X320). D. Arteriole in kidney showing hyaline replacement of media (hematoxylin and eosin X320).
recording. Among this group it was found that 4 cases or 40 per cent had wall-to-lumen ratios below 1:2 in both kidney and pancreas. This compares with the findings in cases having multiple blood pressure recordings.

![Distribution wall-to-lumen ratios of arterioles in kidney according to age in decades.](image1)

![Distribution wall-to-lumen ratios of arterioles in the pancreas according to age in decades.](image2)

**TABLE 3.—Increased Thickness of Ventricle in 80 Cases of Cardiac Hypertrophy: Average Ratio of Wall-to-Lumen.**

<table>
<thead>
<tr>
<th>Increased thickness of:</th>
<th>Cases</th>
<th>Per cent</th>
<th>Average ratios of wall-to-lumen arterioles of:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Kidney</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>11</td>
<td>22</td>
<td>1:1.87</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>7</td>
<td>14</td>
<td>1:2.13</td>
</tr>
<tr>
<td>Both ventricles</td>
<td>6</td>
<td>12</td>
<td>1:1.60</td>
</tr>
</tbody>
</table>

**Comment**

A study of the arterioles of the kidneys and pancreas in 50 cases of cardiac hypertrophy of undetermined cause shows wall-to-lumen ratios in both kidney and pancreas of less than the normal ratio of 1:2 in 20 cases (40 per cent). These ratios bear no relationship to age. The arterioles having wall-to-lumen ratios of less than 1:2 demonstrate pathologic changes found in arterial hypertension. The increased weights of the hearts studied were due to generalized hypertrophy of the heart; in only 11 cases (22 per cent) was the thickness of the left ventricle alone increased and in only 7 cases (14 per cent) was the thickness of the right ventricle alone increased.

Kaplan, Clark and de la Chapelle reviewed 43 cases of congestive heart failure with predominant left ventricular hypertrophy of unknown origin and studied the arterioles of the kidney and adrenal gland. In 30.9 per cent of these cases mild or severe renal arteriolar sclerosis was present. Of 269 patients without hypertension also studied by these authors 12 per cent showed renal arteriolar sclerosis which bore a relationship to age. Of 154 patients having essential hypertension, 82.5 per cent of those dying in congestive heart failure showed renal arteriolar sclerosis. These authors concluded that although the role of antecedent hypertension cannot be excluded in the individual case of hypertrophy of the left ventricle of unknown cause its absence in the majority of these cases seems likely.

Moritz and Oldt, using Kernohan's technic, obtained wall-to-lumen ratio in arterioles of controls from 1.0 to 1.9 and in arterioles of hypertensives from 1.0 to 1.36. The distribution curves of these ratios showed a wide overlapping with only 20 per cent of hypertensives having a wall-to-lumen ratio less than that seen in any control.

Gross and Lisa give strong support for considering hypertension as the cause for undetermined cardiac hypertrophy by reporting renal arteriolar sclerosis in each of 18 cases of cardiac hypertrophy with normal blood pressure and moderate to severe coronary disease.
Conclusions

From the present study it seems that 40 per cent of cases of cardiac hypertrophy of undetermined origin are probably due to antecedent hypertension. This study, however, does not throw any light on the cause of cardiac hypertrophy of unknown origin in cases encountered at necropsy when sclerosis of the arterioles in various organs cannot be demonstrated.

REFERENCES

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