Atherosclerotic Disease of the Coronary Arteries

A Pathologic-Radiologic Correlative Study

By JOSEPH H. EUSTERMAN, M.D., RICHARD W. P. ACHOR, M.D., OWINGS W. KINCAID, M.D., and ARNOLD L. BROWN, JR., M.D.

Atherosclerotic disease of the coronary arteries is the leading cause of death in the United States. Significant disease of this type is found at necropsy in three fourths of the adults examined. It is generally agreed that present medical treatment is inadequate to cope with this problem in a curative sense. Hence various indirect and direct surgical approaches have been devised in an effort to increase myocardial blood supply with the hope of reducing the morbidity and mortality arising from coronary atherosclerosis.

Recently, direct surgical procedures have become favored by some surgeons who have associated themselves with the problem. These procedures include (1) replacement of the occluded arterial segments with autogenous or artificial grafts, (2) anastomosis of extracardiac arteries to a distal, patent segment of an occluded coronary artery, and (3) coronary endarterectomy. Blumgart and associates have presented a comprehensive review of the problems concerned with the pathologic anatomy of such direct coronary surgery as has been proposed. Though the difficulties are immense, continued study seems warranted.

Essential to obtaining the best possible results from surgical treatment is accurate preoperative information concerning the location and severity of the occlusive process in the coronary arteries. Most workers think that such evaluation is best obtained by radiologic visualization of the coronary arteries. In recent years several technics have been devised, using the experimental animal and man for the express purpose of such arteriographic visualization. However, it was thought that a basic study has been overlooked, namely, whether or not arteriographic evaluation of the coronary arteries in man provides a truly accurate picture of stenotic or occlusive coronary disease. This correlative radiologic and pathologic study, utilizing coronary arteriograms made at necropsy, was therefore designed and undertaken to determine whether or not such coronary arteriograms do, in fact, accurately reflect the existing pathologic anatomy of the coronary arteries.

Methods

Fifty human hearts were obtained at random during necropsy 1 to 18 hours after death from various diseases. Each heart was separated from the heart-lung block by dividing the aorta and pulmonary artery about 5 cm. above their valves. The pulmonary veins were similarly divided at the pulmonary hilum after examination of the left atrium had been completed. The inferior and superior venae cavae were also divided at the time of removal of the heart-lung block. The aorta was then trimmed away to about 1 to 2 cm. above the level of the coronary ostia after making certain that no congenitally abnormal ostia were present superiorly. The heart was next impaled on two radiolucent Lucite spikes; the respective coronary ostia were identified and 5 ml. of 85 per cent methylglucamine diatrizoate (Cardiograft) was injected manually into each via a tapered cannula on the end of a 10-ml syringe. Hemostats were then placed on the proximal 0.5 cm. of each main right and left coronary artery, and the heart was suspended above an x-ray cassette. Roentgenographic exposures were made by means of a conventional machine and a focal-film distance of 53 inches (135 cm.). The exposure time employed


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Cross sections of coronary arteries illustrating grades of luminal occlusion. a. Grade 1, 0 to 24 per cent stenosis. b. Grade 2, 25 to 49 per cent stenosis. c. Grade 3, 50 to 74 per cent stenosis. d. Grade 3+, 75 to 99 per cent stenosis.

was three-twentieths second with 15 ma. at 67 to 76 kv., depending on the size of the specimen. Anteroposterior and left posterior oblique (or right anterior oblique) exposures were made of each heart and these films were developed immediately. The heart was then returned to the necropsy suite for its routine examination.

Approximately 48 to 72 hours later the specimen was removed from its formalin bath and the coronary arteries were inspected in detail by serial sectioning at intervals of 2 to 3 mm. The degree of atherosclerotic stenosis was estimated by gross examination and graded according to the following system (White and colleagues): 0 to 24 per cent stenosis in at least one area, grade 1; 25 to 49 per cent stenosis, grade 2; 50 to 74 per cent stenosis, grade 3; 75 to 99 per cent stenosis (or less than complete occlusion grossly), grade 3+; and 100 per cent occlusion, grade 4 (fig. 1).

The coronary arteries were arbitrarily divided into 16 segments according to the method of White and colleagues, namely, the proximal, middle, and distal segments of the left anterior descending, left circumflex, right main, right marginal branch, and right posterior descending branch, plus the left main coronary artery (fig. 2).

Each segment, when present, was graded by gross inspection as to its maximal atherosclerotic narrowing. These lesions were further classified as being nonfocal (more than 5 mm. long) or focal (less than 5 mm. long). Similarly all deviations from the three predominant patterns of coronary-artery distribution were recorded. These three principal patterns are (1) predominantly right coronary-artery distribution, (2) predominantly left coronary-artery distribution, and (3) balanced arterial distribution (figs. 3, 4, and 5). Sections were taken for microscopic study only when the degree of narrowing could not be classified by gross inspection or when representative samples of narrowing were desired.

From the coronary arteriograms the degree of nonfocal and focal atherosclerotic narrowing was estimated in each case by the same system of grading, that is, 1, 2, 3, 3+, and 4. Whenever possible, the arteries were arbitrarily divided into the same 16 segments as previously described.

Whenever marked discrepancies between the pathologic and roentgenographic methods of grading were observed, the coronary artery in question was re-examined to confirm or deny the original estimate concerning the degree of luminal stenosis or occlusion present; in no instance was significant disparity from the original estimation found on re-examination (fig. 6). However, poor filling of various arterial segments did occasionally occur in the presence of minimal disease involving these segments, and this of course resulted in marked discrepancies in grading by two methods (pathologic and radiologic); these segments were excluded from the study.

The left main coronary artery was not visualized sufficiently well in 26 cases because of its short length, and this difficulty was compounded by having to clamp it proximally or by occluding part of its length in several instances with a threaded Lucite plug. These procedures were necessary to prevent the contrast medium from draining out by retrograde flow.

*Figure 1*

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In 22 hearts the left circumflex branch became the obtuse marginal branch rather than continuing around the atrioventricular sulcus as a true left circumflex artery. Thus 22 hearts did not show a mid or distal left circumflex coronary artery.

Consequently, in this study comprising the coronary arteries of 50 hearts, 479 segments were graded anatomically and arteriographically. The grades of luminal stenosis, both nonfocal and focal, estimated by the two methods were then
Table 1

Diffuse (Nonfocal)* Coronary Luminal Stenosis: Accuracy of Arteriographic Estimation as Determined at Necropsy

<table>
<thead>
<tr>
<th>Nonfocal luminal stenosis, grade†</th>
<th>Coronary segments examined</th>
<th>Same</th>
<th>Grade by arteriography Less</th>
<th>More</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (0-24%)</td>
<td>292 (61%)</td>
<td>226</td>
<td>77</td>
<td>66</td>
</tr>
<tr>
<td>2 (25-49%)</td>
<td>101 (21%)</td>
<td>55</td>
<td>54</td>
<td>35</td>
</tr>
<tr>
<td>3 (50-74%)</td>
<td>41 (9%)</td>
<td>7</td>
<td>17</td>
<td>31</td>
</tr>
<tr>
<td>3+ (75-99%)</td>
<td>32 (7%)</td>
<td>1</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>4 (100%)</td>
<td>13 (2%)</td>
<td>2</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>479 (100%)</td>
<td>291</td>
<td>61</td>
<td>107</td>
</tr>
</tbody>
</table>

*Lesions more than 5 mm. length.
†Determined by gross inspection.

correlated to determine the percentage of exact or inexact agreement and also the degree of inexact agreement.

Results

Since 19 per cent of the 479 segments examined grossly showed focal disease in addition to nonfocal disease, correlations between the anatomic grades of coronary atherosclerosis revealed by inspection of the vessels themselves and those revealed by arteriography were determined for both nonfocal and focal disease. Table 1 shows the findings for nonfocal disease. The actual amounts of luminal stenosis or occlusion were graded exactly the same by the two methods in 61 per cent of the 479 segments, were underestimated by arteriography in 22 per cent, and were overestimated by arteriography in 17 per cent. It can be seen from table 1 that when the degree of nonfocal stenosis was less than 50 per cent the accuracy of arteriographic grading was significantly higher than when it was 50 per cent or more, the accuracy being surprisingly low under the latter circumstance. Also evident from table 1 is the fact that when the nonfocal luminal stenosis was 50 per cent or
more the severity of involvement was underestimated by the arteriograms in most instances.

In table 2 the results of arteriographic grading in the 89 cases of focal luminal stenosis or occlusion are correlated with the results of grading by gross inspection. It can be seen that the focal disease was graded the same by the two methods in 11 per cent of instances, underestimated by the arteriographic method in 86 per cent, and overestimated by this method in only 3 per cent. In grading focal as opposed to nonfocal involvement, the degree of luminal stenosis was not a factor affecting the accuracy of grading of arteriograms.

Regarding the degree of error, the severity of nonfocal disease was underestimated from the arteriograms in 107 instances—in 58 per cent by only one grade and in 42 per cent by two or more grades. In 75 per cent of 81 instances in which the severity of nonfocal disease was overestimated by arteriography the error amounted to only one grade, and in 25

Table 2

<table>
<thead>
<tr>
<th>Focal luminal stenosis, grade†</th>
<th>Coronary segments examined</th>
<th>Same No.</th>
<th>%</th>
<th>Grade by arteriography Less</th>
<th>More No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (25-49%)</td>
<td>19 (21%)</td>
<td>2</td>
<td>11</td>
<td>16 84</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>3 (50-74%)</td>
<td>49 (55%)</td>
<td>5</td>
<td>10</td>
<td>42 86</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>3+ (75-99%)</td>
<td>13 (15%)</td>
<td>2</td>
<td>15</td>
<td>11 85</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>4 (100%)</td>
<td>8 (9%)</td>
<td>1</td>
<td>13</td>
<td>7 87</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Total</td>
<td>89 (100%)</td>
<td>10</td>
<td>11</td>
<td>76 86</td>
<td>3</td>
<td>3</td>
</tr>
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</table>

*Lesions less than 5 mm. long.
†Determined by gross inspection.

Figure 6

*Right anterior oblique view of coronary arteriogram (left) showing double lumen of right main coronary artery at point indicated by arrow. Cross section of right main coronary artery (right) showing that double lumen was result of recanalized thrombus 6 cm. long. Magnification increased from × 20.*
Atherosclerosis of Coronary Arteries

Number correlated

<table>
<thead>
<tr>
<th>Segment</th>
<th>Left main</th>
<th>LAD</th>
<th>Circ.</th>
<th>Right main</th>
<th>Right main post.</th>
<th>Desc.</th>
<th>Mid. LAD</th>
<th>Mid. LAD</th>
<th>Desc.</th>
<th>Right main</th>
<th>Left main</th>
<th>Circ.</th>
<th>Right main</th>
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</thead>
<tbody>
<tr>
<td>Number correlated</td>
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<td>47</td>
<td>49</td>
<td>47</td>
<td>36</td>
<td>35</td>
<td>45</td>
<td>28</td>
<td>49</td>
<td>47</td>
<td>28</td>
<td>44</td>
<td>47</td>
</tr>
<tr>
<td>% over-estimated</td>
<td>25%</td>
<td>19%</td>
<td>26%</td>
<td>17%</td>
<td>3%</td>
<td>12%</td>
<td>33%</td>
<td>4%</td>
<td>12%</td>
<td>21%</td>
<td>14%</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>% identical findings</td>
<td>63%</td>
<td>51%</td>
<td>41%</td>
<td>51%</td>
<td>15%</td>
<td>65%</td>
<td>73%</td>
<td>4%</td>
<td>66%</td>
<td>55%</td>
<td>66%</td>
<td>75%</td>
<td>73%</td>
</tr>
<tr>
<td>% under-estimated</td>
<td>12%</td>
<td>30%</td>
<td>33%</td>
<td>32%</td>
<td>15%</td>
<td>23%</td>
<td>17%</td>
<td>33%</td>
<td>33%</td>
<td>13%</td>
<td>11%</td>
<td>16%</td>
<td>18%</td>
</tr>
</tbody>
</table>

Figure 7

Accuracy of arteriographic estimation of diffuse (nonfocal) coronary luminal obstruction by segments. More heavily shaded areas in midportion of graph represent percentage of correctly estimated segments in which the luminal stenosis was graded 1 on gross inspection.

Discussion

The only study found in the literature in which estimation of coronary luminal disease by arteriography was checked by actual inspection of the vessels was that of Lemmon and co-workers, in which they obtained "essential agreement and good correlation" in eight of 13 cases (62 per cent). This agrees closely with our 61 per cent for nonfocal luminal stenosis; however, this agreement obviously is little more than coincidence when one considers the difference in method and sample size in the respective studies. It is also apparent that the incidence of minimal occlusive disease (grade 1) was a significant factor in the better correlative values obtained for nonfocal than for focal disease.

A limiting factor and possible cause for error when evaluating the results of this type of study, particularly when estimating focal disease by arteriograms, is present in the definition of segmental limits, that is, proximal, middle, and distal, in each major coronary artery.
artery. We can say only that we realized this difficulty from the start and made every effort to be as accurate as possible in defining segmental limits both on gross inspection and on estimating luminal disease by arteriography.

Another limiting factor was the necessity for applying hemostats to the proximal portion of the right main and left main coronary arteries to prevent reflux of contrast medium. The limited time (about 10 minutes) available for injecting the hearts and making roentgenograms in two planes prevented the use of careful placement of two “stick” ligatures; this was tried early in the study but not only proved too time-consuming but also provided a possible source for leakage of medium should the vessel wall be penetrated by the suture needle. Similarly, various types of plugs and adhesives were tried without success. Hence, the most proximal 5 to 10 mm. of the right and left main coronary arteries were not visualized on the arteriograms.

Perhaps a justifiable criticism might be made of the method of grading atherosclerosis of coronary arteries by gross rather than histologic estimation of the degree of coronary luminal narrowing. However, the principal concern was, first, not the type of process that caused the luminal stenosis or occlusion, but rather whether the obstruction and its site were readily demonstrable. Secondly, Lober found no appreciable difference in results in grading coronary sclerosis by several methods, namely, by relative area of lumen, intimal infiltration, relative thickness of intima, elastic degeneration, and outside diameter of artery. Also since ours was a postmortem study, we thought that the oft-used factor of tortuosity of coronary arteries would be difficult to interpret and should not be employed as a means of increasing the accuracy of estimation of coronary atherosclerosis by either gross inspection or arteriography, especially since tortuosity may be influenced largely by myocardial systole versus diastole.

The rather poor agreement of arteriographic with anatomic findings obtained in this study, particularly with regard to severe nonfocal involvement and focal involvement of any severity, was surprising. Furthermore, the results in estimating luminal disease in the proximal and middle segments of the main coronary arteries, which are believed as a group to represent portions of the coronary arteries that are technically the most amenable to surgical attack, were most disappointing. These findings suggest that coronary arteriography is not yet as absolute a method for selecting patients for direct coronary operations as many have thought and hoped it would be.

Until and unless arteriographic estimation is proved accurate in the great majority of cases by surgical or necropsy study, its use either for selection of patients to undergo direct coronary operations or for evaluation of coronary disease for diagnostic, therapeutic, or prognostic purposes should be accepted conservatively and hesitantly—accepted as an investigative method rather than as a technic of proved accuracy.

Summary and Conclusions

Fifty human hearts were studied to determine whether coronary arteriograms made at necropsy provided accurate information on coronary stenosis and occlusion. The coronary arteries of each heart were divided arbitrarily into 16 segments, a total of 479 of these segments being studied to determine (1) whether the arterial stenoses or occlusions were nonfocal or focal in character and (2) the degree of luminal obstruction present. The disease was termed “focal” if the length of obstruction was less than 5 mm. Luminal obstruction was graded as follows: 0 to 24 per cent stenosis, grade 1; 25 to 49 per cent, grade 2; 50 to 74 per cent, grade 3; 75 to 99 per cent, grade 3+; and 100 per cent occlusion, grade 4.

From the viewpoint of nonfocal disease, luminal obstruction was graded exactly the same by arteriography as by gross anatomic examination in 61 per cent of the 479 segments. The actual amount of luminal stenosis or occlusion was underestimated by arteriog-
raphy in 22 per cent and overestimated in 17 per cent.

Only 11 per cent of the 89 segments showing coexisting focal involvement were graded the same by the two methods. The involvement was underestimated by arteriography in 86 per cent and overestimated in only 3 per cent.

In nonfocal disease, arteriographic estimation of severe luminal obstruction (grades 3, 3+, or 4) appeared to be markedly inaccurate. In focal disease, however, severity of stenosis did not affect the accuracy of arteriographic estimation.

In those segments of the coronary arteries deemed most susceptible technically to direct surgical intervention, arteriographic estimation of coronary stenosis or occlusion was least reliable. Therefore, too much dependence on the reliability of coronary arteriograms for the exact evaluation of coronary disease seems unwarranted at this time. More correlative studies incorporating necropsy specimens, surgical inspection, and increased experience in roentgenographic interpretation of coronary arteriograms are greatly needed.

References

“Aortic Insufficiency”

Two of the infectious scourges of Dublin in the early eighteen hundreds were typhoid and typhus fevers. These were first differentiated on clinical grounds by another giant of the Irish School, Dominic Corrigan (1802-1880). Although his long career was studded with honors, and crowned with a baronetcy, Corrigan’s name is immortalized because of work done during his early twenties in a hospital of only six beds. By carefully selecting his patients for clinical investigation from Dublin’s sprawling slums, where syphilis was endemic, he was able to correlate the bounding “Corrigan pulse” with a “permanent patency of the aortic valve.”—K. M. Cahill, M.D. The Golden Era of Irish Medicine. The New England J. Med. 266: 545 (March), 1962.
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