Clinical Pathologic Correlations in Coronary Artery Disease

The extensive clinical utilization of coronary angiography and coronary artery surgery in recent years has heightened interest in the anatomy and pathology of the coronary arterial tree. Much new information has indeed been amassed concerning the patterns of distribution of the coronary arteries, the size and extent of interarterial coronary anastomoses, the nature, location, and extent of coronary artery narrowing and occlusion, and the correlation of these findings with pathologic changes in the myocardium and with clinical manifestations of coronary heart disease. Many years ago these matters were the subjects of extensive clinicopathologic studies based on the postmortem injection-plus-dissection technic developed by Schlesinger.1 We are, therefore, interested here in reviewing these early findings as well as the recent observations and assessing their significance for the many difficult problems that arise in the clinical management of coronary artery disease today.

Anastomoses

The most effective protection against the otherwise dire effects of coronary occlusions is afforded by the interarterial collateral circulation of the heart. In 1669 Lower described the development of anastomoses following arterial occlusion, but he did not state whether he had observed interarterial anastomoses in the coronary arteries of the normal heart.2 In a prolonged controversy, anatomists have maintained that interarterial coronary connections are normally present in man. Since aqueous solutions injected into one coronary artery appear immediately in the others, they are evidently connected at least by arteriolar and capillary vessels. Physiologists, however, have insisted that functionally the coronary arteries are end arteries inasmuch as acute experimental ligation or clinical occlusion of a large artery always produces myocardial infarction. Anastomoses present in the normal heart, therefore, are not of sufficient size and number to be functionally significant since they do not prevent myocardial infarction.

The development of larger, functionally important interarterial anastomoses has been demonstrated repeatedly following gradual experimental or atherosclerotic occlusion of a coronary artery.3-5 These collateral channels between coronary arteries serve to nourish myocardium beyond complete occlusions that would otherwise undergo necrosis, and they also serve as bypasses or detours to connect proximal and distal portions of occluded arteries. It has been shown experimentally that dogs and pigs may survive gradual complete occlusion of one or more main coronary arteries with little myocardial damage.6 The clinical counterpart of these experiments, i.e. the occasional complete absence of clinical symptoms and of myocardial infarction or fibrosis despite multiple, old coronary artery occlusions, emphasizes the functional significance of the compensatory collateral vessels.

The hearts of patients with angina pectoris usually show one or more occlusions of the coronary arteries, a rich collateral development, and variable myocardial fibrosis or infarction.7 While there is a general relationship between the incidence of coronary occlusion and the occurrence of angina...
pectoris, other modifying factors, such as the
precise location of occlusions, the importance of the
vessels involved, the adequacy of the collateral
circulation, the rates at which occlusions or
narrowing develop, the activity, psychological and
physical condition of the patient, such as anemia or
thyroid function, and the temporary influence of
emotion and of vasomotor reflexes, are also of great
importance.\(^8\), \(^9\) Although damage to the heart may
be reduced by the development of the collateral
circulation, the margin of safety, or, as it may be
termed, "the coronary reserve," is lessened.

By the Schlesinger lead-agar or barium-gelatin
injection technic the functionally important colla-
teral channels were found to be generally more
than 40\(\mu\) in diameter in fixed sections, which
correspond to 80\(\mu\) in fresh tissue. These large
anastomoses were ordinarily absent in normal
human hearts, but were demonstrated in hearts
with hypertrophy, coronary arterial narrowing or
occlusion, and in hearts of patients with anemia.\(^9\)
Several postmortem injection studies done with
varying materials and technics, have presented
conflicting evidence concerning the size of interar-
terial coronary anastomoses in normal human
hearts. Some investigators\(^{10-13}\) have concluded that
large functionally significant anastomoses are nor-
mafly present. Pitt,\(^{14}\) on the other hand, and the
many recent clinical angiographic studies\(^{15}\) have
confirmed Schlesinger's initial conclusions. Although
angiographic dyes are water soluble, they are
usually visible by X-ray only in the arterial branches
larger than 100\(\mu\) in diameter mainly because of the
limits of radiographic resolution. These intercoro-
nary anastomoses are not visualized in normal
human hearts, but do appear in the presence of
cardiac pathology and therefore provide informa-
tion of great functional and clinical significance. It
is of interest that both the earlier studies by the
Schlesinger technic and the more recent angiogra-
phic studies visualize the collateral channels by X-
ray.

Parallel to these anatomic observations, many
physiologic studies have amplified and confirmed
the protective significance of intercoronary anasto-
moses disclosed by the morphologic injection tech-
nics.\(^{16, 17}\)

The general older view of coronary arterioscle-
rotic heart disease as simple progressive myocardial
damage with narrowing and occlusion therefore is
not tenable. Instead, the final condition of the
myocardium is the resultant of opposing anatomic
and physiologic factors, i.e. the opposing morpho-
logic processes of atherosclerotic obstruction versus
the compensatory development of large collateral
channels and also variations in blood supply and
demand.

The time required for the development of
functionally significant anastomoses has been stud-
ied in animals. Available evidence indicates that
although sizable interarterial anastomoses become
visible within days after sudden coronary obstruc-
tion, several weeks are necessary for their rich
development, and several months may elapse
before their full potentiality is realized.\(^8\) A pressure
gradient between occluded and nonoccluded arterial
segments and hypoxia are important factors in
the development of these collateral vessels. The
slow development of these channels as well as of
the inflammatory reaction to necrosis emphasizes
the importance of rest and reduced activity for
many weeks after acute myocardial infarction,
contrary to the current tendency to early ambula-
tion. Similar efforts to reduce the cardiac require-
ment for blood would seemingly apply to patients
before infarction develops, when angina pectoris
first appears, or when the frequency or intensity of
the attacks suddenly increases. Such changes in
cardiac pain signal a new imbalance in blood
supply and demand in the heart. Ample evidence
exists that reduced cardiac work favors healing of
the infarct, reduces the extent of myocardial
damage, lessens liability of rupture, and provides
time for the development of these anastomotic
channels. The slow development of a richer
anastomotic circulation is also apparently respon-
sible for the occasional clinical improvement of
patients with angina pectoris, the collateral chan-
nels acting to offset the narrowing or occlusion.

Coronary Angiographic Studies

Studies in living patients have confirmed many
earlier anatomic and experimental observations and
have extended our knowledge of the coronary
circulation.\(^8, 15\) The angiographic group differs
from the old postmortem series in that it represents
an earlier stage of the disease compatible with
survival. In general, the postmortem findings are
anatomically more reliable, but give, however, only
inferential insight into functional blood flow. In
many comparative analyses the angiographic evi-
dence of coronary narrowing and occlusion con-
forms closely to the anatomic findings. The almost
invariable appearance of collateral channels when
stenosis is marked is verified by angiography. It is
stated, indeed, that "the presence of a collateral
circulation is helpful in defining the degree of stenosis. In addition, it will aid in predicting the results of revascularization procedures."\textsuperscript{19} A rapid runoff of the injected material indicates a rich collateral network that may be valuable in bypass surgery. Similarly, areas of infarction devoid of blood supply can be identified, thereby forestalling vain attempts to improve blood supply to the region.

A number of technics have been used for the measurement of myocardial blood flow during selective coronary arteriography. Indocyanine, krypton, xenon, and other substances have been used. The accuracy and usefulness of these methods are still under study.

**Hazards of Coronary Arteriography**

Coronary angiography is not devoid of risk.\textsuperscript{18, 20} Transient episodes of cardiac arrhythmias, acute cardiac ischemia, acute pulmonary edema, vascular hemorrhage at the site of puncture, vascular thrombosis, damage to the coronary arteries by the catheter, focal myocardial necrosis, and cardiac perforation are among the complications. Untoward incidents occur in 1–7\% of patients, depending on the technic employed and the experience of the group.\textsuperscript{21} In a series of 900 cases significant, but nonlethal complications occurred in 2.2%.\textsuperscript{22–25} In experienced hands a mortality of approximately 0.1\% may be achieved.\textsuperscript{26} Mortality rates above 0.3\% are considered unacceptable.\textsuperscript{27}

Experienced personnel, careful monitoring of cardiac rhythm, and adequate facilities for immediate resuscitation and external stimulation and countershock are mandatory.

**Indications for Coronary Arteriography**

Which patients should be advised to undergo the unavoidable mortality, morbidity, stress, and expense of this procedure? Angiography provides information necessary for surgical procedures such as bypass surgery in which the location of occlusions, of collateral blood flow runoff, and of myocardial damage are important considerations. Whether the operation itself is indicated may be decided by the angiographic findings. In patients with angina pectoris and aortic stenosis, it is important preoperatively to assess the relative significance of the valvular and coronary lesions.

The authors do not believe that coronary angiography should be undertaken merely to establish a diagnosis of angina pectoris, except under rare circumstances. The presence of arterial narrowing or occlusion does not establish a clinical diagnosis of angina pectoris. There is ample evidence that gradually developing occlusion of one or more arteries may occur without any cardiac symptoms. Conversely, some patients, particularly those with arterial hypertension, marked valvular disease, congenital heart disease, myocardial infarction, or pericarditis may have angina pectoris or cardiac pain mimicking angina pectoris, without coronary heart disease. Rarely a patient, such as an airplane pilot, or bus or truck driver, may be requested by employers to obtain angiographic clearance, but the wisdom of such a requirement may be debated.

It must be reiterated that the doctor-patient relationship has the welfare of the patient as its prime objective. Every ethical principle rejects the performance of angiography in man solely for the discovery of new knowledge unrelated to any therapeutic benefit to the patient.

**Surgical Relief of Coronary Occlusion**

The therapeutic problem in coronary artery disease is created by stenosis or complete occlusion of a vessel with consequent diminished coronary blood flow. To achieve direct relief of coronary disease by introducing a new source of arterial blood supply to the ischemic but viable myocardium, the following procedures have been performed in the past on man: (1) application of grafts of neighboring tissues (pectoral muscle, omentum, lung, stomach, jejunum); (2) production of pericardial adhesions; (3) myocardial insertion of an actively bleeding artery; (4) anastomosis of the coronary venous system with neighboring arteries; (5) ligation of internal mammary arteries; (6) endarterectomy; and (7) resection of atheromatous arterial segments with graft replacement. These procedures have been subjected to the test of animal experimentation, but, in addition, patients have undergone operations, and favorable effects on angina pectoris have been recorded. Despite many early enthusiastic reports, they have all now been generally discarded.

Currently, aortocoronary-vein bypass is being enthusiastically hailed as a major conquest, and some 20,000 operations evidently have been performed in the U.S.A. in the past 12 months.

The morphologic characteristics of coronary atherosclerosis are indeed favorable to surgical intervention. The obstructing lesions are in the main stems or primary branches, are mostly localized and segmental, are almost entirely epicardial, and 70\% lie within 4 cm of the coronary...
ostia.4, 28 The preoperative angiographic portrayal of the sites of coronary obstruction, the appraisal of the collateral runoff, and the extraordinary advances in surgical technic and in medical management during and following operation favor success.

Information on which to evaluate the operation is as yet meager.27, 29, 30 Some of the urgent questions that must be answered before the procedure can be confidently advised to patients are as follows: Is survival of patients with angina pectoris increased? What is the incidence, degree, and duration of improvement? Are myocardial infarction and congestive failure prevented? Is myocardial function improved? What is the duration of patency of the vein grafts and the quantity of blood flow through them?

Fragmentary data indicate that in some series, after 1 year, 22% of vein grafts are occluded, 18% of patients have sustained a myocardial infarction, and cardiac function is worsened in 50% of those with previous myocardial damage.30 In another series in which 105 vein grafts were assessed angiographically, 20% were occluded 2 weeks postoperatively and 50% were occluded in 1 year.31 In a series of 450 patients, 11% had acute myocardial infarction within 30 days after operation.32 In some centers where the operative death rate is only 3%, operative mortality increases to 15% if the myocardium is severely damaged.30 The interpretation of lessened angina pectoris after surgery is also beset with many difficulties of interpretation. For example, the nerve pathways from the heart to the nerve roots are not clearly defined. They traverse a wide pathway and may be transected by the operative procedure with abolition of the pain,33 but without changing the coronary blood flow, or indeed affecting the heart in any way. It is noteworthy in this connection that 80–90% of patients report complete or partial relief of angina pectoris, but the objective assessment of the results of operation with exercise testing and study of left ventricular function suggests lesser degrees of improvement.34

At the present time we believe that the only definite indication for bypass surgery is disabling angina pectoris unresponsive to medical treatment in patients without severe myocardial damage in whom the operative risk is commensurate with the anticipated improvement. The results in patients with refractory congestive failure have been unsatisfactory.27, 30 The extension of bypass surgery to patients with acute coronary obstruction (cardiac pain) without infarction and to patients with infarction and continuing pain or hypotension should be considered at present as experimental. A somewhat more detailed discussion with which we are in agreement has been presented recently by C. K. Friedberg.35

A central registry for data from the centers practicing these procedures is urgently needed. Controlled prospective studies comparing the results with randomized groups of similar patients managed without surgery are necessary.

HEMMAN L. BLUMGART
PAUL M. ZOLL

References
1. SCHLESINGER MJ: An injection plus dissection study of coronary artery occlusions and anastomoses. Amer Heart J 15: 528, 1938
2. LOWER R: Tractatus de corde item de motu et colore sanguinis, et chyle in eum transitu. Amstelodami, 1669
3. BLUMGART HL, SCHLESINGER MJ, DAVIS D: Studies on the relation of the clinical manifestations of angina pectoris, coronary thrombosis, and myocardial infarction to the pathologic findings, with particular reference to the significance of collateral circulation. Amer Heart J 19: 1, 1940
8. ZOLL PM, NORMAN LR: The effects of vasomotor drugs and of anemia upon interarterial coronary anastomoses. Circulation 5: 833, 1952

Circulation, Volume XLVII, June 1973


29. KOCHEUKOS NT, KIRKIN JW: Coronary bypass operations for ischemic heart disease. Mod Conc Cardiovasc Dis 41: 47, 1972


