Myocardial Consequences of Coronary Artery Bypass Graft Surgery

The Paradox of Necrosis in Areas of Revascularization

BERNADE H. BULKLEY, M.D., AND GROVER M. HUTCHINS, M.D.

SUMMARY Myocardial infarction after coronary artery bypass graft (CABG) surgery has been described clinically in up to 30% of patients but there is little morphologic information about the character and pathogenesis of this myocardial injury. We studied myocardium in the distribution of bypassed and nonbypassed coronary arteries for the presence of contraction band necrosis as compared to coagulation necrosis, in 58 autopsied patients who died less than 1 month after surgery. Operation related necrosis consisting of focal subendocardial contraction band necrosis was present to some degree in 48 (83%) patients. Regional transmural necrosis was present in 22 (38%) patients and was of two types. Contraction band necrosis occurred in 18 patients and was in the distribution of a patent bypassed coronary artery in 15 of them. Coagulation necrosis was found in four patients, and in each was in the distribution of a new graft-related coronary artery occlusion. The results suggest that coronary artery reflow through widely patent grafts following the period of operative nonperfusion, rather than graft or intrinsic coronary artery occlusion, accounts for the majority of operation-related myocardial "infarcts" associated with CABG surgery. Thus, prevention of intraoperative myocardial injury must also focus on characteristics of the phase of myocardial reperfusion.

THE STATUS OF THE MYOCARDIUM AFTER AORTOCORONARY BYPASS SURGERY remains an issue of uncertainty and controversy. Although this procedure has proved of value in the symptomatic treatment of angina pectoris, the mechanism of improvement remains unclear. Symptomatic improvement occurs in over 80% of patients, but for the majority of patients little evidence exists that this operation improves ventricular function or prolongs life. The incidence of operation related myocardial infarction is approximately 10%, with a range between 2 and 30%, depending upon the method of detection, i.e., new Q-waves, contrast ventriculography, or radionuclide imaging. Despite these observations there is little if any morphologic information about the character and the pathogenesis of the early myocardial lesions after aortocoronary artery bypass surgery. In this study we evaluated the myocardium in the distribution of both the bypassed and nonbypassed coronary arteries in 58 autopsied patients who died early (<30 days) after operation to determine the nature of the myocardial injury associated with this procedure and its relationship to the local vasculature. Particular attention was paid to whether myocardial lesions were coagulation necrosis or contraction band necrosis since the mode of development as well as the pathological appearance of the two lesions are distinctive.

Materials and Methods

All patients at The Johns Hopkins Hospital who died within one month of an aortocoronary artery bypass graft operation, and on whom autopsy examinations were performed, were included in this study. Postmortem coronary arteriography using a barium-gelatin-pigment injection mass was performed on all hearts. Hearts were then fixed with formalin in a distended state. Stereoscopic radiographs were prepared of the intact heart and its transverse sections and samples of myocardium for histologic examination were taken in the distribution of each of the major coronary arteries and each coronary artery bypass graft. Additional sections were taken from septum, and anterior, posterior, and lateral left ventricle and margin of the right ventricle at mid ventricle level to determine overall myocardial injury. A minimum of ten sections per heart were examined. Histologic sections were reviewed for extent, type and age of myocardial injury. Necrosis was graded on a scale of 0–4 +, with 4 + corresponding to greater than 30% of the area of a transverse slice of left ventricular (LV) myocardium; 3 +, 20–30%; 2 +, 10–20%; and 1 +, less than 10%, as determined from analysis of cross-sections through the LV ventricle, one toward the base, one at mid LV and one halfway between mid LV and apex. In addition, the anastomosis site with part of the proximal and distal intrinsic coronary artery was removed "en bloc," and for each, stereoscopic radiographs in two planes prepared. After light decalcification, the tissue was routinely processed, embedded with paraffin and serially sectioned transversely at 8 µ. Every fifteenth section was retained and stained with hematoxylin and eosin, elastic-van Gieson or phosphotungstic acid-hematoxylin.

For each patient the clinical record including operative and anesthesia reports were reviewed, as were the gross heart specimen, stereoscopic radiographs, gross photographs, and the histologic sections of myocardium, coronary arteries, and bypass grafts. Patency of graft and intrinsic coronary artery at the graft-artery anastomosis was determined from the radiographs, gross examination, and review of serial histologic sections. The point of maximum narrowing of the coronary artery lumen at the proximal end of the arteriography was determined from sections of the proximal pre-arteriography graft and coronary artery. A similar point of maximum lumen narrowing at the distal end of the arteriography and a representative section of coronary artery

From the Cardiovascular Division of the Department of Medicine and the Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, Maryland.

Supported by grant P50-HL-17655-03 with The National Institutes of Health, Public Health Service, Department of Health, Education and Welfare and the Stetler Research Fund for Women Physicians.

Address for reprints: Dr. Bernadine H. Bulkley, Cardiovascular Division, The Johns Hopkins Hospital, Baltimore, Maryland 21205.

Received April 6, 1977; revision accepted June 27, 1977.
distal to the anastomotic site were selected. The outlines of the lumen, internal elastic lamina, and external elastic lamina of the coronary artery at each level were projected, drawn on tracing paper, and the area of the lumen of coronary artery wall determined using a planimeter. The percent occlusion of the coronary artery lumen at the proximal and distal ends of each anastomosis compared to the adjacent lumen was calculated. Narrowings of the luminal area of greater than 75% were considered to be significant.

Results

Clinical Findings

Of the 67 autopsies at The Johns Hopkins Hospital after coronary artery bypass surgery, 58 of the patients had died within one month of operation (table 1). These patients ranged in age from 37 to 75 years (average 56 ± 4) and 15 (26%) were women; 54 (93%) were class III-IV (New York Heart Association) with regard to angina pectoris and four patients without severe angina had grafts placed into critically narrowed vessels at the time of valve replacement. Of these 58 patients, 23 died in the operating room, 13 died within 24 hours of operation, and 22 died between 1 and 30 days of operation. The 58 patients had 114 coronary artery bypass graft anastomoses: 109 utilized saphenous veins; 5, internal mammary arteries. End-to-side anastomoses were made at 106 sites and jump grafts at eight.19 Single grafts were placed in 18 patients; two grafts in 26; three in 12; and four, in two patients. The average number of grafts per patient was 2.0. Additional operative procedures included aneurysmectomy or infarct-plication in nine patients and aortic or mitral valve replacements in nine. Of the 35 patients that died after leaving the operating room, a new myocardial infarct was detected by electrocardiogram (new Q-waves) in three (9%).

Morphologic Findings

 Coronary Vasculature

Morphologic findings in the intrinsic coronary arteries, and in the vascular grafts are summarized in tables 1 and 2. Of the 114 grafts, 93 (82%) were patent and 21 (19%) were totally occluded at the distal portion of the coronary artery to graft anastomosis. All total graft occlusions included the anastomosis site. Lesser degrees of narrowing, between 75 and 99%, of the intrinsic coronary artery at the distal anastomosis site were present in 14 (12%) of the 114 grafts. Mechanisms of narrowings and occlusions of these vessels

<table>
<thead>
<tr>
<th>Time of Death Relative to Operation</th>
<th>Intra-operative</th>
<th>1-84 Hours</th>
<th>1-84 Days</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>23</td>
<td>13</td>
<td>22</td>
<td>58</td>
</tr>
<tr>
<td>Age (mean ± sd) years</td>
<td>56 ± 8</td>
<td>56 ± 7</td>
<td>56 ± 4</td>
<td></td>
</tr>
<tr>
<td>No. of women (%)</td>
<td>6 (26%)</td>
<td>4 (31%)</td>
<td>5 (23%)</td>
<td>15 (26%)</td>
</tr>
<tr>
<td>Preoperative myocardial infarct</td>
<td>10 (43%)</td>
<td>6 (46%)</td>
<td>11 (50%)</td>
<td>27 (47%)</td>
</tr>
<tr>
<td>Clinically diagnosed postoperative MI (Q-wave)</td>
<td>-</td>
<td>0</td>
<td>3 (14%)</td>
<td></td>
</tr>
<tr>
<td>No. of coronary arteries narrowed &gt;75%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 ( 4%)</td>
<td>0</td>
<td>0</td>
<td>1 ( 2%)</td>
</tr>
<tr>
<td>1</td>
<td>2 ( 9%)</td>
<td>1 ( 8%)</td>
<td>6 (27%)</td>
<td>9 (16%)</td>
</tr>
<tr>
<td>2</td>
<td>6 (26%)</td>
<td>8 (62%)</td>
<td>6 (27%)</td>
<td>20 (34%)</td>
</tr>
<tr>
<td>3 or more</td>
<td>14 (61%)</td>
<td>4 (31%)</td>
<td>10 (45%)</td>
<td>28 (48%)</td>
</tr>
<tr>
<td>Left main</td>
<td>8 (36%)</td>
<td>4 (31%)</td>
<td>3 (14%)</td>
<td>15 (26%)</td>
</tr>
<tr>
<td>Grafts per patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 graft</td>
<td>5 (22%)</td>
<td>4 (31%)</td>
<td>9 (41%)</td>
<td>18 (31%)</td>
</tr>
<tr>
<td>2 grafts</td>
<td>10 (43%)</td>
<td>6 (46%)</td>
<td>10 (45%)</td>
<td>26 (45%)</td>
</tr>
<tr>
<td>3 grafts</td>
<td>6 (26%)</td>
<td>3 (23%)</td>
<td>3 (14%)</td>
<td>12 (21%)</td>
</tr>
<tr>
<td>4 grafts</td>
<td>2 ( 9%)</td>
<td>0</td>
<td>0</td>
<td>2 ( 3%)</td>
</tr>
<tr>
<td>Average grafts per patient</td>
<td>2.2</td>
<td>1.9</td>
<td>1.7</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Myocardial Injury

1. Preoperative

- Focal subendocardial fibrosis
  - Transmural fibrosis
  - 3 (13%) 2 (15%)
  - 10 (17%)

2. Operative

- Focal subendocardial necrosis
  - Regional necrosis (3-4+)
  - 18 (78%) 11 (85%)
  - 19 (96%)
  - 48 (83%)
  - 9 (90%)
  - 9 (91%)
  - 22 (38%)

Bypass Grafts (Total)

- Widely patent
  - 39 (76%)
  - 16 (64%)
  - 24 (63%)
  - 79 (69%)

Narrowed

- >75–99
  - 6 (12%)
  - 3 (12%)
  - 5 (13%)
  - 14 (12%)
  - 6 (12%)
  - 6 (24%)
  - 9 (24%)
  - 21 (18%)

Major Cause of Death

- Cardiogenic shock
  - 14 (61%)
  - 4 (31%)
  - 6 (27%)
  - 24 (41%)

- Arrhythmia

- Pulmonary embolus

- CVA

- Sepsis

- Other

- Unknown

- 5 (22%)

- 3 (13%)

- 4 (18%)

- 12 (21%)
TABLE 2. Operative Myocardial Injury: Regional Transmural Myocardial Necrosis in 22 Patients

<table>
<thead>
<tr>
<th></th>
<th>Time of Death Relative to Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intra-Operative</td>
</tr>
<tr>
<td><strong>Total number of patients</strong></td>
<td>23</td>
</tr>
<tr>
<td>I. Patients with necrosis</td>
<td></td>
</tr>
<tr>
<td>Coagulation Necrosis</td>
<td></td>
</tr>
<tr>
<td>Gift distribution</td>
<td>9</td>
</tr>
<tr>
<td>Nongraft distribution</td>
<td>0</td>
</tr>
<tr>
<td>Contraction Band Necrosis</td>
<td></td>
</tr>
<tr>
<td>Gift distribution</td>
<td>9</td>
</tr>
<tr>
<td>Nongraft distribution</td>
<td>0</td>
</tr>
<tr>
<td>II. Myocardium in graft distribution</td>
<td></td>
</tr>
<tr>
<td>Total Number of Grafts</td>
<td></td>
</tr>
<tr>
<td>Grafts Occluded:</td>
<td></td>
</tr>
<tr>
<td>With contraction band necrosis</td>
<td>18 (40%)</td>
</tr>
<tr>
<td>With coagulation necrosis</td>
<td>0</td>
</tr>
<tr>
<td>Patent Grafts:</td>
<td></td>
</tr>
<tr>
<td>With contraction band necrosis</td>
<td>18 (40%)</td>
</tr>
<tr>
<td>With coagulation necrosis</td>
<td>0</td>
</tr>
</tbody>
</table>

Myocardial Lesions

General

In 36 (62%) patients preoperative myocardial injury included focal fibrosis in the subendocardium and the tips of papillary muscles in ten, and healed transmural myocardial infarcts in 26 (table 1). In 48 (83%) patients there was operative myocardial injury of some degree, but in 22 (38%) patients there were areas of regional necrosis of 3-4+ severity equivalent to so-called transmural injury, in that necrosis involved greater than 2/3 of the thickness of left ventricular wall. The "transmural" injury in this group of 22 patients is the major focus of this study. Small foci of myocardial necrosis, present mostly in the subendocardium, were also found in 26 patients without regional transmural necrosis, and in the remaining myocardium in many cases where severe regional injury was present. There were ten (17%) patients with no identifiable operative myocardial necrosis, other than that related to left ventricular vents or suture placement. In three patients postoperative myocardial infarcts were found secondary to occlusion of coronary arteries by thrombus overlying ulcerated atherosclerotic lesions. Neither these three infarcts nor the 26 preoperative myocardial infarcts is included in this analysis of operative myocardial necrosis.

Regional Transmural Myocardial Necrosis

The morphologic findings in the 22 (38%) patients with regional transmural necrosis are summarized in tables 2 and 3. The myocardial injury was of two types: coagulation necrosis and contraction band necrosis. The more commonly recognized form of necrosis, coagulation necrosis, usually develops in the setting of permanent vessel occlusion. In its earliest stage (as early as 1-2 hours), coagulation necrosis may be recognized by thin wavy fiber formation; by 6 to 12 hours cytologic changes of necrosis of myocardial fibers and an inflammatory response become evident (fig. 1). Regional transmural coagulation necrosis was present in four (11%) of the 35 patients who survived operation and in each instance it was in the distribution of a newly occluded bypassed vessel. In each of the four patients, the histological age of the infarct was compatible with having developed at the time of operation. Although thin wavy fiber change was not observed in the 23 patients who died at operation, it is possible that the time lapse in this group may not have been sufficient to allow this myocardial lesion to develop.

Contraction band necrosis, a distinctive type of myocardial injury, develops in myocardium that has been reperfused after a period of transient nonperfusion, but also may be induced by certain nonischemic insults such as catecholamine exposure. The histological changes of contraction band necrosis include the appearance of transverse eosinophilic sarcoplasmic condensations of contractile elements, and interstitial and cellular swelling (fig. 1).

TABLE 3. Correlation of Vascular Patency with Necrosis in Graft Distribution

1. Contraction band necrosis: 15 patients
   Number of grafts placed 35
   Number of vessels bypassed* 38
   Necrosis (3-4+) in vessel distribution 30/38 (79%)
     Vessel widely patent 28/29 (97%)
     75-99% narrowed 2/6 (33%)
     100% occluded 0/3
   Number of major coronaries not bypassed 0/10
     Necrosis (3-4+) in vessel distribution 0/0
     Vessel widely patent 0/0
     75-99% narrowed 0/0
     100% occluded 0/0

2. Coagulation necrosis: 4 patients
   Number of grafts placed 5
   Number of vessels bypassed 5
   Necrosis (3-4+) in vessel distribution 4/5 (80%)
     Vessel widely patent 0/1
     75-99% narrowed 0/1
     100% occluded 4/5 (100%)
   Number of major vessels not bypassed 0/7
     Necrosis (3-4+) in vessel distribution 0/0
     Vessel widely patent 0/5
     75-99% narrowed 0/1
     100% occluded 0/1

*Three grafts were placed along major branchpoints.
Subsequently, myocardial cell nuclei disappear, an inflammatory process develops and necrotic myocardium is gradually removed by macrophagic activity to be replaced by fibrous tissue. The vasculature undergoes a simultaneous series of alterations giving the myocardium a grossly hemorrhagic appearance. Initially there is a congestion and hyperemia which is followed by extravasation of blood into the interstitium and by about 24 hours intimal fibrin deposits can be found in small vessels in the areas of necrosis. A fibrous scar forms the end point of both coagulation and contraction band necrosis.

Regional transmural necrosis was of the contraction band type in 18 patients, or in 82% of the patients with transmural necrosis; in 15 of these necrosis occurred in the distribution of a bypassed coronary artery. All but one of the latter patients died within 48 hours of operation suggesting the necrosis developed intraoperatively or in the immediate postoperative period.

**Relationship of Regional Transmural Necrosis to Vascular Patency**

Although 21 grafted arteries had new distal occlusions myocardial infarcts occurred in the distribution of the new occlusions in only 4 (19%) patients, or in 27% of patients who survived operation. In each case the injury was coagulation necrosis. In the patients with coagulation necrosis (fig. 2) there was no injury in the distribution of the one bypass graft that was widely patent nor were there necroses in the distribution of the nonbypassed vessel regardless of the degrees of narrowing (table 3).

In contrast to the transmural coagulation necrosis in the distribution of newly occluded vessels, regional transmural necrosis developed in the distribution of 30 (32%) of the 93 patent grafts, and in each instance it was of the contraction band type. This injury occurred in 15 patients in whom 35 bypass grafts had been placed (table 3). As three of these bypasses were placed at a branchpoint, a total of 38 vessels were bypassed by these grafts (fig. 3). Thus, necrosis developed in the myocardium in the distribution of 30 of the 38 vessels, and on the average each patient showed two separate areas of regional myocardial necrosis. Of the 38 vessels bypassed, 29 were widely patent, and necrosis developed in the distribution from 28 (97%) of them. Of the remaining nine grafted vessels, six had 75–99% narrowing distally and myocardial necrosis developed in their myocardial infarcts.
dium of distribution in two (33%); three had new total occlusions, and their myocardium of distribution showed no coagulation or contraction band necrosis. In the three branching vessels, one branch was occluded by the new anastomosis and one widely patent, and in each instance necrosis was present only in the distribution of the patent branch. One of the patients survived 48 hours and no coagulation necrosis was evident in the myocardium in the distribution of the obstructed branch vessel. In these same 15 patients, ten major coronary arteries were not bypassed, and there was no transmural myocardial injury in the distribution of any of these ten vessels, despite their degree of narrowing by old atherosclerotic plaque: one was widely patent, seven were 75–99% narrowed, one was 100% occluded. Thus, 30 natural or bypassed vessels were widely patent at autopsy, and regional transmural necrosis was present in the myocardium of their distribution in 28 (93%). Eighteen arteries, grafted or ungrafted, were narrowed by greater than 75% or occluded, and 3–4+ myocardial necrosis developed in the distribution of only two (11%) of them.

Three other patients had 3–4+ myocardial necrosis of the contraction band type, in the distribution of nongrafted vessels. In two of them, operated upon in the first year of bypass operations at this institution, regional injury occurred in the distribution of patent nongrafted vessel due to a coronary perfusion cannula which inadvertently transiently obstructed flow during operation. In these 2 patients there was no injury in the distribution of their other vessels grafted or ungrafted regardless of patency. The one other patient with an occluded graft to the left anterior descending coronary artery who died 4 days after operation had regional transmural contraction band necrosis in the distribution of the widely patent, dominant right coronary artery, and no injury in the distribution of the newly occluded grafted artery. After 4 days it is less easy to be confident that myocardial injury was intraoperative.

Comparison of Patients with and without 3–4+ Regional Transmural Necrosis

As can be seen in table 4 there were no significant differences between the 22 patients who developed transmural myocardial necrosis and the 36 who did not, with regard to age, sex, history of preoperative myocardial infarction or congestive heart failure. There was a somewhat greater incidence of three vessel and left main coronary artery disease in the patients with severe injury as opposed to those patients without severe regional transmural necrosis, but the differences were not statistically significant. Coagulation necrosis developed in four patients who had less severe coronary disease than the overall group studied; they had an average of 1.5 coronary arteries narrowed compared to 2.6 for the group as a whole. No significant differences could be determined between the two groups with regard to operative procedure, duration of cardiopulmonary bypass, cumulative anoxic arrest time, or single maximum period of anoxic arrest, and comparison of the periods of survival for

Figure 2. Patient with coagulation necrosis in the distribution of an occluded internal mammary artery (IMA) to left anterior descending coronary artery (LAD) anastomosis. Death occurred two days after operation. A. Postmortem coronary arteriogram viewed in the anatomic position. The IMA graft is occluded at its distal end and has its distal anastomosis at the arrow on the right. The critical stenosis bypassed is indicated at the upper arrow. B. Transverse section of right (RV) and left (LV) ventricles showing graft (IMA) anastomosed to the LAD. The infarct (arrow) is in the interventricular septum. C. Coagulation necrosis with thin wavy fiber change, nuclear pyknosis, and acute inflammatory cell infiltrate in the myocardium supplied by the operatively occluded grafted artery. (Hematoxylin and eosin, × 350.)
Thus, myocardial distribution of necrosis, in incidence regarding the distribution from the pericarditis. myocardial clinical detection of those with necrosis patients (38%) is biased only 14% to in injury related to myocardial the patients with and without necrosis also showed no differences. All 35 patients who died at operation or within 24 hours of operation were exposed to continuous intravenous pressor therapy but there were no differences between the 13 with necrosis and the 22 without regard to dosages or type of pressor agent used insofar as could be determined from the operative and postoperative records.

Discussion

Coronary artery bypass surgery is unequivocally successful in the symptomatic relief of angina pectoris, a success which usually occurs without improving, and frequently impairing, ventricular function despite patent of the majority of bypass grafts. To determine the character and possible pathophysiologic of the myocardial injury related to coronary artery bypass surgery, we examined the 58 patients who came to autopsy within 30 days of this operation. In the majority (62%) of the patients studied there was no significant operative injury; in 22 patients (38%) there was regional transmural necrosis. In only 14% of the patients with transmural necrosis (and 9% of those with necrosis dying after operation) was the injury apparent clinically by electrocardiogram. Although our patient population is biased to the non-survivor, the low incidence of clinical detection in our patients suggests that ECG far underestimates the true incidence of new operative related myocardial necrosis, an underestimation which may well stem from the problem of the postoperative period including pericarditis.

Although an autopsy study cannot provide precise incidence information, it does provide pathophysiologic data regarding the type and possible mechanisms of the injury associated with aortocoronary bypass procedures. From this study it appears that most operative related infarctions are in the distribution of bypassed arteries, but are not true "infarctions" in that most are associated with patent and not occluded vessels. In the 22 patients with transmural regional myocardial necrosis, there were 34 regional areas of injury in the distribution of grafts and 30 (88%) of them were in the distribution of patent grafts and distal coronary arteries. Thus, myocardial infarction after operation does not necessarily mean that the new graft is occluded and that reoperation should be performed, for the new "infarct" is more apt to have developed in the region of myocardium supplied by a well constructed, widely patent bypass graft. Almost paradoxically the myocardial injury is occurring in regions of myocardium newly exposed to unobstructed blood flow. Furthermore, in comparing the groups of patients with and without severe operative necrosis, there were no significant differences between the two groups with regard to age, sex, incidence of congestive heart failure.

Table 4. Comparison of Patients with and without Severe Operative Necrosis

<table>
<thead>
<tr>
<th>With Necrosis*</th>
<th>Without Necrosis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>22 (38%)</td>
</tr>
<tr>
<td>Age (avg.) years</td>
<td>35-75 (50)</td>
</tr>
<tr>
<td>Sex: M:F</td>
<td>19:3</td>
</tr>
<tr>
<td>% Male</td>
<td>86%</td>
</tr>
<tr>
<td>Preoperative MI</td>
<td>9 (41%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>No. Coronary Arteries Narrowed &gt;75%</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>2</td>
<td>6 (27%)</td>
</tr>
<tr>
<td>3</td>
<td>13 (59%)</td>
</tr>
<tr>
<td>Left Main</td>
<td>7 (32%)</td>
</tr>
<tr>
<td>Average (3.0)</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Operative Procedure

Plication/Aneurysm | 1 (5%) | 7 (19%) |
Valve replacement | 6 (27%) | 5 (14%) |
AVR | 6 (27%) | 3 (8%) |
MVR ± AVR | 2 | 2 |
No. SVBG's per patient (avg.) | 2.0 | 1.9 |
Pump time (min): | 188 ± 75 | 181 ± 70 |
Anoxic arrest period (min): | | |
Single maximum | 35 ± 16 | 25 ± 15 |
Cumulative | 64 ± 41 | 50 ± 27 |
Heart weight (mean = SD) | 518 ± 118 | 541 ± 163 |

Survival

Operation | 9 (41%) | 14 (39%) |
Hours | 4 (18%) | 8 (22%) |
Days | 9 (41%) | 14 (39%) |

*No feature showed a difference significant at P = 0.05 level by the Chi square or unpaired t-test.
Includes time period for valve replacements and for intraoperative resuscitation when patients could not be separated from bypass.

Figure 3. Patient with contraction band necrosis in the distribution of a widely patent saphenous vein bypass graft (SVBG) from the aorta (Ao) to the left anterior descending (LAD) coronary artery. Death occurred two days after operation. A. Postmortem arteriogram showing widely patent distal SVBG to LAD anastomosis at the arrow. B. Transverse section through right (RV) and left (LV) ventricles showing dark hemorrhagic regional transmural contraction band necrosis in the anterior LV and interventricular septum (IVS). The area of contraction band necrosis corresponds to the distribution of the successfully bypassed LAD. C. Contraction band necrosis of myocardium in the distribution of the LAD. Note transverse sarcoplasmic bands, nuclear loss, sarcoplasmic swelling and congestion of capillaries. (Hematoxylin and eosin, × 231.)
severity of coronary artery disease, nor were there
differences between the number of grafts placed, the total
cardiopulmonary bypass pump time, periods of anoxic
arrest or hypothermic ventricular fibrillation or exposure to
pressor therapy. Again, the techniques of operation could
not explain the differences between those patients who died,
and did or did not develop the regional necrosis.

There are two interdependent aspects of this seeming
paradox of myocardial necrosis in these postoperative
patients. One is that approximately three-quarters of the
time necrosis developed in the distribution of patent grafted
vessels; the second is that approximately three-quarters of the
time necrosis did not develop in the distribution of newly
occluded grafted coronary arteries. With regard to the
latter, we know from both animal experiments and human
studies\textsuperscript{27, 28} that when a coronary artery is occluded,
coagulation necrosis results. In the somewhat different situ-
ation of a newly occluded grafted coronary artery, however,
collateral blood supply is likely well developed in the dis-
tribution of the critically stenosed vessel, protecting myocard-
dium from infarction from a new occlusion. This is somewhat
analogous to patients with severe coronary artery
disease who come to catheterization or autopsy with one or
more totally occluded coronary arteries but no evidence of
infarction. Although the numbers are small, it may be of
significance that the four patients who developed infarcts in
the distribution of vessels with new coronary occlusions had
less severe coronary disease and, therefore, may have had
less well developed collaterals than the group that did not
develop necrosis.

Less easy to explain is the necrosis in the distribution of
widely patent vessels, which represents the majority (82%) of
the operative related transmural injury in our patients.
Perhaps the best clue to its etiology is that the injury was a
regional contraction band necrosis. Contraction band
necrosis may be caused by ischemia due to transient in-
terruption of blood flow, and also by certain drugs such as
isoproterenol.\textsuperscript{11–14} The latter may induce necrosis without
coronary blood flow interruption by a direct toxic effect on
myocardium, possibly caused by increased calcium
permeability.\textsuperscript{24} When nons ischemic drug induced contraction
band necrosis occurs, however, it is a diffuse lesion not
respecting the distribution of any given vessel. Similarly,
when hypotension is a cause of myofibrillar degeneration
the lesion tends to be a diffuse subendocardial insult. Thus
although hypotension or pressor therapy may have
aggravated the necrosis in some of our patients, it is difficult
to explain the regional character of the injury by hypoten-
sion or drugs.

What was particularly striking about the severe contrac-
tion band injury noted in our patients in this study was not
only its regional distribution, but also its presence ex-
clusively in the distribution of vessels which were patent, and
in 93%, widely patent, suggesting an association with cor-

nary blood flow per se, and thus an ischemic etiology. Con-
traction band necrosis of ischemic origin requires two
sequential phases for its development: a period of nonper-
fusion in which the myocardium becomes ischemic, followed
by a period in which the previously ischemic myocardium is
reperfused.\textsuperscript{37} It is not clear, however, whether the myocard-
dium at the time of reflow is always dead with reflow merely
marking the region of irreversibly damaged tissue.

Findings in our patients, which represent a unique human
model of transient interruption of coronary artery perfusion
followed by reflow, suggest that reflow itself may be causing
necrosis. Despite the same degree of coronary stenosis, the
same operative milieu, the same periods of nonpulsatile
pump perfusion, or aortic-cross clamp, anoxic arrest and
ventricular fibrillation, and similar exposure to pressor
amines, myocardial contraction band necrosis developed in
regions newly exposed to unobstructed reflow. In the same
hearts, areas of myocardium in which reflow was impaired by
new or pre-existing arterial narrowings such severity of
injury did not occur. And, in the myocardium in the distribu-
tion of new occlusions, coagulation necrosis did not occur.
The latter situation is perhaps best illustrated by the three
narrowed coronary arteries that were bypassed immediately
proximal to a branchpoint. With virtually identical con-
ditions for developing necrosis, necrosis developed only in
the distribution of the patent and not the occluded branch.
Thus, it appears that myocardium which has the same
potential for developing contraction band necrosis may sur-

vive if reflow is inhibited.

Although there is virtually no information in humans, experi-
mental studies in animals have suggested that reflow itself
may be deleterious\textsuperscript{25, 26, 28–30} and may limit the
usefulness of revascularization procedures within hours of
acute coronary occlusion.\textsuperscript{31, 32} During ischemia a number of
biochemical and structural alterations occur including intra-
cellular acidosis, depletion of high energy phosphates, and
loss of integrity of cell and mitochondrial membranes for
both myocardial cells and vascular endothelium. But at what
point such ischemic alterations become irreversible is not
clear. Reflow of sufficiently ischemic tissue will lead to
severe structural and metabolic changes, including calcium
and sodium influx, the loss of needed co-factors, nucleotides,
enzymes and ions, cell and organelle swelling and
mineralization of mitochondria.\textsuperscript{37} That such reflow
phenomena of themselves are critical events in the onset of
necrosis for some cells exposed to potentially reversible
ischemic damage is highly likely. One might wonder whether
myocardial preservation could be enhanced in patients un-
dergoing aortocoronary artery bypass surgery by altering
the method of reflow after periods of non-perfusion, either
by introducing reflow more slowly or by manipulating the
pH, oxygen or calcium content of the reflow medium. Such
efforts will be of value not only to the problems of myocar-
dial preservation during coronary artery bypass surgery, but
also to the efforts at surgically reperfusing myocardium in
patients after acute coronary occlusion.

References
1. Ross RS: Ischemic heart disease: An overview. Am J Cardiol 36: 496,
1975
Failure of successful grafting to improve resting left ventricular function
3. Hutchinson JE III, Green GE, Mekhjian HA, Kemp HG: Coronary
bypass grafting in 376 consecutive patients, with three operative deaths. J
Thorac Cardiovasc Surg 67: 7, 1974
4. Hultgren HW, Miyagawa M, Buck W, Angell WW: Ischemic myocar-
5. Brewer DL, Bilbro RH, Bartel AG: Myocardial infarction as a complica-
graft surgery for coronary artery disease. Survival and angiographic
results in 1,000 patients. Circulation 48 (suppl III): III-184, 1973
7. Rose MR, Glassman E, Isom OW, Spence FC: Electrocardiographic
and serum enzyme changes of myocardial infarction after coronary
coronary artery bypass surgery for angora pectoris. Am J Cardiol 33:
221, 1974
DA, Wallace RB, Davis GD, Elveback LR, Danielson GK: Relation of
intraoperative or early postoperative transmural myocardial infarction
to patency of aortocoronary bypass grafts and to diseased ungrafted
coronary arteries. Am J Cardiol 35: 767, 1975
10. Klausner SC, Botvinick EH, Shames D, Roe B, Fishman N, Ulliot D,
Ebert P, Chatterjee K, Parmley WW: The value of radionuclide infarct
imaging to confirm the diagnosis of significant peri-operative myocardial
infarction during revascularization. (abstr) Am J Cardiol 37: 148, 1976
the myocardial cell to injury. Arch Pathol 85: 189, 1968
12. Jennings RB, Sommers HM, Herdson PB, Kaltenbach JP: Ischemic in-
of progressive systemic sclerosis: A cause of cardiac dysfunction. Circula-
tion 53: 483, 1976
14. Hutchins GM, Anaya OA: Measurements of cardiac size, chamber
volumes and value orifices at autopsy. Johns Hopkins Med J 133: 96,
1973
15. Bulkley BH, Hutchins GM: Accelerated “atherosclerosis”: A
morphologic study of 97 saphenous vein coronary artery bypass grafts.
Circulation 55: 163, 1977
16. Hutchins GM, Bulkley BH: Mechanisms of occlusion of saphenous vein-
17. Griffith LSC, Bulkley BH, Hutchins GM, Brawley RK: Occlusive changes
at the coronary artery-by-pass graft anastomosis: Morphologic study of 95 grafts.
J Thorac Cardiovasc Surg 73: 668, 1977
19. Furlong MB Jr, Gardner TJ, Gott VL, Hutchins GM: Myocardial infar-
cion complicating coronary perfusion during open-heart surgery. J
Thorac Cardiovasc Surg 63: 185, 1972
20. Bulkley BH, Roberts WC: Atherosclerotic narrowing of left main cor-

MYOCARDIAL CONSEQUENCES OF CABG SURGERY/Bulkley, Hutchins 913

Beddingfield G, Manley JC: Late results of saphenous vein bypass graft-
22. Maurer BJ, Oberman A, Holt JH Jr, Kouchoukos NT, Jones WB,
Russell RD Jr, Reeves TJ: Changes in grafted and nongrafted coronary
arteries following saphenous vein bypass grafting. Circulation 50:
293, 1974
23. Campeau L, Crochet D, Lesperance J, Bourassa HG, Grondin CM:
Postoperative changes in aortocoronary saphenous vein grafts revisited.
Angiographic studies at two weeks and at one year in two series of con-
secutive patients. Circulation 52: 369, 1975
25. Rona G, Chappel CI, Balazs T, Gaudry R: An infarct-like myocardial
lesion and other toxic manifestations produced by isoproterenol in the rat.
Arch Pathol 67: 443, 1959
26. Bloom S, Davis DL: Calcium as mediator of isoproterenol-induced
27. Sommers HM, Jennings RB: Experimental acute myocardial infarction.
Histologic and histochemical studies of early myocardial infarcts induced
by temporary or permanent occlusion of a coronary artery. Lab Invest
13: 1491, 1964
and myocardial infarcts: Ulceration of atherosclerotic plaques precipitat-
ing coronary thrombosis. Am Heart J 93: 468, 1977
29. Whalen DA Jr, Hamilton DG, Ganote CE, Jennings RB: Effect of a tran-
sient period of ischemia on myocardial cells. I. Effect on cell volume
30. Kloner RA, Ganote CE, Whalen DA Jr, Jennings RB: Effect of a tran-
sient period of ischemia on myocardial cells. II. Fine structure during the
first few minutes of reflow. Am J Pathol 74: 399, 1974
31. Lang TW, Corday E, Gold E, Meerbaum S, Rubin S, Constantine C,
Hirose S, Osher J, Rosen V: Consequences of reperfusion after coronary
artery occlusion. Effects of hemodynamics and regional myocardial
metabolic function. Am J Cardiol 33: 69, 1974
effects due to hemorrhage after myocardial reperfusion. Am J Cardiol
33: 82, 1974
Myocardial consequences of coronary artery bypass graft surgery. The paradox of necrosis in areas of revascularization.
B H Bulkely and G M Hutchins

_Circulation_. 1977;56:906-913
doi: 10.1161/01.CIR.56.6.906
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/56/6/906