Late Benefit of Coronary Surgery on Mortality from Myocardial Infarction

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The effect of surgical revascularization on long-term survival of patients with coronary artery disease has been extensively reported by the Veterans Administration Cooperative Study of Surgery for Coronary Disease (VACSS),1 the European Coronary Surgery Study (ECSS),2 and the National Heart, Lung, and Blood Institute–sponsored Coronary Artery Surgery Study (CASS).3 Ten- to 12-year follow-up results of these studies generally concur in demonstrating a long-term survival advantage of surgical revascularization for patients with multivessel disease and preexisting left ventricular dysfunction, which typically result from prior myocardial infarction. However, long-term outcomes with respect to myocardial infarction are not as well documented, and results to date have not yielded distinctive findings. This, in part, reflects the facts that the diagnosis of myocardial infarction is made with less definitive certitude than is mortality and that greater logistic complexity is required to collect and interpret relevant clinical and electrocardiographic records.

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The diagnosis of myocardial infarction in a randomized trial of revascularization is potentially subject to a variety of subtle biases. Prospective clinical follow-up requires analysis of hospitalization records and both objective and reproducible methods of electrocardiographic analysis, particularly to detect silent infarction that can occur in up to 25% of patients.4 Electrocardiogram (ECG) acquisition at specified intervals after randomization and equivalently obtained in both treatment groups is necessary to avoid ascertainment bias that could result from more frequent ECG sampling in surgery patients. Even though appropriate ECG follow-up avoids sampling bias, q wave regression was shown in CASS5 to be more common in postsurgical patients than in medical patients. Thus, relatively silent q wave infarctions may be undetected if the interval between ECGs is long. The VACSS used a composite of medical record retrieval, prospective ECG sampling, and central blinded review to minimize bias.6

The report of 10-year VACSS follow-up by Peduzzi et al6 in this issue of Circulation shows a 10-year cumulative 36% incidence of combined fatal and nonfatal myocardial infarction for patients randomized to surgery that is similar to the 31% for those randomized to medical treatment alone (p=0.13). Cumulative all-cause mortality plus infarction at 10-year follow-up was 54% in surgical patients and 49% in medical patients (p=0.20). The corresponding cumulative 10-year results in CASS3 are 34% in surgery patients and 31% in medical patients (p=0.41). The lower event rates in CASS patients probably reflect inclusion of internal mammary artery as a graft conduit during the later phases of CASS, less severe ischemic symptoms at baseline and better risk factor profile of CASS patients. Although there was an initial 13% perioperative infarction rate in VACSS surgical patients, the cumulative infarction rates of the two randomized groups converged by 5 years.6 This pattern of initially higher infarction rates in surgically treated patients with convergence of event rates between the two randomized groups 5–10 years later is similar for both ECSS and CASS.5,8

Although VACSS 10-year cumulative incidence of fatal and nonfatal myocardial infarction is minimally affected by coronary revascularization, postinfarction mortality is substantially lower for patients who previously were randomized to surgery instead of medical therapy. The 28-day case fatality rate for surgery patients with diagnosed infarction is 17.7% compared with 28.2% for medical patients.6 This striking difference in fatality rates after diagnosed infarction persisted even after analysis based on the Cox proportional hazards model that excluded perioperative infarctions from consideration and adjusted for baseline differences in left main coronary disease prevalence, clinical risk, and angiographic risk. In addition, there is a trend at 10-year follow-up toward a higher incidence of non-q wave infarctions in surgically treated patients (15%) than in medically treated subjects (12%; p=0.08), albeit without a concomitant reduction in q wave infarction. These results suggest a long-term benefit of surgery that had not been suspected at the time these randomized trials were
designed. Coronary bypass surgery appears to shift the type of infarction from q wave events, which carry a 32.1% fatality rate in medically treated patients, toward potentially less damaging non-q wave events that have a 10.4% mortality in surgical patients.6

Indirectly supporting the VACSS observation is the fact that the ECSS and CASS ratios of 5-year nonfatal infarctions to all-cause mortality are higher in surgery patients compared with medically randomized patients. In CASS the ratio of nonfatal infarction to all-cause mortality was 2.4 to 1 for surgery patients and 1.3 to 1 for medical patients.5 The corresponding ratios for ECSS patients are 1.9 to 1 for surgery patients and 0.6 to 1 for medically treated patients.7 These differences in ratios suggest that surgery may shift the case presentation mix away from immediately lethal manifestations of acute critical coronary ischemia towards nonfatal infarction. The most probable explanation for this surgical benefit is the availability of additional myocardial perfusion distal to obstructing lesions. The increased number of patent coronary conduits (grafts or native vessels) divides the left ventricular myocardial territory into a larger number of smaller domains with greater potential for overlap and development of collateral supply. Peduzzi et al8 additionally relate 1-year graft patency to the incidence of myocardial infarction and postinfarction mortality. Patients with all grafts patent had a substantially lower incidence of infarction than did patients who had partial or complete graft occlusions. Moreover, of those who died during 10 years of follow-up, the occurrence of a prior infarction was much more common for those patients with complete or partial 1-year graft occlusion than for patients with patent grafts. These observations lend credence to the concept of the long-term benefit of multiple alternative coronary conduits, whether patent native vessels or grafts. It would, however, be of interest to know for a similar duration of follow-up the extent to which not only survival but also incidence of left ventricular dysfunction and occurrence of heart failure is influenced by initial surgical treatment in randomized patients.

Prior analysis of all-cause mortality in VACSS has shown a survival advantage for surgically treated patients in the high-risk clinical and angiographic subsets and, conversely, a trend toward better survival with medical therapy in the low-risk subsets.1 CASS, after 10 years of follow-up,3 also confirms a surgical advantage for patients with ejection fraction less than 0.50 and three-vessel disease and, conversely, an advantage of medical treatment compared with surgery for patients in low-risk subsets (i.e., ejection fraction greater than or equal to 0.50). Although the current report from the VACSS does not specify the particular patient subsets for whom postinfarction mortality was most improved by surgery, it is likely that patients in the highest-risk clinical and angiographic subsets gained the most.

To some extent, it is disappointing that a beneficial effect of coronary surgery on postinfarction mortality does not lead to lower overall mortality. However, all-cause mortality is diluted by noncardiac deaths as well as cardiac but noninfarction-related deaths. In CASS, 37% of deaths in medical patients followed for 10 years were unrelated to acute coronary events.3 An additional factor may be the fact that diagnosed myocardial infarction constitutes only a portion of the spectrum of lethal or potentially lethal critical ischemic events, raising the possibility that the patient presentation mix may be influenced by coronary disease treatments. Patient awareness heightened by prior surgery could alter patient response time after onset of chest pain. Newer β- and calcium channel-blocking drugs, unavailable at the time of VACSS, ECSS, and CASS and taken by many patients with known coronary disease, could also alter the modes of initial clinical presentations.

The VACSS report6 highlights the subset of patients who survive their infarction with sufficient time for diagnosis of infarction to be made rather than those patients with immediately fatal events occurring out of hospital. A portion of patients dying prior to hospitalization who are currently classified as sudden death may have critical coronary ischemia that immediately presents as lethal arrhythmia or electromechanical failure without sufficient time for documentation of ischemic necrosis and infarction. Because of the difficulty of distinguishing between acute infarction and sudden death, it has been past epidemiological practice to include sudden unexpected deaths (i.e., medically unattended deaths without obvious noncardiac etiology) within the rubric of myocardial infarction. In reports from the 1970s, the proportion of medically unattended deaths with implied or autopsy-verified infarction to all presumed acute infarction cases was 26%9 and 21%.10 Thus, it would be interesting to learn from the VACSS whether the beneficial effects of surgery on postinfarction survival might extend to patients dying suddenly without a diagnosis of myocardial infarction. A beneficial effect of surgical treatment on sudden death incidence was suggested by a nonrandomized, observational CASS registry study,11 which showed a 4-year sudden-death incidence of 1.6% in surgical patients and 5.2% in medical patients (p<0.0001 by log-rank test). The effect of coronary surgery on incidence of sudden death was particularly evident for the patient subset with three-vessel disease and history of heart failure (9% for patients treated surgically and 31% for those treated medically).

These new observations from the VACSS6 regarding postinfarction mortality raise several important questions. Does more complete surgical revascularization afford long-term advantages? To what extent should patients with lesions of lesser severity receive bypass grafts at the time of surgery that is focused primarily on revascularization of other critically obstructed vessels? Does revascularization of totally occluded vessels, either by surgery or angioplasty, offer long-term benefit as a means of providing border zone perfusion and collateral supply? These
are not easy questions to answer. Certainly there usually is viable myocardium interspersed with necrotic cells in regions of hypoperfusion resulting from coronary occlusion. Viability of myocytes in areas of infarction may be critically dependent on alternative sources of perfusion to help maintain tissue integrity, minimize adverse regional wall expansion, and maintain systolic function. Techniques to assess quantitatively, in discrete areas of myocardium, the relative perfusion potential and actual contributions from alternative sources of blood supply that include native arteries, collaterals, and surgically placed grafts, are not readily available in humans. Perhaps combined analyses of regional sources of blood supply, corresponding segmental wall motion measurement, and quantitation of local myocardial viability in the setting of myocardial infarction could be compared in patients with and without prior revascularization. The final outcome of atherosclerotic coronary disease is clearly a complex function not only of revascularization but also of atherosclerotic disease progression, acute myocardial ischemic insults, and vascular topography. These unique 10-year observations of the VACSS by Peduzzi et al6 confirm the necessity for long-term patient follow-up and continuing critical data analysis.

References
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