EDITORIAL

An alternative interpretation of the results of the Coronary Artery Surgery Study

ROLF M. GUNNAR, M.D., AND HENRY S. LOEB, M.D.

IT IS PERPLEXING that the CASS investigators have found that patients who are considered for coronary artery bypass grafting have such a benign course with medical treatment that it would be almost impossible for surgical intervention to improve upon it.¹ This is not consistent with the results of the European trial² nor with the Veterans Administration experience at Palo Alto and Hines Hospitals.³,⁴ It is also not consistent with the survival curves for medically treated patients in the CASS registry as reported in 1982.⁵ The results of these studies are consistent with historical reports of medical mortality in patients with angina pectoris.⁶ In making this comparison, one must consider that the more recent series permitted significant numbers of patients in the medical treatment groups to have coronary bypass surgery and that these crossover patients were considered alive but lost to follow-up at the time of surgery. Therefore, in more recent studies there has been some apparent improvement in survival of medically treated patients because of surgical interventions.

What, then, is the explanation for the difference between the CASS results and those of previous randomized studies? We think the answer can be found in reviewing the data recently reported on the randomizable but nonrandomized patients in CASS.⁷ There were 2099 patients who met study criteria for randomization; 780 entered the randomized trial and 1319 were considered “randomizable” but did not participate in the randomized study. Four patients in the latter group were dropped from analysis because they died before the average time to surgery at the relevant CASS site. For analysis the remaining 2095 patients were divided into the following four groups according to initial treatment category: randomized to medical treatment (n = 390); randomized to surgical treatment (n = 390); nonrandomized, receiving medical treatment (n = 745); and nonrandomized, receiving surgical treatment (n = 570). In comparing the angiographic data from these patients, it appears that the first three of these four groups were similar with regard to incidence of left main coronary artery disease (1.5% to 2.3%), obstruction of the proximal left anterior descending coronary artery (27.4% to 32.8%), and three-vessel disease (23% to 34.6%). However, in the fourth group (nonrandomized, surgical treatment) the incidence of left main, proximal left anterior descending, and three-vessel disease was 9.1%, 46.1%, and 46.1%, respectively, all significantly higher than in the other three groups.

It appears, therefore, that of the original 2095 patients who met both clinical and angiographic criteria for randomization (“randomizable” patients), a significant number with angiographic features of higher risk were offered and accepted surgical treatment (the nonrandomized, surgical group). After the exclusion of many such higher-risk patients, the remaining patients, including those actually undergoing the randomization process, would be expected to have a favorable prognosis regardless of whether they received medical or surgical therapy.

The question that must be answered is whether the baseline characteristics of the randomized patients were the same as those of the patients in the randomizable but nonrandomized group receiving surgical treatment. However, the study group did not emphasize this comparison. They compared the two medically treated groups, the two surgically treated groups, and then the two randomized groups. We emphasize the significant differences in angiographic features between the nonrandomized patients receiving surgical treatment and the two randomized groups. This is a matter of understanding what question needs to be asked. The statisticians who have analyzed the CASS results apparently believe that the question to be asked is whether patients who could be randomized in the CASS trial did better with medical or surgical treatment, while the clinician asks whether the patient recommended for surgery is better off with surgical or

From the Department of Medicine, Loyola University Stritch School of Medicine, Maywood, IL, and the Hines Veterans Administration Hospital, Hines, IL.

Address for correspondence: Rolf M. Gunnar, M.D., Department of Medicine, Loyola University Stritch School of Medicine, 2160 South First Ave., Maywood, IL 60153.

Vol. 71, No. 2, February 1985
medical care. In analyzing the patients who were randomizable but not randomized, we noted that only 43.3% were taken from randomization to have surgical treatment. The usual reason given for excluding randomizable patients from the randomized trial was clinical judgment. It must be concluded that a majority of the patients (56.7%) in the randomizable group were considered by clinical judgment not to be surgical candidates, since they were removed from randomization to have elective medical treatment. It is therefore not surprising that the CASS group would come to the conclusion that medical therapy is as good as surgical therapy, since most of the randomized patients compared best with the randomizable patients who the clinicians believed should have medical therapy.

The study does not address the issue of the efficacy of surgical vs medical treatment in patients recommended for surgery by the conscientious physician. This may make for clean statistics, but it creates a problem for the clinician to interpret the meaning of the study. It should be obvious to those of us who have carried out randomized trials, but perhaps not to the casual reader, that one way to enlarge the pool of patients in a randomized study is to add patients who have mild angina, are very stable, and for whom the clinician has no bias toward advocating surgery. This, we think, is what happened in CASS. It is certainly what happened in the Veterans Administration study in hospitals that had low percentages of their patients randomized.4

Therefore, a justified conclusion from the CASS results is that for patients with stable mild angina or for patients asymptomatic after myocardial infarction who have undergone coronary arteriography, clinical decision making as to therapy (which included elective surgery in 27%) resulted in excellent overall survival. Extrapolation from CASS results to the management of patients with coronary artery disease who have not undergone arteriography is not justified, nor can it be concluded from CASS that for all patients with mild symptoms or for postmyocardial infarction patients without symptoms medical and surgical treatment will yield similar results. Clinical judgment (however defined) after complete study remains an important element in the decision-making process as it was in the CASS trial. Patients with three-vessel disease and obstruction of the proximal left anterior descending artery should probably receive surgical treatment, as should patients with left main coronary artery obstruction.

We think the attempt to negate the efficacy of aorto-coronary bypass surgery to cut the costs of medical care is misdirected. We should recognize the efficacy and indications for this operation, look carefully at the long-term consequences of the surgery, and reduce the cost of the operation by reducing unit costs rather than by convincing those who are less familiar with these studies that surgical treatment is not effective.

References
7. CASS Principal Investigators and Their Associates: Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery. Comparability of entry characteristics and survival in randomized patients and nonrandomized patients meeting randomization criteria. J Am Coll Cardiol 3: 114, 1984
An alternative interpretation of the results of the Coronary Artery Surgery Study.
R M Gunnar and H S Loeb

Circulation. 1985;71:193-194
doi: 10.1161/01.CIR.71.2.193

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1985 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/71/2/193.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally
published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the
Editorial Office. Once the online version of the published article for which permission is being requested is
located, click Request Permissions in the middle column of the Web page under Services. Further
information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/