Coronary artery bypass in patients with type 2 diabetes: Experience from the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial

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Objective: Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) was a study of management strategies for diabetic patients with myocardial ischemia and coronary artery disease. In a 2 × 2 design, early revascularization versus medical management with or without late revascularization and insulin sensitization versus insulin provision were examined. No advantage for either strategy was seen, except in the group undergoing early coronary artery bypass grafting (CABG). In that group, a reduction in subsequent myocardial infarction was noted. The purpose of our report was to characterize the conduct and short-term outcomes for CABG that led to this result.

Methods: Data from the BARI 2D CABG stratum were collected, including the baseline demographic and cardiovascular characteristics, technical details of the operation, and perioperative morbidity and mortality, and analyzed.

Results: A total of 347 patients were studied. The average cardiac function was normal, and most had multivessel disease. Almost all had undergone CABG by way of a median sternotomy using an internal mammary artery, and one third were off pump. The perioperative morbidity and mortality were low and compared well with larger outcomes databases.

Conclusions: BARI 2D showed that early CABG in patients with type 2 diabetes and myocardial ischemia and multivessel disease reduced the subsequent myocardial infarction rates. The present results have demonstrated that this was achieved using off-pump surgery in certain cases, standard myocardial protection, and routine use of the internal mammary artery or other arterial grafts. (J Thorac Cardiovasc Surg 2014;148:1268-72)

The association between coronary artery disease (CAD) and type 2 diabetes mellitus (DM) is well known. The original Bypass Angioplasty Revascularization Investigation (BARI) trial, which had included patients who had undergone revascularization late in their course of CAD, demonstrated a dramatic reduction in survival among those with DM compared with those without DM, regardless of whether they had undergone percutaneous transluminal coronary angioplasty or coronary artery bypass grafting (CABG).[1] Among the patients with DM, a significant benefit was found for CABG, in particular, with an internal mammary graft, relative to percutaneous transluminal coronary angioplasty. However, it was noted that patients receiving insulin had a worse outcome than those requiring oral agents only to control their DM. BARI 2 Diabetes (BARI 2D) was thus planned to determine the treatment strategies that might reduce the excess mortality associated with CAD in patients with type 2 DM. Early revascularization versus optimal medical management with delayed or no revascularization and insulin sensitization versus insulin provision to achieve glycemic control were tested in a 2 × 2 design. No advantage was documented for either strategy in the primary analysis. However, within the CABG stratum, a significant benefit for CABG in reducing subsequent myocardial infarction (MI) was observed.[2] In the present report, we have described the methods used in the conduct of CABG in the BARI 2D centers to better place this important finding into context.

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Abbreviations and Acronyms

BARI	=	Bypass Angioplasty Revascularization Investigation
BARI 2D	=	Bypass Angioplasty Revascularization Investigation 2 Diabetes
CABG	=	coronary artery bypass grafting
CAD	=	coronary artery disease
DM	=	diabetes mellitus
IMA	=	internal mammary artery
MI	=	myocardial infarction
PCI	=	percutaneous coronary intervention

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METHODS

The details of the design of BARI 2D have been previously presented.[1] The trial was sponsored by the National Institutes of Health, with additional support from industry. The industry sponsors did not have access to the outcomes data and did not participate in the data analysis or preparation of our report. The institutional review board at each participating site approved the protocol (ClinicalTrials.gov NCT00006305). All patients provided written informed consent. An independent data and safety monitoring board approved the study protocol and monitored the conduct of the study and safety of the patients.

A 2 × 2 factorial design was used to randomly assign patients to 2 treatment strategies. In the first strategy, the patients were randomized to early (within 4 weeks) revascularization or medical therapy. In the second strategy, the patients were assigned to either insulin-sensitization therapy or insulin-provision therapy. The target for these therapies was a glycated hemoglobin level of <7.0%.

Before randomization, the patients were assigned to a stratum of percutaneous coronary intervention (PCI) or CABG as the method of coronary revascularization by the physician responsible using the clinical criteria in place at each respective institution. This was not meant to be a study of CABG versus PCI but, rather, a real world application of the revascularization strategy. Patients in the medical therapy arm underwent subsequent revascularization during follow-up if they had progression of angina or had developed acute coronary syndrome or acute myocardial ischemia. Each participating institution was required to adhere to specific surgical requirements as set forth by the BARI 2D trial.

For the purpose of the present analysis and to reflect the results of the BARI 2D trial, we focused on the patients randomized to early revascularization, who had undergone CABG as their initial revascularization procedure.

The conduct of the operation and perioperative care was left to the individual surgeons and their institutional protocols. The decision to perform a case on pump versus off pump was determined by the perceived quality of the targets and surgeon preference. Similarly, the myocardial protection schemes in the on-pump group were left to the surgeon's discretion. The use of ≥1 internal mammary arteries was not mandated but was encouraged. Incomplete revascularization was allowed, but it was expected that all stenosis contributing to the patient's clinical symptoms and areas of ischemia would be bypassed. The management of insulin use in the perioperative period was not mandated by a specific central protocol but was left to the individual centers to use their established protocols, noting the importance of attention to glycemic control in the perioperative period.

In addition to recording the number of diseased vessels, the myocardial jeopardy index was calculated for each patient. This is the ratio of jeopardized and anatomically relevant segments downstream of significant lesions relative to all viable left ventricular segments and is reported as a percentage.[3] A multivariate analysis of the surgery was performed that included the baseline characteristics, cardiovascular and DM factors on presentation, conduct of the operation, and outcomes.

RESULTS

Of the 1176 patients assigned to prompt revascularization in the BARI 2D trial, 95.4% had undergone revascularization within 6 months of entry. A total of 347 patients underwent CABG as their initial assigned revascularization. The present report describes the results for that group of patients.

The demographic characteristics of the 347 patients who were assigned to revascularization and underwent CABG are listed in Table 1. Of these patients, 98% were from the CABG stratum (ie, CABG was the intended method revascularization before randomization). Their mean age was 63 years, and 75% were men. The BARI 2D trial was an international multicenter study; 40% of the CABG patients were from the United States, 32% from Brazil, 17% Canada, 7% Mexico, and 5% from Central Europe. Most of the patients were white; however, black and Hispanic patients were well-represented in the CABG cohort.

The cardiovascular clinical history is presented in Table 2. One third of the patients had had a previous MI and 8% a previous cerebrovascular accident or TIA. Within 6 weeks of study entry, 58% were classified as having stable angina and 10% unstable angina. Of the patients, 12% had undergone previous PCI, and just more than one half of these had received a stent. Only 1 patient had undergone previous CABG. The average ejection fraction was 58%, with less than one fifth of patients having an abnormal ejection fraction, as defined by a left ventricular ejection fraction <50%. Most patients in the present cohort had multivessel disease, defined as ≥2 major vessels with ≥50% stenosis.

TABLE 1. Baseline characteristics (n = 347)

Characteristic	Value
CABG stratum (%)	97.7
Male gender (%)	74.9
Mean age at study entry (y)	62.9 ± 8.6
Age category (%)	
<50 y	8.1
50-59 y	27.7
60-69 y	43.2
≥70 y	21.0
Race/ethnicity (%)	
White, non-Hispanic	69.7
Black, non-Hispanic	11.8
Hispanic	14.4
Asian, non-Hispanic	4.0
Geographic region (%)	
United States	39.5
Canada	16.7
Mexico	7.2
Brazil	31.7
Czech Republic/Austria	4.9

CABG, Coronary artery bypass grafting.

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