

Late results of coronary bypass in patients with peripheral vascular disease

II. Five-year survival according to sex, hypertension, and diabetes¹

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Two hundred sixteen of a series of 1000 patients initially presenting for elective surgical treatment of peripheral vascular disease underwent coronary bypass as a staged or simultaneous procedure, while bypass was warranted but never performed in 35 others who were documented by angiography to have severe coronary artery disease (CAD). Myocardial revascularization was associated with an approximate 10-fold reduction in the early mortality of vascular reconstruction, and these differences were statistically significant among hypertensive patients ($p=0.045$) and nondiabetics ($p=0.018$). During a mean follow-up interval of 4.6 years, fatal cardiac events occurred in 3.7% of patients with normal coronary arteries or mild to moderate CAD, in 12% of those receiving coronary bypass, and in 26% of the group with severe, uncorrected CAD. The protection from cardiac-related death offered by myocardial revascularization was most apparent among men ($p=0.023$), hypertensives ($p=0.05$), and nondiabetics ($p=0.031$). Cumulative 5-year survival after coronary bypass in men (76%) and nondiabetics (78%) exceeded that for comparable women (60%) and diabetics (43%). Because of their low operative risk (0.7%), superior 5-year survival (81%), and few late cardiac deaths (6.3%) following coronary bypass, nondiabetic men appear to have the most to gain from a comprehensive approach to associated CAD preceding peripheral vascular operations.

Index terms: Aortocoronary bypass • Vascular surgery

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During the past two decades, several large series have demonstrated that associated coronary artery disease (CAD), hypertension, and diabetes mellitus seriously limit

Table 1. Mean ages according to clinical features

Clinical features	No.	Mean age (Years)
Men	685	64.4
Women	315	63.4
Normotensive	403	63.8
Hypertensive	597	64.3
Nondiabetic	170	64.1
Diabetic	830	64.2

late survival following successful peripheral vascular reconstruction. DeBakey et al¹⁻³ initially discovered that cumulative 5-year survival was approximately 25% less than otherwise would be expected among patients having both CAD and hypertension, and despite subsequent improvement in the medical management of these risk factors, Hollier et al⁴ recently described a similar disparity of nearly 20% after aortic aneurysm resection. Crawford et al^{5,6} reviewed extensive personal experience with aortic replacement for either aneurysms or occlusive disease and found that actuarial 5-year survival was 84–89% for patients who had no other complicating features, 59% for those with hypertension, 55% for diabetics, and 54% in the presence of traditional clinical indications of CAD. Campbell et al⁷ reported that the incidence of fatal cardiac events far exceeded the late stroke rate after carotid endarterectomy and that cardiac deaths were three times more common in diabetics (38%) than in nondiabetics (14%) during comparable periods of observation.

These data generally are consistent with a number of previous studies from the Cleveland Clinic.⁸⁻¹¹ In comparison with patients who had no coronary involvement by conventional criteria, cumulative 5-year survival for those suspected to have CAD was 15% less after extracranial procedures, 20% less after lower extremity revascularization, and 27% less after aortic aneurysm resection. Each of these differences was caused in large measure by late cardiac mortality, and all were statistically significant. In an attempt to enhance long-term survival as well as perioperative risk, routine preoperative coronary angiography and selective myocardial revascularization were employed in 1000 consecutive patients under consideration for elective peripheral vascular operations at this center beginning in

1978.¹² The impact of our comprehensive approach to associated CAD on early results and late survival already has been calculated according to age and the clinical cardiac status.¹³ In this, the second report covering a follow-up interval of 3–7 years (mean, 4.6 years), we address the influence of sex, hypertension, and diabetes.

Materials and methods

The format of this investigation has been presented elsewhere.^{12,13} In summary, cardiac catheterization was performed in virtually every new patient scheduled for elective peripheral vascular reconstruction at the Cleveland Clinic during the study period of 1978–1982. Preliminary or simultaneous coronary bypass was recommended to those found to have severe surgically correctable CAD in an effort to prevent fatal myocardial infarctions within the foreseeable future.

Patient information

Sex, hypertension, and diabetes: The series consisted of 685 men and 315 women (*Table 1*). For the purpose of this report, the diagnosis of hypertension was applied to patients with reproducible elevation of systolic or diastolic blood pressure at or above 180 or 90 mmHg, respectively, as well as to those who required antihypertensive management to maintain normal blood pressure at the time they entered the study. A total of 597 patients qualified as hypertensive under these criteria.

Diabetes mellitus was defined as consistent elevation of the fasting or 2-hour postprandial blood sugar level above 140 mg/dL, or abnormal glucose tolerance testing, either of which required formal management with insulin or oral hypoglycemic agents. Elevated glucose values that were inconsistent or corrected by dietary measures alone were considered to represent simple glucose intolerance. This type of intolerance was discovered in 107 patients, but 170 others had established diabetes that was under medical treatment and are included in this report.

Coronary angiography: Each patient underwent coronary angiography and left ventriculography, and the results were classified according to the following criteria (*N*=patients):

1. Normal coronary arteries. (*N*=85)
2. Mild to moderate CAD, with measurable disease of one or more coronary arteries but no lesion exceeding 70% stenosis. (*N*=317)

Table 2. Operative deaths after peripheral vascular reconstruction

Clinical features	No.	Coronary angiographic classification										Total cardiac deaths	
		Normal or mild to moderate CAD		Advanced compensated CAD		Severe correctable CAD				Severe inoperable CAD			
		No.	%	No.	%	With bypass		No bypass		No.	%	No.	%
Men	584	5/217	2.3	8/175	4.6	2/162	1.2	1/12	8.3	2/18	11	18	3.1
Women	262	1/135	0.7	1/75	1.3	1/38	2.6	1/4	25	2/10	20	6	2.3
Normotensive	346	1/161	0.6	1/94	1.1	0/77	—	0/6	—	2/8	25	4	1.2
Hypertensive	500	5/191	2.6	8/156	5.1	3/123	2.4	2/10	20	2/20	10	20	4.0
Nondiabetic	715	5/308	1.6	7/207	3.4	1/170	0.6	2/15	13	1/15	6.7	16	2.2
Diabetic	131	1/44	2.3	2/43	4.7	2/30	6.7	0/1	—	3/13	23	8	6.1
Total	846	6/352	1.7	9/250	3.6	3/200	1.5	2/16	12	4/28	14	24	2.8

CAD = coronary artery disease.

3. Advanced but compensated CAD, with greater than 70% stenosis of one or more coronary arteries but no immediate indication for myocardial revascularization because of adequate intercoronary collateral circulation or because the involved vessel supplied myocardium already replaced by scar. ($N=289$)

4. Severe, correctable CAD, with greater than 70% stenosis of one or more coronary arteries serving unimpaired myocardium and representing immediate or predictable risk for myocardial infarction. ($N=251$)

5. Severe, inoperable CAD, with greater than 70% stenosis of multiple coronary arteries representing inadequate targets for coronary bypass because of diffuse, distal disease or generalized ventricular impairment. ($N=58$)

Statistical analysis

Paired data were compared using the Fisher exact test. Life table calculations were performed according to Cutler and Ederer¹⁴ and were analyzed for statistical significance using the method described by Lee and Desu.¹⁵ Patients who died during the immediate postoperative period following peripheral vascular reconstruction have been omitted from cumulative data in order to permit survival comparisons between this study group and other patients with vascular disorders whose operations preceded our current approach to preoperative evaluation. It should be noted, however, that the operative mortality rate of coronary bypass is included in all comparisons involving the subset with severe, correctable

critical feature of the planned approach to associated coronary disease in this series, the importance of its surgical risk is a fundamental consideration.

Results

Vascular surgical mortality

Peripheral vascular procedures now have been performed in a total of 846 of the original 1000 patients who were evaluated by coronary angiography. As indicated in *Table 2*, operative mortality had a linear correlation with the extent and surgical treatment of associated CAD irrespective of other factors, such as sex, hypertension, or diabetes. In the group with severe, correctable coronary involvement, early risk was 1.5% for 200 patients who underwent synchronous or preliminary myocardial revascularization in comparison with 12% for 16 others who did not ($p=0.045$). Similar trends suggesting the protection provided by coronary bypass were identified in nearly every subset, and they achieved statistical significance among hypertensive patients ($p=0.045$) and nondiabetics ($p=0.018$).

Late mortality

Of all 1000 patients entering this study, 12 (5.5%) died after 216 coronary procedures and another 24 (2.8%) after elective peripheral vascular reconstruction. Complete follow-up information was available for 945 (98%) of the remaining 964 patients during a mean interval of 4.6 years. As described in a previous report, 266

Table 3. Perioperative and late cardiac deaths within 7 years for the entire series

Clinical features	No.	Coronary angiographic classification										Total cardiac deaths	
		Normal or mild to moderate CAD		Advanced compensated CAD		Severe correctable CAD				Severe inoperable CAD			
		No.	%	No.	%	With bypass		No bypass		No.	%		
Men	685	10/242	4.1	33/204	16	13/174	7.5	6/24	25	14/41	34	76	11
Women	315	5/160	3.1	12/85	14	12/42	29	3/11	27	8/17	47	40	13
Normotensive	403	7/185	3.8	15/102	15	8/82	9.8	2/15	13	8/19	42	40	9.9
Hypertensive	597	8/217	3.4	30/187	16	17/134	13	7/20	35	14/39	36	76	13
Nondiabetic	830	12/348	3.4	28/232	12	17/183	9.3	8/30	27	13/37	35	78	9.4
Diabetic	170	3/54	5.5	17/57	30	8/33	24	1/5	20	9/21	43	38	22
Total	1000	15/402	3.7	45/289	16	25/216	12	9/35	26	22/58	38	116	12

CAD = coronary artery disease.

additional patients (28%) died during the observation period, and fatal cardiac events were responsible for three times the number of deaths caused by any other source of late mortality.¹³ The data in *Table 3* demonstrate that long-term cardiac mortality, like perioperative risk, generally may be stratified according to angiographic results, and in this study ranged from 3.7% among 402 patients with unimpressive catheterization findings to 38% in 58 others having severe, inoperable CAD.

In comparison with smaller subsets of patients who did not undergo operation and who had severe but correctable CAD, coronary bypass was associated with significant reductions in late cardiac mortality among men ($p=0.023$), patients with hypertension ($p=0.05$), and nondiabetics ($p=0.031$). With the exception of those having inoperable CAD, however, relatively few cardiac deaths have occurred within the current follow-up interval among normotensive patients, irrespective of whether they received myocardial revascularization. Furthermore, there is no evidence thus far to suggest that coronary bypass has reduced the incidence of fatal cardiac events either in women or in diabetics. The late cardiac mortality among all of those with severe, correctable CAD in these two groups exceeded 20% and was marginally higher in operated patients.

Cumulative survival

As presented elsewhere, actuarial 5-year survival currently ranges from only 22% among

patients found to have severe, inoperable coronary lesions to 85% for those having normal coronary arteries or mild to moderate CAD.¹³ Five-year survival was 72% in patients with severe, correctable CAD who underwent myocardial revascularization, a figure that surpasses both the late results (64%) in patients with advanced but compensated CAD and survival (43%) in 35 others for whom coronary bypass was warranted but never performed ($p=0.001$).

Sex: *Figure 1* illustrates survival for 667 men and 308 women and includes, as do all the life table data in this report, the operative mortality of coronary bypass in the late calculations for this particular subset. Overall survival was 70% for men and 74% for women ($p=NS$), but in similar candidates, the influence of coronary bypass on late mortality appeared to be more favorable in men. Five-year survival among men with severe, correctable CAD was 76% when myocardial revascularization was performed and 44% when it was not ($p=0.0008$). In comparison, cumulative survival was 60% in women who received coronary bypass and 41% for those with severe, uncorrected CAD ($p=NS$). The difference in survival between the male and female bypass groups approached, but did not quite attain, statistical significance ($p=0.07$).

Hypertension: Late survival among 399 normotensive patients and 577 others with hypertension is depicted in *Figure 2*. Five-year survival was 74% in normotensive patients and 69% in those with hypertension ($p=NS$), and there likewise

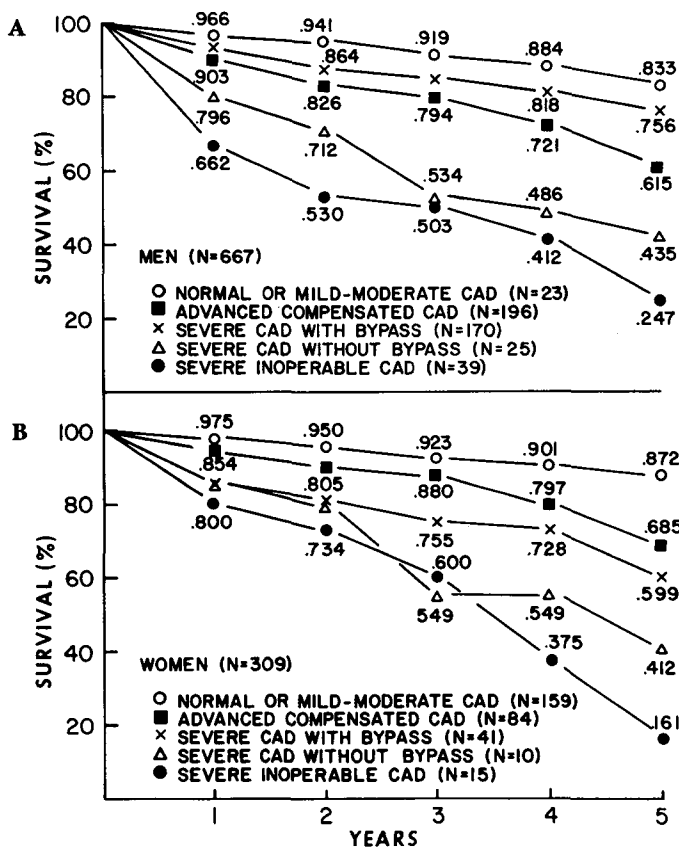


Fig. 1. Cumulative 5-year survival according to the angiographic classification of associated coronary artery disease (CAD) in men (A) and women (B).

was no significant difference in survival between the bypass subsets in these two groups (77% and 69% respectively). Although its late results were comparable in both groups, myocardial revascularization may have greater relative benefit among hypertensive patients with severe, correctable CAD because only 30% of hypertensive bypass candidates survived 5 years without operations ($p=0.0004$).

Diabetes: Figure 3 presents cumulative survival for 814 nondiabetic patients and 162 diabetics. Five-year survival for these respective groups was 74% and 57% ($p=0.0001$), making diabetes the only independent risk factor in this analysis that was associated with an unfavorable influence on overall life expectancy. There was significant improvement ($p=0.0001$) in late survival among nondiabetic patients with severe, correctable CAD who underwent coronary bypass (78%) in comparison with those who did not (40%). While only five diabetics warranted myo-

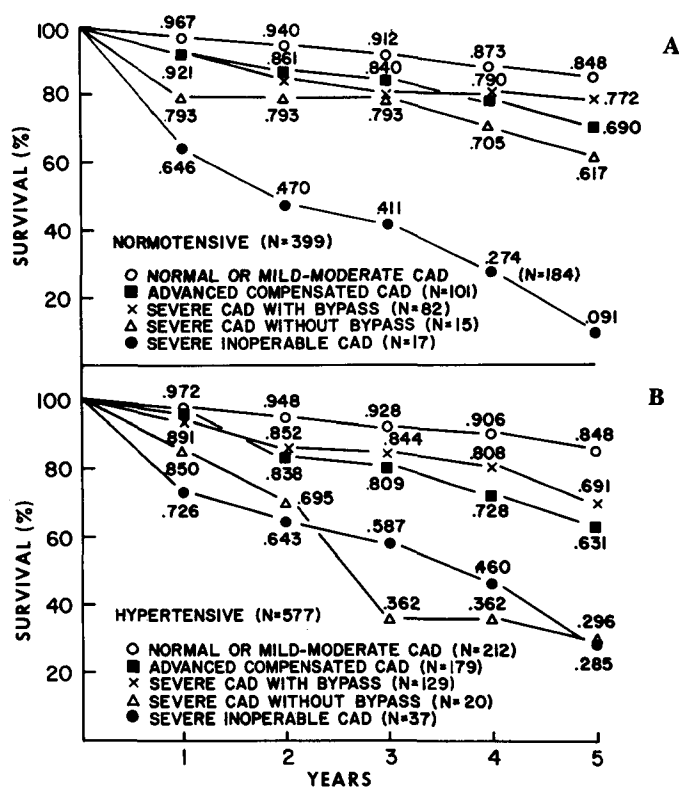


Fig. 2. Cumulative 5-year survival according to the angiographic classification of associated coronary artery disease (CAD) in normotensive patients (A) and hypertensive patients (B).

cardial revascularization but did not receive it, late survival after bypass in the diabetic patients (43%) was measurably worse than that calculated for similar nondiabetic patients ($p=0.0002$). The operative mortality of cardiac procedures (12%) among diabetics in this series substantially contributed to their poor outcome.

Nondiabetic men: Since all preliminary information suggested that late survival after peripheral vascular reconstruction was particularly enhanced by myocardial revascularization in selected men and nondiabetic patients, the data illustrated in Figure 4 were collected to determine the results of a comprehensive approach to associated CAD in a composite group of 562 nondiabetic men as well as in the 414 patients making up the remainder of this series. Overall 5-year survival was 73% and 69%, respectively. Nondiabetic men with severe CAD underwent coronary bypass with an operative mortality of 4.9% and a cumulative survival of 81%, a figure that was

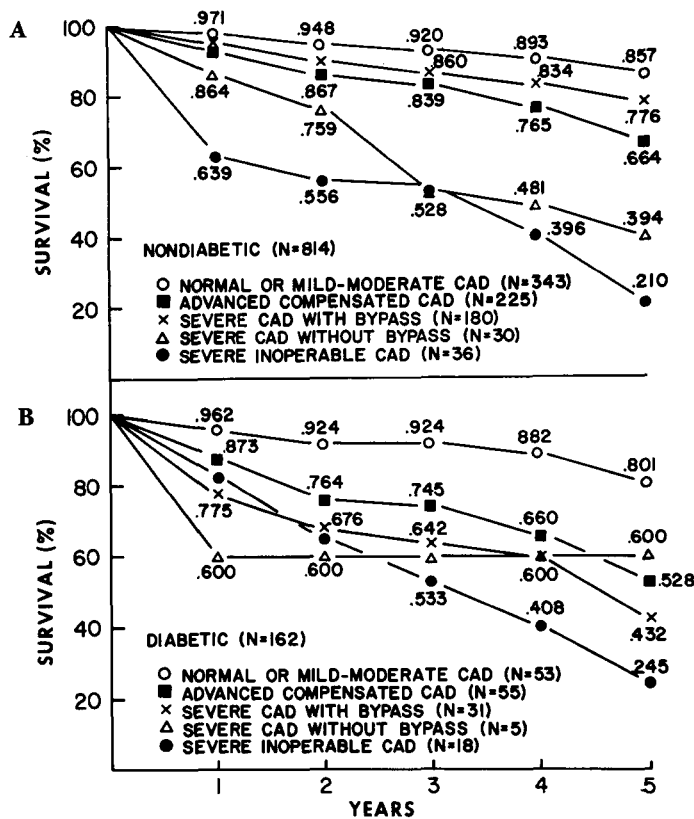


Fig. 3. Cumulative 5-year survival according to the angiographic classification of associated coronary artery disease (CAD) in nondiabetic patients (A) and diabetic patients (B).

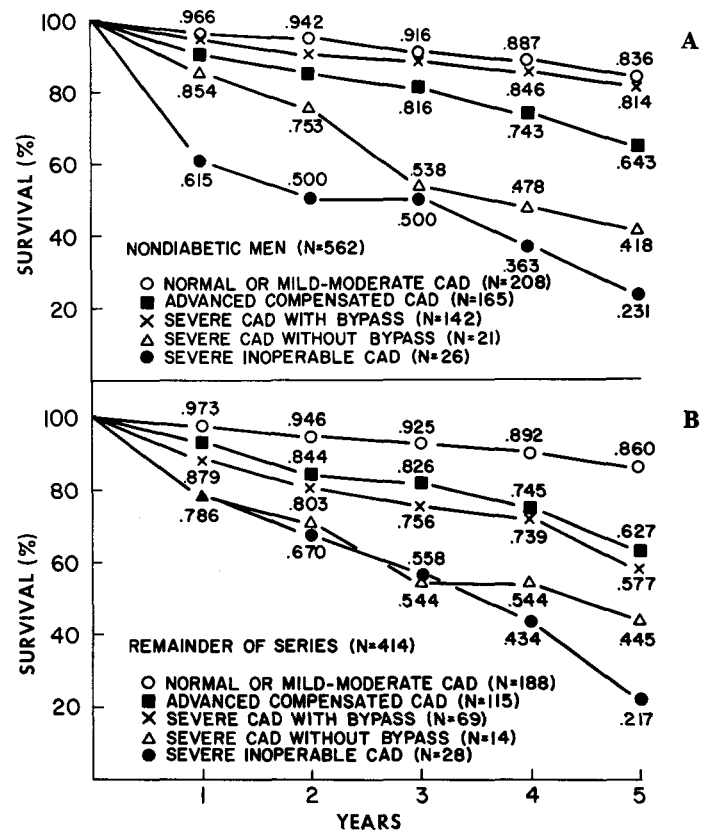


Fig. 4. Cumulative 5-year survival according to the angiographic classification of associated coronary artery disease (CAD) in nondiabetic men (A) and remainder of the series (B).

virtually identical to the survival of nondiabetic men having normal coronary arteries or only mild to moderate CAD. Five-year survival in the unoperated subset of nondiabetic men with severe, correctable CAD was 42%, and this difference was statistically significant ($p=0.0002$).

In comparison, myocardial revascularization in the remainder of the series was associated with an early risk of 7.0% and 5-year survival of 58%, a figure that was nearly 30% (actuarial) less than that for patients in the same cohort with unimpressive angiographic lesions. Cumulative survival among the remaining unoperated patients with severe, correctable CAD was only 44%, but this difference did not achieve statistical significance ($p=0.26$). There was a clear distinction ($p=0.003$) between the survival rates after coronary bypass in nondiabetic men (81%) and the remainder of the series (58%), and there also was a significant difference in the crude incidence of subsequent cardiac death despite bypass (6.3%

and 23%, respectively) between these two subsets ($p=0.029$).

The information depicted in Figure 5 adds further substance to the conclusion that nondiabetic men with severe, correctable CAD received the greatest benefit from myocardial revascularization, irrespective of whether they had traditional evidence of coronary involvement before angiography. In nondiabetic men who had no clinical indications of ischemic heart disease, coronary bypass was associated with late survival (84%) that was equivalent to comparable asymptomatic patients, while in those who were suspected to have CAD by conventional criteria, 5-year survival after bypass (80%) was superior ($p=0.0007$) to others with similar clinical findings (56%). Within the remainder of the series, however, late survival after myocardial revascularization was disappointing in patients without standard indications of CAD (55%) and represented little improvement in comparison with

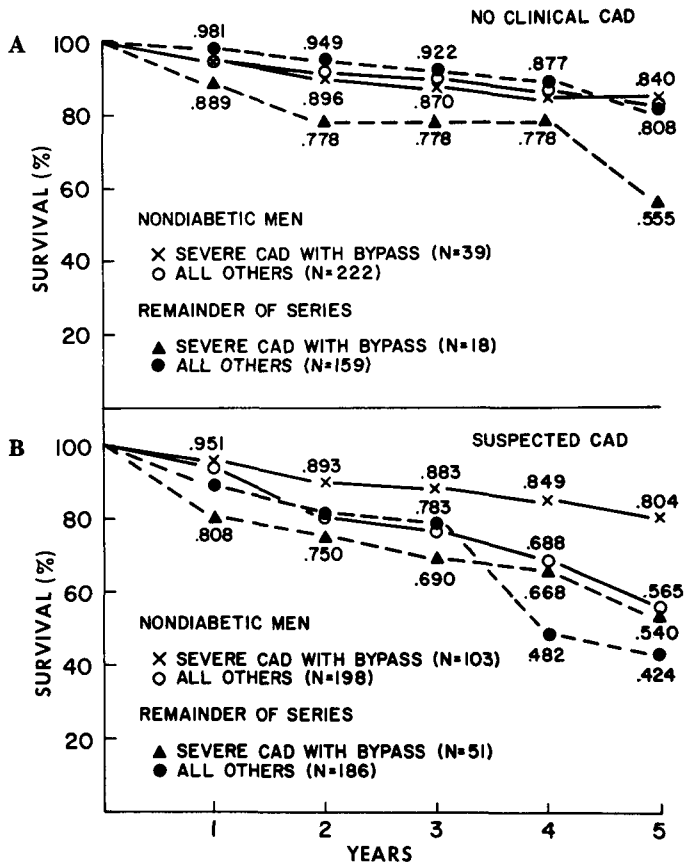


Fig. 5. Comparison of cumulative 5-year survival between nondiabetic men and the remainder of this series according to the angiographic classification of associated coronary artery disease (CAD) and the clinical cardiac status in patients with no clinical CAD (A) and suspected CAD (B).

survival among others suspected on clinical grounds to have CAD (54%).

Discussion

Although no conclusive studies have addressed the influence of sex on long-term survival following peripheral vascular procedures, the unfavorable impact of diabetes is indisputable. In perhaps the most cited example of the limited life expectancy among diabetics, DeWeese and Rob^{16,17} reported that 92% of this subset died within 10 years after femoropopliteal bypass and that none with additional evidence of incidental coronary disease survived even 5 years. Källero et al^{18,19} subsequently confirmed these observations in a large series of patients who underwent lower extremity revascularization in the presence of atherosclerosis involving the popliteal artery and

its trifurcation vessels, a feature that is especially common among diabetics. Compared with other patients requiring limb salvage, those with trifurcation and distal involvement had a significantly higher incidence of perioperative myocardial infarction (10%), early mortality (5.2%), late death (48%), and fatal cardiac events (24%) within 4 years of follow-up. Experience at the Cleveland Clinic also suggests that diabetic tibioperoneal disease is associated with a substantial decline in 5-year survival after aortofemoral reconstruction.²⁰

While the surgical risk of coronary bypass appears to assume an inverse correlation with body surface area and accordingly is higher in women, the late benefit of myocardial revascularization generally has not been prejudiced by sex as an independent variable.^{21,22} At this center, Loop et al²² found that the overall survival of men and women is similar both 5 years (93% and 91%, respectively) and 10 years (78% and 79%) after bypass even though graft patency is superior among men ($p < 0.001$). Nevertheless, other cooperative surveys have suggested that the expectations of coronary bypass may be compromised in candidates who have systemic atherosclerosis or other concurrent illnesses. Describing the results of the Coronary Artery Surgery Study (CASS) in patients over 65 years of age, Gersh et al²³ reported 5-year survival of 71% for those having two or more related medical disorders, compared with 89% for a subset in which CAD was an isolated finding. The European Coronary Artery Study Group calculated that the 5-year mortality after bypass in patients who also had peripheral vascular disease (11%) slightly exceeded the figure (8%) for those who did not.²⁴ The most revealing data in the randomized European study, however, concerned the outcome of nonoperative cardiac management. When myocardial revascularization was not performed, late survival was only 66% among entrants with associated peripheral vascular disease, compared with 85% in all others under medical treatment.

A critical review of both the CASS investigation and our data supports the conclusion that hypertension alone does not significantly affect survival after coronary bypass despite the fact that it is an important adjunctive risk factor in patients with suspected *but uncorrected* CAD. In comparison, the durability of myocardial revascularization in patients with peripheral vascular

disease seems to be seriously jeopardized by diabetes mellitus, possibly because of progressive deterioration in the distal coronary circulation during the first few postoperative years. The relative absence of diabetes among older men with aortic aneurysms probably accounts for the exemplary 5-year survival in this study of patients over 70 years of age who received coronary bypass.¹³ Notwithstanding this particular subset, however, the prevalence of diabetes among all men (16%) and women (19%) in the entire series was equivalent and does not clarify the comparatively poor cumulative survival after bypass in the latter group. Conceding that generalized vascular disease in women frequently is associated with refractory tobacco addiction and often pursues a relentless course when it does occur, the disappointing results following myocardial revascularization in this group may, as in diabetics, be attributable to the eventual occlusion of small coronary arteries or the grafts that supply them.

After 8 years of critical review, nondiabetic men appear to have the most to gain from a comprehensive approach to associated coronary disease preceding peripheral vascular reconstruction. Despite the early mortality from coronary bypass itself (4.9%), a factor reflecting the age of the candidate more than any other consideration, nondiabetic men in this series with severe CAD who received myocardial revascularization had few fatal complications at the time of arterial procedures (0.7%), a low risk for cardiac death within the subsequent 5 years (6.3%), and a cumulative survival that was virtually identical to that of patients with only trivial coronary involvement (81%). The superiority of late results in this subset was statistically significant and may encourage others who have been reluctant to pursue even selective angiography that the surgical treatment of serious coronary disease *does* make a difference in a large and important group of vascular patients.

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