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Surgical treatment of infrainguinal arterial occlusive disease in women

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Purpose: This study reviewed the outcome of 131 women who underwent infrainguinal bypass in 150 limbs from 1984 to 1991 for limb-threatening ischemia (95%) or disabling claudication (5%).

Methods: These women were compared with 209 men who underwent infrainguinal arterial reconstruction of 231 lower extremities for limb threat (89%) or claudication (11%) during the same interval. On average, women were 3 years older than men (mean age 72 vs 69 years, $p < 0.005$) but were less frequently cigarette smokers (56% women, 68% men, $p < 0.05$). Fifty-two percent of women had diabetes and 67% had hypertension, similar to the male patients. Infrainguinal disease distribution necessitated bypass to the above-knee popliteal artery in 10%, to the below-knee popliteal artery in 25%, and to the tibial or pedal arteries in 65% of women, comparable to the disease distribution in men. Autogenous vein grafts were performed in 90% of both groups.

Results: Early postoperative (30-day) mortality was 4% for women and 2% for men (not significant). Life-table survival after 3 years, however, was only 54% in women, compared with 72% in men ($p < 0.05$). Multivariate analysis indicated that diabetes increased the mortality rate 2.5-fold in women, which was not true in men. Three-year life-table survival of women with diabetes was only 39%, compared with 78% in women without diabetes ($p < 0.001$). Primary graft patency in women was 59% at 1 year and 54% at 3 years, significantly less than the 73% and 70% graft patency rates observed in men ($p < 0.005$). Secondary graft patency improved in women to 75% and 69% after 1 and 3 years, but this was still significantly less than the secondary patency rates of 89% and 86% observed in men ($p < 0.001$). Multivariate analysis indicated that female sex decreased secondary graft patency 2.4-fold and was the only variable associated with graft failure. Cumulative 3-year limb salvage in women was 82%, not statistically different than the 89% limb salvage rate observed in men.

Conclusions: Women and men requiring arterial reconstruction for infrainguinal occlusive disease had comparable operative mortality and limb salvage rates, but long-term survival and graft patency were significantly reduced in women. Our results indicate that sex substantially influences the outcome of patients after infrainguinal bypass. (J VASC SURG 1993;17:67-78.)

Numerous reports have documented the efficacy of infrainguinal arterial bypass for limb salvage.[1-3] Furthermore, the results of these procedures have been analyzed in specific populations, including diabetic, octogenarian, and dialysis groups.[4-6] Although these series have included female patients, we are unaware of a specific analysis of infrainguinal revascularization in women. Vascular bypass surgery in other anatomic regions has been evaluated in women. We previously reported our experience with surgical treatment of aortoiliac occlusive disease in women and noted results comparable to those in men, despite a subset of young women with "small aortas."[7] Other authors have also described young women with advanced aortic arteriosclerosis and small vessels.[8-10] In addition, considerable data have been published concerning women who require coronary artery bypass grafts (CABG). Compared with men, these women are usually older, more often have diabetes, and have a higher incidence of congestive heart failure and peripheral arterial occlusive disease.[11,12] Furthermore, smaller-sized coronary

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arteries and reduced patency of CABG in women compared with those in men have been noted, although this has not consistently translated into reduced long-term survival.[11-14] On the basis of these data, we suspected that women who require treatment for infrainguinal bypass might also be older and have smaller infrainguinal arteries in comparison with men and, therefore, might experience different treatment outcomes. This retrospective review was performed to specifically analyze the outcome of women in our practice who required infrainguinal arterial bypass for atherosclerotic occlusive disease. These women were then compared with a contemporaneous cohort of men who underwent infrainguinal revascularization at the same institution.

PATIENTS AND METHODS

All patients who underwent infrainguinal arterial revascularization for arterial occlusive disease at the Dartmouth-Hitchcock Medical Center between 1984 and 1991 were identified from a computerized patient registry. Patients operated on for aneurysmal disease or trauma were excluded. Demographic information and risk factors were recorded, including angina pectoris within 1 year, a history of myocardial infarction, hypertension (blood pressure higher than 160/90 mm Hg or antihypertensive treatment), cerebrovascular disease (previous stroke, transient ischemic attacks, or carotid endarterectomy), diabetes mellitus (DM; requiring either oral hypoglycemic agents or insulin), and smoking history. Indication for operation was stratified by claudication, rest pain, and tissue loss.

Preoperative cardiac evaluation was individualized according to surgeon preference and urgency of revascularization. Angina, history of myocardial infarction, arrhythmia, congestive heart failure, and DM plus inactivity usually prompted cardiology department consultation. Dipyridamole-thallium scanning to identify ischemic myocardium and echocardiography to evaluate ventricular function were used selectively, on the basis of this clinical evaluation. Although these studies occasionally led to coronary arteriography, they more often influenced the intensity of perioperative monitoring. Only one patient underwent CABG before infrainguinal bypass on the basis of these preoperative evaluations. Four additional patients had undergone CABG and one had undergone coronary angioplasty at a mean time of 8 months before infrainguinal bypass. Continuous epidural anesthesia was usually used in this series. Pulmonary artery catheter monitoring and perioperative pharmacologic manipulation of cardiac function were selectively applied to high-risk patients. With rare exception, patients recovered in the postanesthesia care unit and were transferred to the floor on the operative day. Preoperative aspirin therapy was continued postoperatively (325 mg daily).

Surgical technique frequently included a two-team approach for simultaneous proximal and distal arterial exposure. In situ saphenous vein graft (ISSVG) procedures were done preferentially, with a long leg incision and a modified Mill's retrograde valvulotome used for valve lysis. Anastomoses were routinely done with loupe magnification. Grafts were examined after completion with a continuous-wave Doppler scan and a combination of arteriography and angioscopy. Completion angioscopy supplanted arteriography in the majority of grafts done in the last 8 months of this study. Systemic anticoagulation (heparin, 150 units/kg intravenously) was routinely reversed with protamine sulfate after bypass inspection. Graft duplex examination was performed before hospital discharge and thereafter at 3- to 6-month intervals as part of our routine surveillance protocol. Vascular laboratory findings that prompted further evaluation included an ankle/brachial index that decreased 0.15 or more; a velocity that was less than 45 cm/sec or focally increased by 2.5 times that in the adjacent graft; or a graft flow less than 60 ml/ml. If two of these criteria were detected, the graft was investigated by arteriography and revised if critical defects were confirmed.

Confirmation of survival was accepted by telephone contact, but graft patency and limb salvage were calculated from the date of most recent examination. Graft patency was determined from vascular laboratory studies including ankle/brachial indexes and graft duplex scans with the use of Society for Vascular Surgery and International Society for Cardiovascular Surgery criteria.[15] Primary, assisted primary, and secondary graft patency; patient survival; and limb salvage were analyzed by life-table methods. Life-table graphs were expressed as dashed lines when the standard error exceeded 10% of the patient survival, graft patency, or limb salvage.[15] Differences in life-table outcomes between men and women were compared by the log rank test of Mantel. Expected survival was compared with that of age-, sex-, and race-matched disease-free controls on the basis of normal United States population data.[16] Chi-square analysis was used to compare the distribution of risk factors, and Student's t test was used to compare age between men and women. A two-tailed test was used in all cases, and significance designated if $p < 0.05$.

Multivariate regression analysis with the Cox proportional-hazards model was used to assess the influence of various risk factors on patient survival, graft patency, and limb salvage. Risk factors analyzed were sex, angina, myocardial infarction, hypertension, cerebrovascular disease, DM, smoking, indication for operation, and distal bypass level. Variables were entered into the regression equation by stepwise techniques if $p < 0.10$ and considered significant in the final regression equation if $p < 0.05$.

During the interval of this study, 381 infrainguinal arterial bypass graft procedures for atherosclerotic occlusive disease were performed in 340 patients. This population consisted of 131 women (39%) and 209 men (61%, Table I). The proportion of women remained relatively constant during this 7-year period. None of the women and only two men were lost to final follow-up.

Women. One hundred thirty-one women underwent infrainguinal arterial bypass of 150 extremities. These women were 39 to 95 years of age (mean 72) and had a high prevalence of cardiovascular disease, DM, and smoking (Table I). The indication for revascularization was limb threat in 95% (ischemic rest pain, 25%; tissue loss, 70%), with only 5% of procedures performed for disabling claudication. Mean preoperative ankle/brachial index was 0.39 (±0.26 SD) in patients with claudication and 0.42 (±0.31) in women with limb threat. These increased postoperatively to 0.83 (±0.18) and 0.89 (±0.33), respectively.

Disease distribution in these 150 legs led to bypass grafts to the above-knee popliteal artery in 10%, to the below-knee popliteal artery in 25%, to the tibial-peroneal arteries in 53%, and to the dorsal pedal artery in 12%. Of the 15 grafts to the above-knee popliteal artery, eight were polytetrafluoroethylene (PTFE) and seven were ISSVG. Of the 37 below-knee popliteal reconstructions, 95% were all autogenous (82% ISSVG, 11% reversed saphenous vein grafts, 2% composite vein) and 5% were PTFE grafts. Of the 98 tibial and pedal artery reconstructions, 97% were all autogenous (70% ISSVG, 11% nonreversed, translocated greater saphenous vein, 6% reversed saphenous vein, 6% composite vein, 3% arm vein, 1% lesser saphenous vein) and 3% were PTFE-vein composite grafts. The recipient artery in the 98 tibial or pedal reconstructions was the tibioperoneal trunk in 4%, anterior tibial in 35%, posterior tibial in 16%, peroneal in 27%, and dorsal pedal artery in 18%. The inflow course for this group of bypass grafts was the common femoral artery in 75%, distal superficial femoral artery in 3%, popliteal artery in 11%, and a tibial artery in 11%.

Table I. Patient characteristics of women and men undergoing infrainguinal reconstruction

	Women	*Men*	*Difference*
Patients *(n)*	131	209	
Limbs *(n)*	150	231	
Bilateral reconstruction	15%	11%	NS
Mean age (yr)	72	69	$p < 0.005$*
Risk factors			
Angina	39%	31%	NS
MI	37%	49%	NS
HTN	67%	70%	NS
CVD	21%	21%	NS
DM	52%	47%	NS
Smoking	56%	68%	$p < 0.05$†
Indication			
Claudication	5%	11%	NS
Rest pain	25%	28%	NS
Tissue loss	70%	61%	NS
Distal graft level			
AK popliteal	10%	11%	NS
BK popliteal	25%	24%	NS
Tibial	65%	65%	NS
Conduit			
ISSVG	70%	71%	NS
Other vein	21%	18%	NS
PTFE	9%	11%	NS

NS, Not significant; ($p > 0.05$); *MI,* myocardial infarction; *HTN,* hypertension; *CVD,* cerebrovascular disease; *AK,* above-knee; *BK,* below-knee.
*Student's *t* test for nonpaired samples.
†Chi-squared analysis.

Overall, of the 150 bypass grafts constructed in women, 137 (91%) were all autogenous vein grafts. ISSVG procedures were done preferentially and were possible in 70% (104/150) of limbs. The remaining autogenous conduits were nonreversed, translocated greater saphenous vein in 7%, reversed saphenous vein in 7%, composite vein in 5%, arm vein in 2%, and lesser saphenous vein in 1%. PTFE or PTFE-vein composite grafts were placed in only 13 limbs, of which eight were to the above-knee popliteal artery.

Of the entire series of 150 infrainguinal reconstructions in women, 25 (17%) were preceded by inflow procedures and 14 (9%) had concomitant inflow procedures. These 39 inflow procedures consisted of eight aortobifemoral, two iliofemoral, nine femoral-femoral, and four axillobifemoral bypass grafts; one abdominal aortic aneurysm reconstruction; two common femoral endarterectomies; and 13 iliac percutaneous transluminal angioplasties. Four patients who underwent prior iliac percutaneous transluminal angioplasty required inflow reconstructions (three repeat iliac percutaneous translumi-

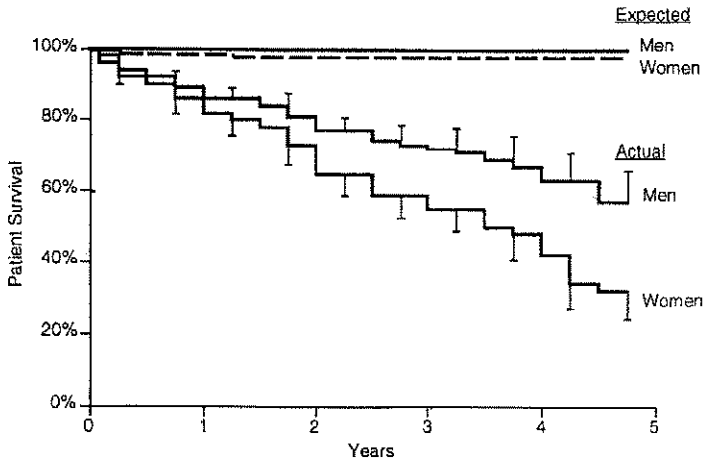

Fig. 1. Life-table analysis of actual and expected patient survival by sex. Despite comparable perioperative mortality, long-term survival in women who required infrainguinal bypass was significantly less than that in comparable men ($p < 0.05$) and much less than that expected for age-matched, disease-free controls.

Table II. Predictors of death in 340 patients after infrainguinal bypass

Group	*n*	*Variable*	*Regression coefficient*	*Relative risk*	*95% Confidence interval*	$p <$
All patients	340	Diabetes	0.70	2.0	1.3-3.0	0.001
		Sex	0.52	1.7	1.1-2.5	0.008
		Angina	0.46	1.6	1.1-2.3	0.025
Women	131	Diabetes	0.92	2.5	1.4-4.4	0.002
Men	209	Angina	0.68	2.0	1.1-3.4	0.02
		Indication	0.57	1.8	1.1-2.9	0.02

Variables significant ($p < 0.05$) in the final model by Cox's proportional hazard stepwise regression analysis (diabetes: no = 0, yes = 1; sex: male = 0, female = 1; angina: no = 0, yes = 1; indication: claudication = 0, rest pain = 1, tissue loss = 2).

nal angioplasties, one abdominal aortic aneurysm) some time after the infrainguinal revascularization. Twenty (13%) extremities had had prior infrainguinal surgical revascularization elsewhere, which had failed. An additional 18 (12%) extremities had undergone a prior unsuccessful ipsilateral infrainguinal percutaneous transluminal angioplasty at a median interval of 6 months before lower extremity bypass.

During follow-up 19 (15%) women required revascularization of the contralateral extremity because of progression of disease not initially requiring treatment. The indication for bypass in these contralateral extremities was rest pain in four and tissue loss in 15. The median interval from initial extremity revascularization to contralateral reconstruction was 8 months (range 1 to 34 months).

Men. During the same period 209 men underwent infrainguinal revascularization of 231 limbs. These men were 42 to 98 years old (mean 69) and also had prevalent medical risk factors (Table I). Indications for bypass were limb threat in 89% (rest pain, 28%; tissue loss, 61%) and disabling claudication in 11%. Target vessels were the above-knee popliteal artery in 11%, below-knee popliteal artery in 24%, and tibial or pedal arteries in 65%. Autogenous vein was used as the conduit in 89% (ISSVG, 71%; other, 18%) and PTFE was required in 11%. Inflow reconstruction preceded infrainguinal bypass in 29 (13%) extremities, was performed concomitantly with 10 (4%) infrainguinal bypasses, and was required subsequent to only one lower extremity bypass. Twenty-two patients (11%) required infrainguinal revascularization of the contralateral limb during follow-up because of disease progression in the contralateral limb at a median interval of 8 months after the index extremity bypass.

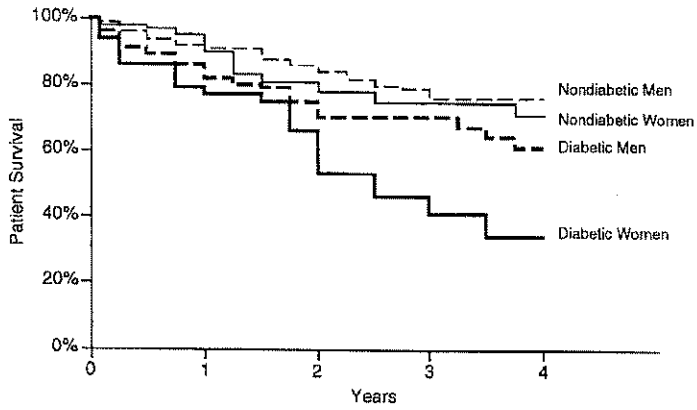

Fig. 2. Life-table analysis of survival in women and men stratified by diabetic status. Survival in women with diabetes was significantly reduced compared with that in women without diabetes ($p < 0.01$). Although there was a trend toward worse survival in men with diabetes, this was not statistically significant.

RESULTS

Compared with their male counterparts, women in this series who underwent infrainguinal revascularization were on average 3 years older when they first came to us for treatment ($p < 0.005$, Table I). Furthermore, significantly fewer women (56%) had a history of cigarette smoking than men (68%, $p < 0.05$). However, the frequency and distribution of other medical risk factors including angina, myocardial infarction, hypertension, cerebrovascular disease, and DM were not significantly different between women and men (Table I). Similarly, there were no sex-related differences in the distribution of clinical indication for revascularization, the level of recipient vessel, or the type of bypass conduit used (Table I).

Five deaths occurred in women within 30 days of bypass, yielding a perioperative mortality rate of 3.8%, slightly higher, but not statistically different from the 2% perioperative mortality rate observed in men. These early deaths in women were caused by myocardial infarction (two), stroke (two), and cardiac failure after an urgent postreconstruction CABG in a patient with crescendo angina. Long-term survival in women was 80% at 1 year and 54% at 3 years after bypass, significantly worse than the 86% and 72% 1- and 3-year survival rates observed in men ($p < 0.05$, Fig. 1). Definite causes of late deaths in women were available in 49 of 50 deceased patients. Cardiac events accounted for 40%, stroke 17%, sepsis 16%, end-stage renal disease 14%, and malignancy 13% of deaths. The survival of both women and men after infrainguinal bypass in this experience was substantially less than expected for age-matched, "normal" controls (Fig. 1).

Multivariate analysis of risk factors that influenced survival of all 340 patients after infrainguinal bypass indicated that DM, female sex, and angina significantly decreased long-term survival. Thus, after infrainguinal bypass, women had a mortality rate 1.7 times that of men; those with DM had a mortality rate twofold higher than those without DM; and patients with angina had a 1.6-fold increase in mortality (Table II). When women were analyzed separately, only DM significantly decreased survival, such that diabetic women had a 2.5 times higher mortality rate (Table II). By the same analysis, DM was not a significant predictor of survival in men. Women without diabetes and men had similar survival, which was substantially better than the survival of women with diabetes (Fig. 2). The 3-year life-table survival in women with DM (39%) was only half that of women without diabetes (78%, $p < 0.001$). Multivariate analysis indicated that angina and indication for operation decreased long-term survival in men. Men with angina had a twofold higher mortality rate, whereas men with tissue loss had a 1.8-fold decrease in survival compared with men with rest pain (Table II).

Primary graft patency in women was 59% at 1 year and 54% at 3 years, significantly lower than the 73% and 70% 1- and 3-year primary graft patency rates in men ($p < 0.005$, Fig. 3). Of the 57 limbs with primary graft failure in women, 86% underwent revision, compared with 60 of 62 (97%) primary graft failures that were revised in men. Twenty-three

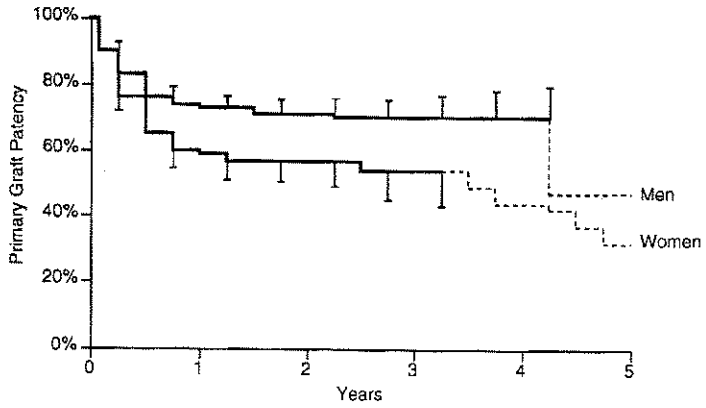

Fig. 3. Primary graft patency after infrainguinal bypass was significantly lower in women compared with that in men ($p < 0.005$).

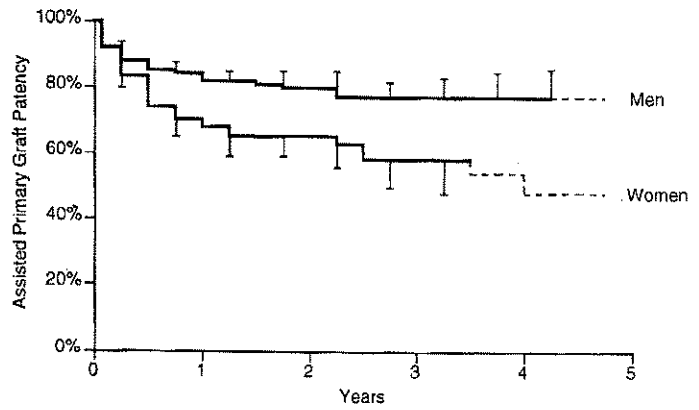

Fig. 4. Assisted primary graft patency after infrainguinal bypass (including any intervention before graft thrombosis) was significantly lower in women compared with that in men ($p < 0.005$).

(47%) of these 50 graft revisions in women were done while the grafts were still patent to correct an underlying graft defect, comparable to the 45% of graft revisions in men that were performed on failing but still patent grafts. Graft revisions in women included patch angioplasty (18), vein interposition (3), and percutaneous vein graft dilatation (2). Of these 23 revisions, 45% resulted in continued graft patency after a mean follow-up of 19 months, yielding a 1-year life-table patency rate of 68%. These interventions extended overall graft patency, yielding an assisted primary graft patency in women of 68% at 1 year and 59% at 3 years. Despite a similarly aggressive graft surveillance and revision policy in both sexes, the assisted primary patency rates in men of 81% and 77% at 1 and 3 years was significantly better than those observed in women ($p < 0.005$, Fig. 4).

Early graft thrombosis (within 30 days) occurred in 12 limbs (9 ISSVG, 1 reversed saphenous vein graft, 1 PTFE graft), which resulted in an early graft failure rate of 8%, similar to the 9% early graft occlusion rate observed in men. Late graft thrombosis occurred in 25 additional limbs after a median interval of 20 months. Of the total of 26 grafts in women that were revised after early and late thrombosis, revision procedures included thrombectomy (23) and thrombolysis (3) in conjunction with patch angioplasty or vein graft interposition. Only 35% of these 26 grafts were patent after a mean follow-up of 15 months, which result in a 1-year life-table patency rate of 36%. Overall, secondary graft patency in

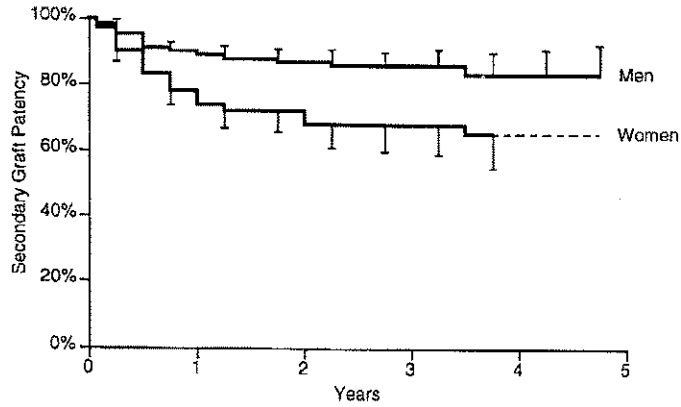

Fig. 5. Secondary graft patency after infrainguinal bypass was significantly lower in women than in men ($p < 0.001$).

Table III. Predictors of graft failure in 381 lower extremities after infrainguinal bypass

	Variable	*Regression coefficient*	*Relative risk*	*95% Confidence interval*	$p <$
Primary patency	Sex	0.46	1.6	1.1-2.3	0.02
Assisted primary patency	Sex	0.67	2.0	1.3-3.0	0.001
Secondary patency	Sex	0.88	2.4	1.4-4.0	0.001

Variables significant ($p < 0.05$) in the final model by Cox's proportional hazard stepwise regression analysis (sex: male = 0, female = 1).

women at 1 and 3 years was 75% and 69%, respectively, significantly inferior to the 89% and 86% secondary graft patency rates observed in men at the same intervals ($p < 0.001$, Fig. 5).

Multivariate regression analysis of graft patency after infrainguinal bypass in all patients revealed that female sex was the only variable that significantly predicted a higher risk for graft failure. This was true for primary, assisted primary, and secondary patency (Table III). By this analysis, women had a secondary graft patency rate that was 2.4-fold worse than that of men. None of the other variables analyzed in this study was significantly predictive of graft patency in the entire population or in women or men considered separately. There was a trend for reduced graft patency in men with a history of smoking, but this did not achieve statistical significance ($p = 0.06$).

Two limbs (1%), both of which had early primary graft failure and failed revision, were amputated within 1 month of bypass in women, similar to the 2% early amputation rate observed in men. Twenty-one additional major amputations were performed in women at a median interval of 6 months (range 1 to 50 months) after revascularization. All but two occurred as the result of graft failure (one patient required above-knee amputation because of uncontrolled infection, whereas another amputation was performed for intractable pain, both despite patent grafts). Cumulative limb salvage in women was 84% after 1 year and 82% after 3 years, slightly less than but not statistically different from the 92% and 89% cumulative limb salvage rates at 1 and 3 years in men (Fig. 6). None of the risk factors analyzed in this study were predictive of limb salvage in the entire group or in women or men considered separately.

DISCUSSION

On the basis of comparison with previous studies, women appear to represent an increasing proportion of all patients undergoing lower extremity revascularization. Before 1970, women accounted for only 15% of femoropopliteal grafts,[17] compared with 39% of patients in our present study. We have previously noted similar trends for women involving aortoiliac disease.[7] Most authors have apparently assumed that graft patency, limb salvage, and survival of women and men after infrainguinal bypass are comparable, since sex-related differences have not been previously analyzed. However, several reports concerning CABG have documented sex-related differences in patient demographics, graft patency, and survival. Women who require CABG have more

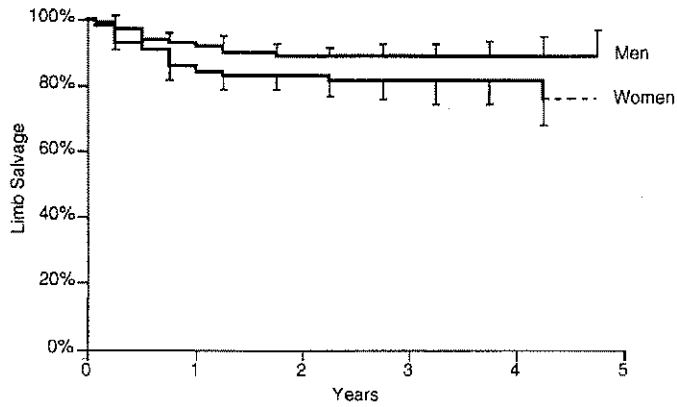

Fig. 6. Limb salvage after infrainguinal bypass appeared slightly higher in men, but this was not statistically different from that in women.

symptomatic angina at presentation, smaller coronary arteries, and reduced coronary vein graft patency when compared with men.[11,12] Furthermore, perioperative mortality has been reported to be greater in women, although differences in long-term survival between men and women after CABG have not been consistently documented.[11-14] In parallel with these differences, we found that graft patency and survival rates for women were worse than those for their male counterparts. Although our study was retrospective, it allowed us to explore possible explanations for these differences among women and men referred from the same geographic region.

Survival among women was substantially influenced by DM, which was present in more than half of these women who required infrainguinal bypass. Studies of patients without peripheral arterial disease have previously documented the greater influence of DM in women compared with that in men in terms of cardiovascular mortality.[18-20] DM was identified as the most pernicious risk factor in women for every cardiovascular endpoint examined in the Framingham study, whereas cigarette smoking was the most influential risk factor among men.[18] Furthermore, after a previous myocardial infarction women with diabetes had a risk of recurrent myocardial infarction that was twofold greater than that for diabetic men, although women without diabetes had a much lower risk compared with men without diabetes. These studies have concluded that DM is an independent risk factor for cardiovascular-related death in women,[18-20] a finding that holds true in our experience for women after infrainguinal bypass.

The predominant cardiovascular cause of late deaths in our series suggests that more careful preoperative screening or better postoperative follow-up and intervention might have increased the longevity of these women. The optimal preoperative cardiac evaluation and treatment of patients who require infrainguinal revascularization is a topic of considerable debate. Some authors have suggested little or no need for extensive preoperative cardiac evaulation, citing a low (<2%) perioperative mortality rate in patients undergoing infrainguinal reconstruction without such evaluation.[21] However, Hertzer et al.[22] have documented significant coronary occlusive disease in 20% to 30% of patients who have aortoiliac disease requiring surgical intervention but who have no symptoms, and they reported improved long-term survival in patients who underwent preoperative CABG. Our practice has been to rely on clinical judgement combined with selective cardiac evaluation, which has also been shown to be accurate for detecting patients at high risk for heart-related problems before operation.[23] With this approach we achieved a reasonably low (<4%) perioperative mortality rate in women but observed poor long-term survival. We can only speculate whether more aggressive preoperative evaluation and treatment, including possible coronary revascularization or carotid endarterectomy might have improved survival by reducing myocardial infarction and stroke in these women. Because other reports have documented a substantially higher perioperative and late mortality for CABG in both female and diabetic patients in this age group, this assumption is not straightforward.[11-13,24,25]

Perhaps most important, our observation of reduced late survival in women underlines the importance of careful medical follow-up in these

high-risk patients. The value of good diabetic control in this subgroup has been previously emphasized.[19] Unfortunately, heightened awareness of potential cardiovascular morbidity at the time of surgical intervention is usually not maintained if the patient survives the postoperative interval. The fact that these women survived a major vascular operation suggests, in fact, that more aggressive treatment of coronary or carotid disease was not necessary at that time. However, future intervention may still be required if coronary or cerebrovascular symptoms develop in these patients. This observation points to the need for prospective evaluation of preoperative CABG versus postoperative surveillance and possible future CABG in those patients in whom symptoms develop.

Because indication for operation, type of bypass conduit, and level of distal revascularization were virtually identical in our female and male patients, the etiologic factors behind the lower graft patency rates in women are unclear. Multivariate analysis failed to identify any significant predictors of graft failure in either women or men. Of note is that DM was not associated with reduced graft patency. A possible explanation for the observed sex-related difference in graft patency concerns blood vessel size. It is generally accepted that women have smaller arteries than men, although this is only documented in the aortoiliac and coronary arteries.[7,12,14,26] We have previously analyzed aortoiliac size measurements in women and found a subset of younger, shorter women with smaller arteries who came to us with more severe initial symptoms.[7] DeLaurentis et al.[26] compared aortograms of men and women and found that 26% of women had "small aortas" compared with only 1% of men. On the basis of these data, it is plausible to assume that women also have smaller infrainguinal arteries compared with men, although we are unaware of specific data to prove this hypothesis. If this is the case, analogous to the CABG experience,[12,14] difference in vessel size may contribute to reduced infrainguinal bypass graft patency in women. It is also possible that compared with men, women have smaller-diameter vein grafts, which might also contribute to reduced graft patency in women. Unfortunately, we do not have specific data regarding this question.

The 2% perioperative mortality rate and 77% 2-year survival rate in our male patients was virtually identical to the 1.5% perioperative mortality rate and 77% 2-year survival rate reported for a male-only Veterans Administration cooperative study.[27] This Veterans Administration study also reported limb salvage rates comparable to those in our male patients (85% vs 94% at 2 years). The secondary vein graft patency rate of 75% at 2 years in the Veterans Administration group was somewhat lower than the 90% 2-year vein graft patency rate of men in our study. On the basis of these similar results in men, we conclude that the differences we observed between survival and graft patency in women and men were the result of worse outcome in women rather than better than expected outcome in men.

We are aware of only two other studies that analyzed sex as a factor in patients undergoing femoropopliteal vein grafting. In one study of patients with intermittent claudication, the 1-year graft patency rate was 70% for women, significantly lower than the 85% patency rate observed in men.[28] In another study there was a trend toward superior performance of femoropopliteal grafts in men when compared to that in women at 2 years.[29] Although this supports our current finding, it does not clarify the possible etiologic basis for reduced graft patency in women.

Despite reduced infrainguinal graft patency in women, these procedures provided very effective limb salvage. Inasmuch as 95% of the women treated in our experience were operated on for limb salvage, this is an important observation. Substantial improvement in primary graft patency was possible through diligent graft surveillance and early intervention even for thrombosed grafts. However, the 45% success rate of intervention before graft thrombosis was significantly better than the 26% success rate of intervention if thrombosis had already occurred. This emphasizes the importance of postoperative graft surveillance in women after lower extremity reconstruction.

In this retrospective study of female and male patients undergoing infrainguinal bypass, we have identified differences that suggest that future efforts should focus on improving graft patency and long-term survival in women. We hope other investigators will review their experience to identify potential sex-related differences so that the etiologic factors behind these differences can be determined and optimal treatment defined.

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DISCUSSION

Dr. Patrick J. O'Hara (Cleveland, Ohio). The authors have called our attention to an important issue about which there is relatively little published data. The results of the treatment of lower extremity occlusive disease appear to be different for men and women in some important respects. What distinguishes today's report is the availability of late results. In their careful review, which uses life-table analysis, the authors have found that women were older, late survival was worse, and graft patency was less for women than men although late limb salvage rates were the same for both sexes. The authors conclude that sex substantially influences outcome after infrainguinal bypass.

This experience is similar to our own at the Cleveland Clinic. Since January 1989, 297 infrainguinal reconstruc-

tions were recorded in our Departmental vascular registry. Of these, 116 or 39% were performed on women. The mean age of the women in our experience was also identical to that reported today and was 5 years older than that of the men. The registry of the Cleveland Vascular Society includes 6855 infrainguinal reconstructions performed from 1975 through 1991. Thirty-four percent were performed on women. Considering only early results, women in this group fared slightly, but significantly, worse than men with respect to graft thrombosis, amputation, and death.

The central question is, of course, why are these differences observed? Like all good papers, this study generates several questions. The authors speculate that blood vessel size may play a role in graft thrombosis. Loop and others from our center have shown that small body surface area correlates more closely with operative mortality after coronary bypass than does the patient's sex alone. Have the authors attempted to correlate graft patency rates with body surface area to evaluate the size issue?

It also may be possible that differences in later survival and graft patency are related to the patient's age at presentation, rather than sex alone. Have the authors compared the late graft patency and survival data for women to that of men who are 3 to 5 years older, or does the statistical analysis compensate for differences in mean age?

Women also may be more likely to undergo endovascular treatment and thus may represent one third of the patients in surgical series, but nearly one half of those in endovascular series. In today's report, 26% of the women had inflow procedures as opposed to 17% of the men. Furthermore, one third of the inflow procedures performed on women were iliac angioplasties. Comparable data were not provided for men in the manuscript, and since myointimal hyperplasia appears to be more frequent in women than in men after carotid endarterectomy, could recurrent inflow disease from failed iliac angioplasty account for the difference in late patency rates observed? Similarly, 25% of the women in this series underwent operation for failed prior infrainguinal bypass or angioplasty. What were the comparable figures for the men? Was the angiographic runoff comparable for the two groups?

Finally, what can we do to improve late graft patency results in women? Is there a role for anticoagulation in this setting?

Dr. Joseph G. Magnant. We are familar with the data that you cited from Dr. Loop from your institution that correlate body surface area with graft patency and survival. We did not collect that information in our study, because we did not anticipate these differences between men and women. It is certainly an interesting observation that deserves further attention.

We recognize that age is an important determinant of survival in any population, but we focused our analysis on modifiable risk factors, such as diabetes and cardiovascular disease. Although the women in our series were slightly older than the men, their expected survival rate normally is longer. Thus the finding of markedly less survival time in women was surprising and could not be influenced by initial age alone. Similarly, we did not find that age had any effect on graft patency in either men or women.

Although slightly more women than men had undergone previous iliac balloon angioplasty, we do not believe this contributed to lower graft patency in women. Only four women required subsequent inflow revision, and none of these revisions caused infrainguinal graft failure. In fact, we are not aware of any of these grafts that failed as a result of recurrence of inflow disease. Similarly, the percentage of secondary infrainguinal grafts in men was comparable to that in women. Our analysis indicated that these factors do not explain the lower graft patency rates that we observed in women. We did not compare detailed angiographic runoff in the women and men, but their initial ankle/brachial indexes were comparable. That these patients did not have concurrent inflow disease is indirect evidence that their outflow or runoff was comparable.

All of these patients, both women and men, were routinely given aspirin after operation. We have no data concerning other anticoagulants in this group. It will be interesting to focus future studies on the subgroup of women with failed grafts to try to identify possible pharmacologic strategies for graft preservation.

Dr. Makis Tsapogas (Stony Brook, N.Y.). The Dartmouth vascular group is to be commended for its valuable contribution to this important topic. There has been for years lively debate on existing differences between men and women in the manifestation, progress, and management of atherosclerotic disease in the lower limb. Many studies, including the present one and our own, have shown that in women, although diffuse symptomatic atherosclerosis appears at a later age, its evolution is more severe once it occurs. It is considered that besides DM, this is mainly because of postmenopausal reduction of estrogens.

I believe that the vascular surgeons have been and will continue to be the leaders in the diagnosis, management, and research of vascular diseases. Prevention of atherosclerosis on the other hand, is an equally important objective. This group, together with colleagues from other disciplines, can also be instrumental in this endeavor. Consideration could therefore be given to the administration of low-dose estrogens, combined with progesterone, particularly in susceptible individuals. The decision is of course based on the benefit/risk ratio. Several studies have shown that besides the beneficial effect on osteoporosis, morbidity and mortality from complications of atherosclerosis, such as myocardial infarction, can be significantly decreased. The small risk for endometrial and breast cancer can be minimized by careful selection of patients. More systematic

studies are needed to clearly define the role of estrogens in the arteries of the lower extremity.

May I have the authors' views on this prophylactic hormone regimen in women for atherosclerosis in general?

Dr. Magnant. We have not routinely used estrogen compounds in the treatment of atherosclerosis in our female patient population. Many of these patients have been taking estrogen on the advice of their own physicians. As you point out, this is a potentially important area, and more data need to be collected regarding the subgroup of elderly women with peripheral, as opposed to coronary, atherosclerosis.

We hope that our report, which has identified important sex-related differences in the outcome of patients with infrainguinal disease, will stimulate other investigators to review their experience to identify etiologic factors that may be modified to improve our results in women.