Potential predictors of outcome in patients with tissue loss who undergo infrainguinal vein bypass grafting

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Purpose: **Aggressive attempts at limb salvage in patients with ischemic tissue loss are justified by favorable initial results in most patients. The identification of patients whose conditions will not benefit from attempted revascularization remains difficult.**
Methods: **This study was designed as a retrospective review of prospectively collected clinical data. The subjects were 210 consecutive patients who underwent infrainguinal vein bypass grafting for ischemic tissue loss in the setting of an academic medical center. Bypass grafting was to the popliteal artery in 56 patients, to the infrapopliteal arteries in 131 patients, and to the pedal arteries in 23 patients. The follow-up examination was complete in 209 of 210 patients. One hundred twenty-five patients underwent blinded review of duplex scan venous mapping and arteriography to determine simplified vein and run-off scores. The outcome measures were the influence of risk factors, venous conduit, and runoff on mortality, limb loss, and graft failure at the 6-month follow-up examination.**
Results: **One hundred seventy patients (81%) were alive and had limb salvage. Nineteen patients (9.1%) died, with need for a simultaneous inflow procedure and end-stage renal disease being most commonly associated with mortality. Thirty-three patients (15.8%) had undergone amputation: 18 after graft failure, and 15 for progressive tissue loss despite a patent graft. Amputation was significantly more common in patients with diabetes (P = .05) and with poor runoff scores (poor runoff, 44.4% vs good runoff, 7.4%; P < .01). Amputation despite a patent graft also correlated with runoff (poor runoff, 41.7% vs good runoff, 4.3%; P < .01). Twenty-five patients had graft failure without amputation, so that only 145 patients (69.4%) were alive, had limb salvage, and had a patent graft. Run-off score was the strongest predictor of outcome, with 70% of patients with poor run-off scores having death, amputation, or graft failure.**
Conclusion: **Aggressive use of infrainguinal vein bypass grafting in patients with ischemic tissue loss results in a high rate of initial limb salvage but significant morbidity and mortality. Arteriographically determined runoff scores appear to potentially identify patients at high risk for a poor initial outcome and may provide a method of selecting patients for primary amputation. (J Vasc Surg 1999;30:427-35.)**

Aggressive attempts at limb salvage in patients who have ischemic tissue loss as the result of severe infrainguinal arterial occlusive disease have been justified by the favorable results of infrainguinal bypass grafting.[1-4] Furthermore, limb salvage provides the best chance for the patient to maintain ambulatory status and living condition,[5,6] and long-term survival rates after successful bypass grafting are significantly greater than after amputations.[1,7] However, patients in whom attempted limb salvage is unsuccessful sustain the risks and costs of the bypass grafting procedure without any benefit, although the level of the subsequent amputation is usually not affected by the failure of the attempted bypass grafting.[4]

The identification of patients with ischemic tissue loss and severe infrainguinal arterial occlusive disease who will not benefit from attempted revascularization remains difficult. Primary amputation is obviously indicated for patients who are bedridden, who have

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severe neurologic impairment, or in whom sepsis or gangrene make foot salvage impossible. Primary amputation may also be appropriate in selected patients who are institutionalized or non-ambulatory with ischemic tissue loss because of poor long-term survival and functional outcome after revascularization procedures.[5] Arterial reconstructive procedures are performed if possible in the remainder of patients with ischemic tissue loss, with reported operative mortality rate associated with infrainguinal bypass grafting being 2% to 8%,[1,7] initial limb salvage rate being 91% to 97%,[4,8] and initial bypass graft patency rate being 85% to 95%.[5,9] Thus, potentially 10% to 32% of patients who agree to undergo an infrainguinal bypass grafting procedure, do not achieve their goal of survival, limb salvage, and hemodynamic improvement in the affected extremity.

To determine the incidence rate of a "bad" outcome as defined by these patient-specific parameters, we reviewed a large group of patients who underwent infrainguinal vein bypass grafting for ischemic tissue loss at a single institution. We also investigated factors that were potentially associated with early graft failure and limb loss in an attempt to identify predictors of poor outcome and subsets of patients who were likely to have less than optimal results.

MATERIALS AND METHODS

Patients and clinical procedures. The records of 210 consecutive patients who underwent infrainguinal vein bypass grafting for ischemic tissue loss between January 1984 and December 1994 were reviewed. The patients with neuropathic ulcers and no evidence of ischemia were excluded from this review. These patients represented 33% of the patients who underwent infrainguinal bypass grafting at the Shands Hospital at the University of Florida and the Gainesville Veterans Affairs Hospital during this time period. All the patients with ischemic tissue loss were considered for arterial reconstruction, except for those who had foot sepsis or tissue loss to such a degree that foot salvage was precluded and those who were irrevocably non-ambulatory. Thus, all the patients who were included in this review were ambulatory or had been ambulatory immediately before the development of the ischemic lesion, and sufficient viable foot tissue was deemed present for healing and limb salvage with successful revascularization. All the patients underwent a routine preoperative evaluation that included a history and a physical examination, a chest x-ray, an electrocardiogram, an echocardiogram, blood work, ankle brachial and toe brachial systolic pressure indices, and selective cardiac testing. Ischemic tissue loss was confirmed by the presence of an ankle brachial systolic pressure index of less than 0.40, a toe brachial systolic pressure index of less than 0.30, or the failure of healing of a lesion that appeared ischemic after at least 4 weeks of local therapy. Ischemic wounds were cultured, and patients underwent treatment with appropriate antibiotics before and after the vascular reconstruction. Nonviable tissue was debrided either before or at the time of the reconstructive procedure, depending on the degree of sepsis present, and during the postoperative period as appropriate. Hyperbaric oxygen therapy was used selectively in these patients.

Preoperative arteriography of the aorta and the run-off vessels using iodinated or CO_2 gas contrast with both cut film and digital subtraction techniques (DSA) was performed in all the patients. CO_2 gas was only used in those patients with contrast allergy or renal insufficiency. Studies were performed with either a Philips Integris 3000 (Philips Medical Systems, North American Co, Atlanta, Ga) with a 1024 matrix DSA unit or a Toshiba Angiorex KXO 2050 (Toshiba American Medical Systems, Tustin, Calif) with a 1024 matrix DSA unit. The contrast injection was performed with 3F or 4F pigtail (Omni Flush, AngioDynamics, E-Z-EM, Queensbury, NY) or selective catheters. The flow rates for iodinated contrast ranged from 7 to 12 mL/s for 2 to 4 seconds for aortic injections to 4 to 5 mL/s for 4 to 5 seconds for external iliac artery injections. CO_2 gas was injected either manually or with a power injector, with volumes of 60 mL for aortic injections and 40 mL for external iliac artery injections. Whenever tibial or pedal vessels failed to opacify, injection catheters were positioned more distally and contrast delivery was augmented with intra-arterial injection of vasodilators (nitroglycerin, 100 μg) and elevation of the legs when CO_2 gas contrast was used. Imaging was continued until the distal vessels were opacified and began to fade, tiny unnamed vessels opacified, or a soft tissue blush had appeared. Preoperative extremity vein mapping of the lower and upper extremities with duplex ultrasound scanning was also performed in all the patients.

The bypass grafting procedures were performed with either general inhalation or epidural anesthesia and standard vascular surgical techniques. The bypass grafts were constructed with greater saphenous, lessor saphenous, and arm veins that were more than 2.5 mm in diameter with preoperative duplex scan mapping, placed most commonly in a nonreversed configuration. Intraoperative, pre–bypass grafting arteriography was used extensively to aid in the selection of the ideal distal target for the bypass graft,[10] and completion arteriography or video angioscopy was performed to assess the technical adequacy of all bypass grafts and to exclude vein segments that contained areas of sclerosis from use as bypass graft conduit. Cut-film, intraoperative, pre–bypass grafting arteriograms were performed by means of insertion under direct vision of a 21-gauge needle into the artery chosen as the distal bypass graft target from the preoperative arteriogram and by positioning an x-ray plate below the injection site to cover the entire run-off bed, including the foot. The x-ray plate was then exposed with a portable x-ray machine, after the injection of 10 to 15 mL of iodinated contrast. All the patients were administered 325 mg of aspirin per day beginning on postoperative day 1, and postoperative anticoagulation therapy (heparin beginning 12 to 48 hours after surgery followed by long-term anticoagulation therapy with warfarin) was used for indications that have been previously identified.[11] Bypass graft patency was confirmed at hospital discharge with a palpable graft pulse or palpable pedal pulses that were not present before the bypass grafting procedure plus an increase in the ankle brachial systolic pressure index in the affected extremity by 0.20 or more or duplex ultrasound scan graft imaging.

Follow-up and data collection. The patients were seen in the outpatient clinic after hospital discharge at 2 weeks, 1 month, 3 months, and 6 months. For the purpose of this study, the follow-up period was terminated at that point, although our clinical practice is to follow each patient every 6 months thereafter for as long as the bypass graft is patent. Graft patency was confirmed at each clinic visit after the initial visit as described previously. The patients who had a decrease in their ankle brachial indices of 0.15 as compared with the discharge value or who had a duplex ultrasound graft scan examination that showed localized velocities of more than 180 cm/s or less than 30 cm/s were considered to have a failing graft and underwent contrast arteriography. Graft stenoses >50% were repaired surgically, as were significant lesions in the inflow and run-off arteries.

Follow-up examination was complete in 209 of the 210 patients. Patient demographics (age, sex), comorbidities (diabetes mellitus, hypertension, coronary artery disease, cerebrovascular disease, end-stage renal disease, smoking history, previous arterial procedures), the extent of tissue loss, operative procedures, operative outcomes, and follow-up data were obtained from a review of prospectively collected preoperative data sheets, clinic charts, and complete medical records. Bypass graft levels were determined from a review of the dictated operative record and classified as popliteal, tibial, peroneal, and pedal. Bypass graft level then was further categorized as "good" (popliteal and tibial) or "bad" (peroneal and pedal) to investigate the influence of collateral foot perfusion (peroneal bypass grafts) or a limited run-off bed (pedal bypass grafts) on outcome. Tissue loss was classified as limited (ischemic ulceration <5 cm in diameter or gangrene confined to the toes without forefoot sepsis) or extensive. Complications were defined with the National Veterans Affairs Surgical Quality Improvement Program criteria.[12] Operative mortality rates were defined as in-hospital or 30-day mortality, and limb salvage and graft patency rates were determined from recorded results of physical examination, noninvasive vascular testing, and arteriograms. The data are presented and analyzed with the standards recommended by Rutherford et al.[13]

A subset of 125 patients whose complete preoperative venous mapping studies and preoperative and intraoperative contrast arteriograms were available also underwent blinded review to determine the influence of the quality of the venous conduit used for each bypass graft and the run-off arteries distal to the bypass graft on outcome. Demographics, comorbidities, bypass grafting procedures performed, and outcomes were similar in these 125 patients as compared with the entire group of 210 patients ($P > .05$, for all comparisons). Venous conduit was classified as greater saphenous vein more than 3 mm in diameter, alternative (arm or lessor saphenous vein) or composite vein more than 3 mm in diameter, greater saphenous vein less than 3 mm in diameter, and alternative or composite vein less than 3 mm in diameter, with a scale from 1 to 4, respectively. The vein scores were then categorized into "good" (scores 1 and 2) and "bad" (scores 3 and 4) to also investigate the effect of vein size on outcome. Run-off was classified from review of both preoperative and intraoperative arteriograms with a modification of the grading system proposed by Rutherford et al[13] (Fig 1). All the bypass grafts were performed to infrapopliteal, pedal, or below-knee popliteal arteries with single infrapopliteal vessel runoff. The site of the distal anastomosis of the bypass graft and the run-off artery in the calf were classified as <50% stenotic (grade 1) or >50% stenotic (grade 2). The run-off arteries at the ankle and those in the foot were classified as direct/named (grade 1) or collateral (grade 2). Thus, the run-off scores for bypass grafts to popliteal or infrapopliteal arteries could range from 4 to 8 and for bypass grafts to pedal arteries could range from 3 to 6. The run-off scores were then further categorized as "good" (scores ≤6 for popliteal and infrapopliteal bypass grafts and ≤5 for pedal bypass grafts) or "bad" (scores >6 for popliteal and infrapopliteal bypass grafts and >5 for pedal bypass grafts).

Statistical analysis. Postoperative and 6-month

Run-Off Grade

Target Vessel	**<50 % Stenosis**	**>50% Stenosis**
Anastomosis	1	2
Distal Vessel	1	2
Run-Off Vessels	**Direct/Named**	**Collateral**
Ankle*	1	2
Foot	1	2

*Ankle Collaterals absent with pedal bypass

Fig 1. Method by which run-off scores were calculated. Total run-off scores for bypass grafts to popliteal or infrapopliteal arteries could range from 4 to 8 and for bypass grafts to pedal arteries could range from 3 to 6.

Table I. Characteristics of patients with tissue loss who undergo infrainguinal vein bypass grafting (n = 210)

Patient characteristics	
Age (years)	62.2 ± 11.5
Male	79%
Diabetes mellitus	67%
End-stage renal disease	21%
Hypertension	67%
Coronary artery disease	52%
Cerebral vascular disease	23%
Smoking	87% (44% currently)
Previous vascular procedure	50%

outcomes were compared with comorbidities, extent of tissue loss, bypass graft levels (individual and categorized), and vein and run-off scores (continuous and categorized) with nonpaired Student *t* test, χ^2 test, and Fisher exact test where appropriate. The outcomes that were investigated were mortality, amputation, bypass graft patency, survival with limb salvage, and survival with limb salvage and graft patency. The predictors of outcome with univarient analysis then were analyzed with multiple logistic regression analysis to determine the independent predictors of individual outcomes. Statistical analysis was done with the SPSS version 6.1 statistical software package (SPSS Inc, Chicago, Ill). The results are presented as the mean plus the standard deviation for continuous data, and *P* values of less than .05 were considered significant.

RESULTS

The patients who underwent infrainguinal bypass graft placement for tissue loss were mostly male smokers, approximately 60 years of age, who had diabetes mellitus (20% of whom had end-stage renal disease), hypertension, and a history of coronary artery disease (Table I). Furthermore, one half of these patients had previously undergone a procedure for peripheral arterial occlusive disease (either a reconstruction or an amputation), and one fifth had end-stage renal disease (70% of whom had diabetes mellitus). Bypass grafting was to the below-knee popliteal artery in 56 patients, to the infrapopliteal arteries in 131 patients (posterior tibial, n = 56; anterior tibial, n = 38; peroneal, n = 37), and to the pedal arteries in 23 patients (dorsalis pedis in all). Simultaneous inflow procedures for repair of aortoiliac arterial occlusive disease were performed in 28 patients (aortobifemoral bypass grafting in 14, extra-anatomic or iliofemoral bypass grafting in 14). Conduit used for the bypass graft was greater saphenous vein in 173 patients (non-reversed in 142, in situ in 29, and reversed in 2), composite greater saphenous vein in 17 patients, composite arm vein in 16 patients, and composite greater saphenous and arm vein in four patients. Completion study results (angiography or angioscopy) revealed abnormalities in 20 patients, all of which were corrected. Postoperative anticoagulation therapy with heparin and warfarin was used in 66 patients (31%). Poor run-off ("bad" run-off score) was present in 20.4% of patients, and marginal venous conduit ("bad" vein score) was used in 10.3% of bypass grafting procedures (in the subset of patients in whom run-off and vein scores were reviewed).

Death occurred in 19 patients—17 after surgery (operative mortality rate, 8.1%), and two during the follow-up period. Cardiac complications accounted for 13 of the deaths (68%): 12 during the postoperative period, and one after hospital discharge. The remaining deaths were caused by respiratory failure in two patients, stroke in one patient, and sepsis in one patient (after hospital discharge), and two patients died after they decided to stop dialysis after long and difficult postoperative courses. The factors that were most commonly associated with postoperative mortality were end-stage renal disease (present in nine patients [53%]) and use of a simultaneous inflow procedure (present in five patients [26%]). Indeed, the postoperative mortality rate was 22.5% in patients with end-stage renal disease and 17.2% in patients who underwent an inflow procedure in addition to infrainguinal bypass grafting as compared with only 5.5% in those patients without end-stage renal disease ($P < .05$) and 6.6% in those patients who underwent infrainguinal bypass grafting alone ($P = .2$). Furthermore, the mortality rate was 28.6% in those patients who underwent aortobifemoral bypass grafting for simultaneous repair of the inflow disease as compared with 7.1% in those patients who had extra-anatomic or iliofemoral bypass grafts. Only three deaths occurred after unsuccessful bypass grafting procedures that led to amputations (one necessitated by graft failure after an arteriogram for symptoms in the contralateral leg during the follow-up period, and two by progressive tissue necrosis despite a patent graft), and the postoperative mortality rate after amputation was 9.1% (vs a 9.1% mortality rate in the patients who did not require amputations).

Forty-six graft failures occurred in 45 patients (21.4%): 19 in the postoperative period, and 27 during the first 6 months of the follow-up period after hospital discharge. One graft that was revised after failure during the postoperative period failed again during the follow-up period. Graft disruption as the result of wound breakdown and graft exposure was the most common cause of graft failure during the postoperative period, and graft stenosis was the most common cause of graft failure during the follow-up period (Table II). Breakdown of a pedal wound resulting in graft exposure led to graft disruption in five of eight patients with this problem, and 62.5% of these patients had diabetes mellitus. The bypass graft conduit was saphenous vein in 39 of the grafts that failed (14 of 19 postoperative failures and 25 of 27 failures during the follow-up period) and composite vein in seven. The bypass grafts that failed were to the popliteal artery in nine patients, to the infrapopliteal arteries in 31 patients, and to the pedal arteries in five patients. Successful graft revision was possible in six patients whose grafts failed during the postoperative period and in four patients whose grafts failed during the follow-up period. All the successfully revised grafts were constructed of saphenous vein. No further arterial reconstructive procedures were attempted in three patients whose grafts failed during the postoperative period and in 15 patients whose grafts failed within 6 months of hospital discharge. No differences were seen in the incidence of preoperative risk factors, the site of the bypass graft distal anastomosis (with or without categorization), the use of anticoagulation therapy, the venous conduit type, or the vein score (continuous or categorized) in the patients with postoperative graft failure as compared with those patients whose grafts did not fail ($P > .05$ for all comparisons).

Table II. Causes of graft failure in patients with tissue loss who undergo infrainguinal vein bypass grafting

	Postoperative graft failure (n = 19)	*Post-discharge graft failure (n = 27)*
Graft stenosis	0	10
Graft disruption	7	1
Poor run-off	2	4
Poor vein	2	2
Technical defect	4	0
Hypercoagulable state	2	0
Perigraft infection	0	2
Inflow stenosis	0	1
Unknown	2	7

Amputation was necessary in 10 patients after graft failure in the postoperative period (seven with graft disruption, and three with no remaining venous conduit) and in seven patients during the follow-up period (one with graft disruption, and six with limited remaining venous conduit). Only one patient who underwent no further attempt at arterial reconstruction after graft failure required an amputation during the follow-up period. Progressive tissue loss despite a patent graft and aggressive efforts to achieve wound healing necessitated 15 additional amputations (10 in the postoperative period, and five during the follow-up period). Diabetes mellitus was present in 86.7% of these patients, extensive tissue loss in 70%, end-stage renal disease in 42.9% (vs 18.8% of patients with patent grafts and limb salvage; $P < .05$), and "bad" run-off scores in 60% (vs 10.5% of patients with patent grafts and limb salvage; $P < .001$).

Therefore, amputations were performed in 33 patients overall (15.7%)—20 in the postoperative period, and 13 during the follow-up period—and the indications for amputation in these 33 patients are summarized in Table III. Again, no differences were seen in the incidence of preoperative risk factors, the site of the bypass graft distal anastomosis (with or without categorization), the use of anticoagulation therapy, the venous conduit type, or the vein score (continuous or categorized) in patients who required amputation as compared with those who did not (*P*

Table III. Indications for amputation in patients with tissue loss who undergo infrainguinal vein bypass grafting

Indications	*No. of patients*
Progressive tissue loss despite graft patency	15 (45.5%)
Graft failure without successful revision	10 (30.3%)
Graft disruption caused by graft exposure	8 (24.2%)

Table IV. Outcome in patients with tissue loss who undergo infrainguinal vein bypass grafting

	At discharge	*At 6 months*
Survival rate with limb salvage	83.3%	77.5%
Survival rate with limb salvage and patent graft	81.9%	69.4%

> .05 for all comparisons). The extent of the tissue loss that prompted the infrainguinal bypass grafting was also not significantly different ($P > .05$) between patients who required amputation and those who did not, regardless of whether the amputation was performed for graft failure or progressive tissue loss, despite a patent graft. However, there was a trend for patients with diabetes to have a higher incidence of amputation in the immediate postoperative period (21.3% vs 9.0%; $P = .054$). Furthermore, patients with end-stage renal disease and patients with "bad" run-off scores had significantly higher overall incidence rates of amputation (19.4% vs 6.1%; $P < .05$; 36.8% vs 6.4%; $P < .01$, respectively), and "bad" run-off score was confirmed with multivariant analysis to be an independent predictor of amputation.

One hundred seventy-five patients were alive and had limb salvage at hospital discharge, and 162 patients were alive and had limb salvage 6 months after infrainguinal vein bypass grafting for tissue loss (Table IV). However, only 172 patients at hospital discharge and 145 patients at 6 months had a patent bypass graft as well. Furthermore, nine patients with limb salvage and a patent graft had required a second procedure to maintain or reestablish graft patency. Survival with limb salvage at 6 months was significantly more likely in patients who had "good" run-off scores, who underwent treatment with long-term anticoagulation therapy, who did not have end-stage renal disease, and who did not have diabetes (Table V). Survival with limb salvage and a patent bypass graft was significantly more common only in the patients who had "good" run-off scores (Table V). Multivarient analysis results confirmed run-off score, anticoagulation therapy, end-stage renal disease, and diabetes mellitus to be independent predictors of survival, with limb salvage at 6 months and run-off score to be an independent predictor of survival with limb salvage and graft patency. Indeed, in those patients with diabetes and "bad" run-off scores, 57.1% had undergone amputation, only 41.2% were alive and had limb salvage, and only 29.4% were alive, had limb salvage and had a patent bypass graft at 6 months of follow-up.

Table V. Predictors of outcome in patients with tissue loss who undergo infrainguinal vein bypass grafting

Survival rate with limb salvage at 6 months			
Run-off score	83.2% ("good")	52.2% ("bad")	$P < .01$
Anticoagulation therapy	93.9% (yes)	52.2% (no)	$P < .01$
End-stage renal disease	81.3% (no)	65% (yes)	$P < .05$
Diabetes mellitus	81.3% (no)	71.9% (yes)	$P < .05$
Survival rate with patent graft and limb salvage at 6 months			
Run-off score	75.6% ("good")	34.8% ("bad")	$P < .001$

DISCUSSION

Many factors, such as initial symptoms, degree of occlusive disease, and availability of appropriate bypass graft conduit influence the results of lower extremity arterial reconstruction. Furthermore, despite overall good results with arterial bypass grafting procedures, outcome in an individual patient may be poor. In this series of patients with significant infrainguinal arterial occlusive disease with tissue loss, initial outcome after infrainguinal venous bypass grafting was acceptable (operative mortality rate, 8% [6% in patients who did not have a simultaneous inflow procedure]; initial limb salvage rate in survivors, 93.3%). However, results after 6 months of follow-up were sobering (survival rate with limb salvage, 77.5%; and survival rate with limb salvage and a patent graft, 69.4%). Furthermore, bypass grafting procedures in certain subsets of patients (eg, those with diabetes and "bad" run-off scores) were of questionable value (survival rate with limb salvage at 6 months, <50%). These results appear to be inferior to other reported results of infrainguinal vein bypass grafting for limb-threatening ischemia. However, few studies that have examined only patients with tissue loss who have a high incidence rate of diabetes mellitus and a graft patency rate of 83% and a limb salvage rate of 86% in survivors at 6 months are not significantly different from several other reports. Furthermore, Nicoloff et al[14] have shown that 54% of patients who undergo infrainguinal bypass grafting for limb-threatening ischemia require repeat procedures during the follow-up period to maintain long-term limb salvage and that only 84% of patients who were ambulatory before the procedure remained so afterwards. Thus, although the goal of limb salvage can be achieved in most patients who undergo infrainguinal bypass grafting for tissue loss, careful patient selection is necessary to limit the number of patients who will have limited or no benefit from these procedures.

Postoperative mortality in the current study was primarily caused by cardiac complications. This is not surprising considering the high incidence of coronary artery disease in patients with severe peripheral arterial occlusive disease.[15] Unfortunately, it will likely be difficult to reduce the incidence of cardiac complications in these patients with diffuse atherosclerosis because previous studies from our group have shown that routine extensive cardiac evaluation does not result in better overall postoperative survival.[16] Furthermore, the mortality rate and the incidence of cardiac complications after primary amputation are at least as high or higher than after bypass grafting procedures,[17] and this is particularly true in patients with end-stage renal disease (the only predictor of mortality in the study presented here) who undergo amputation.[18] In contrast, the avoidance of simultaneous aortic inflow procedures, particularly when a complex infrainguinal reconstruction is necessitated, likely can reduce postoperative mortality because we have previously demonstrated the mortality associated with that combination of procedures to be unacceptably high.[19]

Almost one half of the early graft failures that resulted in amputations were caused by graft exposure and disruption, and this problem was primarily the result of the breakdown of pedal wounds in patients with diabetes mellitus. Adequate tissue coverage of the distal anastomatic site in such patients is often difficult, and Blankensteijn et al[20] have suggested that placing the venous bypass graft in the anatomic position may be protective in patients at risk for wound breakdown, such as those with end-stage renal disease. This was the technique most commonly used in the current study, and, despite this approach, a disturbingly high number of patients had this complication. Graft failure during the follow-up period appeared to be primarily caused by graft stenosis, although the exact cause of graft failure was difficult to determine in seven patients. Surprisingly, neither the type nor the size of the venous conduit used for these bypass grafts was found to influence graft failure, although the short length of the follow-up period and the small number of patients studied likely influenced these results. Routine intraoperative or early postoperative duplex ultrasound scan graft imaging as advocated by Bandyk et al[21] potentially could have reduced this seemingly high rate of vein graft stenosis during only 6 months of follow-up. However, this was not used during the time period of this study at our institution.

Progressive tissue loss, despite a patent graft, that resulted in amputation was the most common indication for amputation in this study. Most of the patients who required amputation for progressive tissue loss despite a patent graft had a combination of diabetes mellitus, extensive tissue loss, and severe, distal infrapopliteal and pedal arterial occlusive disease. Dietzek et al[22] also noted that limb loss despite a patent graft was more common in patients with diabetes, extensive tissue loss, and bypass grafts to isolated popliteal or tibial arteries. In addition, Edwards et al[23] found that all patients with end-stage renal disease who required amputation after infrainguinal bypass grafting (90% of whom had diabetes mellitus as well) had a patent bypass graft. Because of this, they suggested that patients with extensive tissue loss and end-stage renal disease were poor candidates for infrainguinal bypass grafting and potentially might be better served with a primary amputation, an approach suggested by other authors as well.[24] On the basis of the results of the current study and those of Dietzek et al,[22] patients with extensive tissue loss, diabetes mellitus, and poor run-off are also at significant risk for amputation, despite a patent bypass graft, and this should be strongly considered when the decision for bypass grafting versus amputation is made.

The predictors of survival with limb salvage with multivariant statistical analysis in this study were run-off score, anticoagulation therapy, end-stage renal disease, and diabetes mellitus, and survival with limb salvage and a patent bypass graft was predicted with run-off score alone. As previously discussed, diabetes mellitus is a risk factor for amputation because of progressive tissue loss despite a patent bypass graft and for wound breakdown leading to graft disruption (which uniformly led to amputation in the present study). In addition, patients with end-stage renal disease have previously been shown to have limited survival and limb salvage after infrainguinal bypass grafting.[23,24] Diabetes mellitus has not been shown to affect bypass graft patency,[25] so it is not surprising that survival with limb salvage and graft patency was not predicted by the presence of diabetes mellitus. In contrast, we have recently shown in a prospective, randomized study that anticoagulation therapy improves bypass graft patency and limb salvage in patients at high risk for bypass graft failure who undergo infrainguinal vein bypass grafting.[11] Thus, it is somewhat surprising that anticoagulation therapy was not a predictor of survival with limb salvage and graft patency at 6 months, although this was likely affected by the retrospective nature of the current study.

Previous studies of the relationship between run-off scores and subsequent bypass graft patency have produced mixed results.[9,26,27] However, poor run-off is acknowledged as an important factor in bypass graft patency, and both Alback et al[9] and Blankensteijn et al[27] found that the run-off score obtained with the system described by Rutherford et al[13] was predictive of long-term bypass graft patency. Those results support the finding of the present study that the use of a modification of the system described by Rutherford et al[13] strongly predicted outcome after infrainguinal vein bypass grafting in patients with tissue loss. The run-off scoring system used here expanded the range of run-off scores related to an infrapopliteal or pedal bypass graft, which may have improved discrimination between patients with "good" and "bad" run-off. Regardless, details of the run-off from the site of the planned distal anastomosis clearly have a significant effect on outcome after infrainguinal bypass grafting.

As previously stated, the identification of patients with limb-threatening ischemia whose conditions will likely not benefit from lower extremity arterial reconstruction is difficult, and because most patients do benefit, the use of lower extremity bypass grafting has been recommended for all patients but a selected few.[1,4] In addition, primary amputation is associated with equal or greater morbidity and mortality rates[17] and much worse function[6] and long-term survival rates,[7] so that this aggressive approach has been widely accepted. However, a substantial number of patients do not benefit from this approach, and it is far from cost effective when early graft failure results in an amputation.[28] The results of this study and others[8,9,26,27] that examined this issue would suggest that it is possible to identify patients with tissue loss who have a low likelihood of survival with limb salvage and a patent bypass graft or survival with limb salvage alone after infrainguinal bypass grafting. Such patients (eg, those with end-stage renal disease and extensive tissue loss or those with diabetes mellitus and poor runoff scores) can then be presented with appropriate expectations for a good outcome after the bypass grafting procedure, and appropriate consideration can be given to a primary amputation. Alternatively, if an infrainguinal bypass grafting procedure is performed in such patients, adjuncts, such as anticoagulation therapy, anatomic routing of the bypass graft, rotation flaps to cover the distal anastomatic sites, and intensive bypass graft surveillance, can be used in an attempt to achieve the best outcome possible. A prospective study of the potential predictors of outcome in patients with tissue loss who undergo infrainguinal vein bypass grafting identified in this study and by others is currently underway in our institution.

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DISCUSSION

Dr Stanley O. Snyder, Jr (Nashville, Tenn). Dr Seeger and his colleagues are to be congratulated for a careful study of a difficult group of patients that included a veteran smoking population, two thirds of whom were diabetic and 20% of whom had end-stage renal disease.

Twenty-five patients had graft failure and did not require amputation. Conversely, progressive tissue loss, despite a patent graft, necessitated amputation. These data stress the importance of attempting to define which patients indeed require either amputation or bypass grafting as their only alternative. Multivariant analysis results confirmed that runoff scores, anticoagulation therapy, end-stage renal disease, and diabetes mellitus were independent predictors of survival with limb salvage at 6 months and that only runoff scores were predictive of survival with limb salvage and graft patency at 6 months.

The clinical relevance of these statistics is debatable because even the worst case scenario of diabetes mellitus and poor runoff scores resulted in 41% limb salvage, with 29% of the patients obtaining limb salvage and a patent graft. The operative mortality rate for attempted limb salvage was not much greater than that of primary amputation, and almost every patient would opt for bypass grafting surgery when there is a 40% to 50% chance for limb salvage. These data will be helpful in providing appropriate education and informed consent for patients. I am not sure that its parameters will aide in predicting outcome for individual patients.

I have several questions, and they relate to some of the patients who were not listed in the series. This group all had available suitable venous tissue, and most had satisfactory saphenous vein. How do you handle patients with ischemic tissue loss and adequate runoff but inadequate autogenous tissue?

Second, did you attempt to quantify the degree of tissue loss in this group?

Third, did any patients with adequate autogenous vein undergo primary amputation because of an inadequate distal target vessel or inadequate runoff?

And, last, your mortality rate for combination proximal inflow procedures and infrainguinal bypass grafting was 17%. I wonder if you have any additional thoughts regarding primary amputation in this group of patients, particularly if they have risk factors of end-stage renal disease and diabetes mellitus?

Thank you.

Dr James M. Seeger. Thank you, Dr Snyder, for your discussion and insightful questions. First, we make every effort to use autogenous tissue, including arm veins, lessor saphenous veins, and superficial femoral veins, for infrageniculate bypass grafts because we have had poor results with prosthetic infrageniculate bypass grafts. Fortunately, with this aggressive use of alternative veins, we seldom see a patient with adequate run-off in whom a bypass cannot be done for limb salvage because no venous conduit is available. Second, as mentioned in this paper, tissue loss was classified as limited if the ischemic ulceration was less than 5 cm in diameter or the gangrene was limited to the toes without forefoot sepsis. No further classification of the degree of tissue loss was done. Third, some patients do undergo primary amputation when absolutely no distal target vessel can be identified after both preoperative and intraoperative, prebypass arteriography, and, in selected patients, direct vessel exploration. In a previous report from our institution by Dr Tom Huber, primary amputation was required in only nine of 114 patients with limb-threatening ischemia when this approach was used. Finally, I agree with you that the group of patients with combined aortoiliac and infrainguinal arterial occlusive disease, diabetes mellitus, end-staged renal disease, and tissue loss are particularly challenging to manage. At present, we consider the degree of tissue loss, the quality of the infrageniculate run-off arteries, and the venous conduit available in deciding between attempted arterial reconstruction and primary amputation. In addition, when attempted arterial reconstruction seems reasonable, we stage the inflow and outflow reconstructive procedures in all but the most robust patients needing the most straightforward procedures to attempt to reduce the mortality associated with these extensive reconstructive procedures.