Comparative decades of experience with glutaraldehyde-tanned human umbilical cord vein graft for lower limb revascularization: An analysis of 1275 cases

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Purpose: **Biological material has been used as an alternative to autogenous vein since the first lower extremity revascularization procedures were performed. Our experience with glutaraldehyde-tanned human umbilical cord vein graft (UVg), which spanned a period of 28 years, forms the basis of this report, with an emphasis on comparative results between the two decades from 1975 to 1985 and from 1990 to 2000.**
Methods: **Between 1990 and 2000, 283 lower extremity bypass grafting procedures were performed in 230 patients (264 limbs), with UVg used as the predominant, or sole, graft material. Our experience with 907 reconstructions in the decade from 1975 to 1985 has been previously documented and now serves as a baseline comparison with the past decade of experience with UVg. Each reconstruction was classified on the basis of the distal anastomotic site with or without distal arteriovenous fistulas (dAVFs). The primary and secondary graft patency rates were determined for each category as was cumulative palliation, which combines the end points of graft failure, amputation, and death.**
Results: **The results from the second decade (1990 to 2000) showed a continuation of improving patency rates for UVg grafts in lower extremity revascularization. Comparison results of complications showed no changes in the low incidence rates of infection, stenosis, dissection, and pseudoaneurysm. The original series results showed a 2.9% requirement for aneurysm surgery, with an incidence rate of biodegradation of 57% (36% aneurysms, 21% dilation), whereas the current series results have shown no aneurysms to date. The comparative 6-year secondary patency rates for past and current popliteal and crural bypass grafts (with or without dAVF) were: popliteal, 53% versus 67%, $P < .05$; and crural, 26% without dAVF versus 47% with dAVF, $P < .05$. The limb salvage rates for the two series at 6 years showed no significant changes between the decades and the types of bypass grafts. Thrombolysis was performed during the decade from 1990 to 2000 in 27 UVg cases, with lysis achieved in 23 cases (85%) and limb salvage achieved in 20 cases (74%). Since 1996, associated endovascular procedures (fluoroscopy, angioplasty) have assumed increasing importance in the reduction of perioperative graft closure and in the enhancement of patency.**
Conclusion: **Our continuing experience with UVg confirms that favorable results can be obtained with this biologic alternative to autologous vein for lower limb revascularization. Concern regarding biodegradation and aneurysm formation even after 5 years are unfounded at this time. Improved patency and limb salvage rates can be achieved in concert with lower nonthrombotic failure rates, increasing performance of associated endovascular procedures, use of tourniquets, and the addition of dAVF for crural bypass grafting. Prospective randomized studies are still necessary for the assessment of the comparative role of all graft materials, a project that continues to evade our specialty.**
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The quest for a suitable alternative to the autologous saphenous vein has preoccupied surgeons, engineers, and textile scientists for decades. Some of these alternatives have proved more useful than others, and many have been abandoned. For example, unmodified heterografts are no longer used because of accelerated biodegradation. Unmodified allografts, despite low immunogenicity, are similarly no longer used because of rejection. Pretreatment of allografts or even xenografts with chemical agents, freezing techniques, or lyophilization can result in biological materials that can retain durable structure and function. Experience with aldehyde processing (tanning) has provided unique insights into the usefulness, liabilities, and challenges that accompany its deployment for biologically derived materials. The pioneering work of Rosenberg et al[1,2] focused on the ability of aldehyde processing to provide strength, flexibility, ease, and reliability of use and to produce a material devoid of antigenicity and shelf-available and sterile for implantation. Many of these objectives were indeed achieved, but some, immunogenicity and biodegradation in particular, required additional effort during the past two decades for resolution. Our

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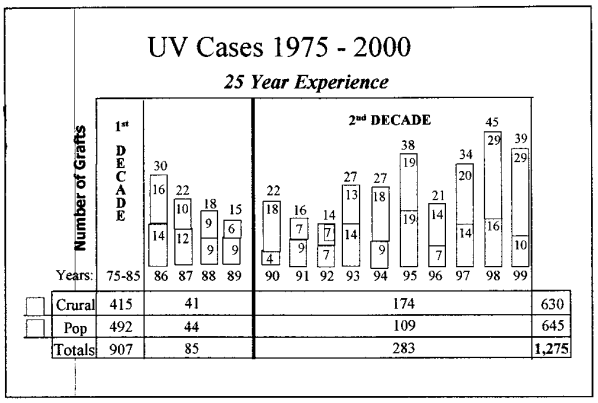

Fig 1. Numbers and types of umbilical vein grafts implanted from 1975 to 2000. Grafts implanted since 1990 were prepared by new manufacturer. Each bar since 1986 represents total umbilical vein bypass grafts for that year. Bottom numbers are popliteals, and above those are crurals. See Dardik et al[15] for details for first decade. *UV,* Umbilical vein graft; *Pop,* popliteal.

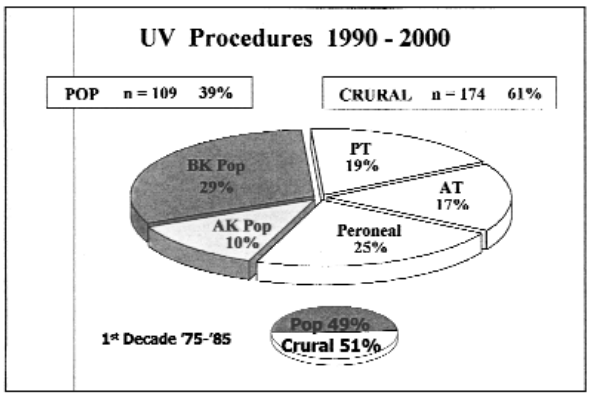

Fig 2. Type, number, and percentage of distal anastomoses of umbilical vein grafts for 1990 to 2000. Shift of 10% occurred from popliteals to crurals in comparison of two decades. *n* indicates the numbers of bypass grafts. *UV,* Umbilical vein graft; *pop,* popliteal; *BK,* below-knee; *AK,* above-knee; *AT,* arterior tibial; *PT,* posterior tibial.

original experimental work with human umbilical vein began in the early 1970s.[3-5] The clinical trials were initiated in 1974 with the glutaraldehyde-tanned umbilical vein graft (UVg).[6-8] Earlier negative experience with bovine heterograft, which was dialdehyde-starch processed,[9] was a key factor in the doubt and skepticism within the vascular community, despite randomized prospective study results that showed satisfactory performance of UVg as an alternative to autologous vein.[10-12] In general, many reports that deal with vascular grafts are characterized, at best, with medium-term follow-up studies and are often devalued with inappropriate case selection, characterization, and clinical/pathologic staging. Established guidelines now can provide a suitable basis on which to perform appropriate prospective randomized studies.[13] The studies cited previously and the recent publication of Johnson and Lee[14] of similar work performed in the 1980s are, amazingly, the only peer-reviewed publications that compare more than one alternative with the saphenous vein for lower limb revascularization. This report documents the continuous experience by a single group during a period of almost three decades in which a single graft was studied in detail. In 1988, the senior author and colleagues reported their 10-year experience (1975 to 1985) with 907 UVg bypass grafts.[15] This report continues that experience and documents for comparative purposes the decade from 1990 to 2000, which reflects modifications that have been made to the graft and to our enlarging experience.

PATIENTS AND METHODS

Between 1990 and 2000, 283 lower extremity bypass grafting procedures were performed in 230 patients (264 limbs), with UVg used as the predominant, or sole, graft material. These grafts generally originated at the femoral artery level and terminated distally (as noted subsequently) as a single graft. In 12 patients, autologous vein was used in the creation of a sequential addition to another remote vessel (eg, a sequential jump to a plantar artery from a femoral peroneal UVg graft). There were no composite configurations. Proximal anastomoses were generally at the common femoral artery level. Because sufficient length of material is always available, we tend to avoid the use of the superficial femoral artery. Proximal superficial femoral artery was used, however, in 14 cases because of obesity. In instances of desmoplasia on the basis of prior surgery, we prefer the use of the external and even the common iliac artery, which accounted for 22 cases. Our experience with 907 reconstructions in the decade from 1975 to 1985 has been previously documented[15] and now serves as a baseline comparison with the most recent decade of experience with UVg. Fig 1 details the numbers and types of bypass grafts that were performed with UVg since 1975, with new data from the decade from 1990 to 2000 summarized in Figs 2 and 3. As in the earlier series, 88% of all the bypass grafts were below the knee. Almost 60% were infrapopliteal grafts, an increase of 10% from the first decade. The demographics and risk factors are depicted in Table I and generally parallel our prior experience and that of others. The male to female ratio was 1.6 to 1, which was slightly less than the 2 to 1 ratio that was noted in the first decade. The mean age was 69 ± 10 years, with a range of 49 to 87 years. Although wide ranges for these risk factors occur within the various subgroup reconstructions, there is clearly an increasing impact of these factors with progressive obliterative disease from the popliteal arteries to the peroneal arteries.

Lower limb bypass grafting surgery had been previously performed in 120 limbs (42%). Two additional patients (0.8%) had failed superficial femoral artery and superficial femoral artery plus popliteal artery angioplasty procedures. Prior inflow procedures that consisted of aor-

Table I. Patient and graft implant data for 1990 to 2000

Group	*N No. of grafts*	*Age (range) in years*	*Male:female ratio*	*Diabetes*	*Smokers*	*Prior bypass grafting*
Popliteal above-knee	34 (12%)	72 (55 to 87)	2.2:1	22%	38%	26%
Popliteal below-knee	81 (29%)	70 (49 to 87)	1.3:1	46%	32%	38%
Posterior tibial	55 (19%)	67 (53 to 84)	2.6:1	48%	43%	45%
Anterior tibial	47 (17%)	67 (57 to 85)	1:1.8	53%	52%	49%
Peroneal	66 (29%)	69 (61 to 88)	2.9:1	70%	62%	48%
Total	283 (100%)	69 (49 to 88)	1.6:1	48%	45%	42%

tic and extra-anatomic reconstructions, profundoplasties, and transluminal angioplasties had been performed in 46 instances (16%). In this study, synchronous inflow reconstruction in the form of angioplasty and stenting was performed in only 10 cases during the last 5 years, which adjusts to 5.6% of the total number of bypass grafting procedures performed during this time interval.

Indications and operative technique. The indications for surgery are made on the basis of the clinical manifestations of the various patterns of occlusive atherosclerosis (Fig 3). The main clinical categories for case selection were: 1, gangrene; 2, critical ischemia (rest pain, nonhealing ulcers, and focal gangrenous lesions); and 3, disabling claudication. Claudication was the indication in 10% of the cases, with the remainder being equally divided between limb salvage for gangrene or critical ischemia. There was one elective case that was performed for the indication of aneurysm of the femoral popliteal system. At our institution, 1091 lower limb bypass grafting procedures were performed during the decade from 1990 to 2000 (range, 72 to 140; mean, 109). During this time, we used as few as 14 UVgs (in 1 year) and as many as 45 during 1998 (Table I). The percentage use of UVgs varies from 20% to 30% per annum.

The indications for the use of UVg are primarily on the basis of the absence or inadequacy of the saphenous vein. In a few instances, the need to facilitate and shorten the time of bypass grafting procedures in individuals with multiple risk factors who would otherwise need a major limb amputation similarly led to the choice of UVg.

The technical requirements for the use of UVg have been previously documented, including the use of the tourniquet, the distal arteriovenous fistula (dAVF) for crural reconstructions, and our intraoperative and postoperative anticoagulation therapy protocol.[16-19] Some of the most important technical points relate to the gentle handling of the graft, the avoidance of standard clamps, the proper trimming of the ends in preparing anastomosis, full-thickness suture bites, and generally, the performance of the distal anastomosis first. It is preferable that this anastomosis be performed with tourniquet control, with the use of a dAVF for tibial and peroneal reconstructions, and then, after completion of the distal anastomosis and removal of the tourniquet, with the passing of the graft through a tunneler in preparation for the proximal anastomosis. We use interrupted sutures at the toe and the heel of tibial and peroneal bypass grafts and continuous technique elsewhere, including "parachute" anastomosis at the femoral level and most importantly for iliac anastomosis. After surgery, the patients undergo heparin therapy during their hospital stay and are converted during this time to undergo Coumadin therapy. The use of clopidogrel bisulfate is being investigated.

Data collection and analysis. The data for all the bypass grafting procedures from 1975 to 2000 were collected as a prospective study with a defined data collection sheet. Analysis, including the life tables, was performed with a computer program that we designed and enhanced during the past decade with the Excel program (Microsoft, Seattle, Wash).[20] All the bypass grafts were classified on the basis of distal anastomotic site with or without dAVF. Unlike the first decade series, in the current decade, bypass graft procedures to the trifurcation and sequential reconstructions were rarely performed and were categorized in relationship to the dominant vessel where the anastomosis was performed with its appropriate runoff. Clinical and noninvasive vascular follow-up studies were carried out at intervals of 3 to 6 months. These studies consisted of ankle-brachial indices, duplex scan studies with documentation of morphology and hemodynamic data, and, if appropriate, pulse volume recordings (without graft compression). The availability of duplex scan sonography has significantly altered our monitoring protocol. Completion sonographic scanning is routine and includes the entire length of the graft. Graft diameter greater than 10 millimeters was considered "dilated" and "aneurysmal" if the pathologic dilatation was localized, segmental, or clearly enlarged in relation to the adjacent vascular structure. Completion angiographic scanning is performed selectively. Duplex scan sonography is readily accepted by the patient and enables an earlier determination of potential "failing" bypass grafts. The indications for revision of grafts that were deemed to be failing were increased peak systolic velocities (>250 cm/s), loss of the reversed flow component in diastole, and a ratio of more than 3.0 (velocity at stenosis/velocity proximal to stenosis).

Complications were tabulated, including nonthrombotic causes. This category consists of cases that needed amputation with patent grafts because of progressive gangrene of the foot or continued wound infection that failed to respond to increased perfusion.

Graft patency and limb salvage rates are expressed with the actuarial life table method.[21] The log-rank test was

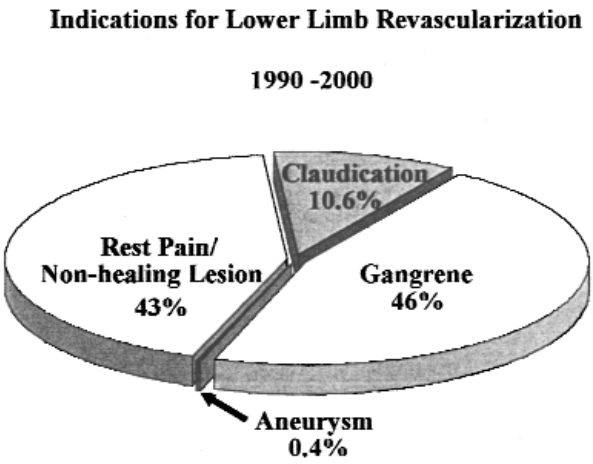

Fig 3. Indications for lower limb revascularization (1990 to 2000).

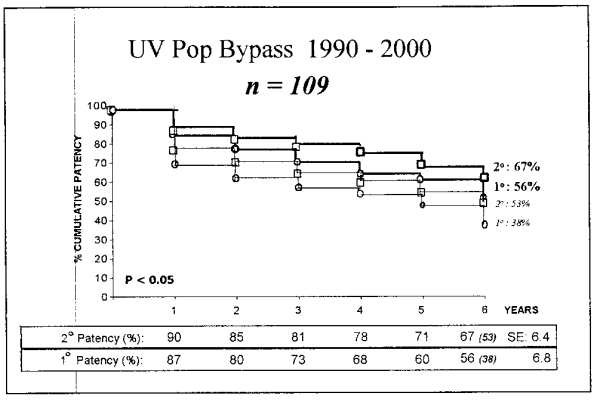

Fig 4. Comparative cumulative graft patency rates for popliteal reconstuctions with use of umbilical vein grafts during decades from 1975 to 1985 *(bold lines)* and from 1990 to 2000 (*light lines* and *italics*). Difference in curves was statistically significant in comparison of decades with log-rank test ($P < .05$). *UV,* Umbilical vein graft; *Pop,* popliteal; *SE,* standard error.

used to test differences between groups. In addition to the documentation of primary and secondary graft patency rates, the assisted patency rates and the cumulative actual palliation rates also were analyzed, the latter combining the endpoints of graft failure, amputation, and death.[22]

RESULTS

The numbers of UVg cases, the indications, and the types of procedures for surgical revascularization are summarized in Figs 1 to 3. The need to secure limb salvage or reverse progressive tissue loss accounted for 89% of the cases. Most of the patients in this study (87%) underwent a single operation. Repetitive ipsilateral procedures were required in 11 patients, which accounted for a total of 15 additional ipsilateral grafts (5%). There were 19 contralateral procedures (7%). These results compare with the authors' previous findings during the first decade of experience with UVg in which a single procedure was possible in 78% of the patients and contralateral procedures in less than 12%.[15] Symmetry of procedures also was once again noted in this series; that is, the type of contralateral reconstruction eventually required was similar to that performed in the original (ipsilateral) limb.

Most of the cases in this series were infragenicular (88%), with a greater number of crural reconstructions (59%) as compared with popliteal reconstructions (41%; Fig 2). This decade has shown a shift of approximately 10% of the below-knee popliteals to crural reconstructions. Most of the latter reconstructions were to the peroneal arteries (41%). The percentage of above-knee popliteal reconstructions in the current decade (12%) was essentially identical to that of the first decade (11%). Eight of the 34 above-knee bypass grafting procedures (24%) were to isolated popliteal segments as compared with nine of the 81 below-knee popliteal bypass grafting procedures (11%). These figures are also similar to the authors' prior experience in which bypass grafting procedures to above-knee and below-knee isolated popliteal segments represented 34% and 15%, respectively, of the total bypass grafting procedures performed to each of these sites.

Cumulative functions. Cumulative graft patency and limb salvage rates are depicted in Figs 4 to 6, with accompanying data in Table II. There were no significant differences between the primary, primary assisted (not depicted), and secondary patency rates of a particular reconstruction. Secondary patency rates for popliteal and crural reconstructions at 5 years for the decade from 1990 to 2000 were 71% and 56% (with dAVF), respectively. These figures were 11% and 6% more than their respective primary patency rates. The 5-year patency rate for popliteal arteries for the series from 1975 to 1985 was 57%. The comparative 5-year tibial/peroneal bypass graft (with or without dAVF) patency rates for the decade from 1975 to 1985 were: tibial, 32%; and peroneal, 34% without dAVF. The results of the decade from 1990 to 2000 were significantly improved as compared with those results that were obtained during the decade from 1975 to 1985 for both the popliteals and the crurals ($P < .05$). The cumulative limb salvage rates for the two series at 5 years also showed an impressive improvement of 80% versus 73% for popliteal arteries ($P < .05$) and 65% versus 58% for crurals ($P < .05$). The cumulative actual palliation data are predictably depressed because of combined failure endpoints (graft failure, amputation, and death). There were no statistically significant differences in a comparison of the patency rates as a function of runoff in popliteal reconstructions, above-knee or below-knee positions, presence or absence of diabetes, and indications for surgery.

Complications. Thrombosis was the major mechanism for graft failure and accounted for the major decline in cumulative patency and limb salvage rates for the entire series. Perioperative (<1 month) thrombosis and reoperation for popliteal arteries for the decade from 1990 to 2000 was 5% and for the crurals was 10%, which was a significant

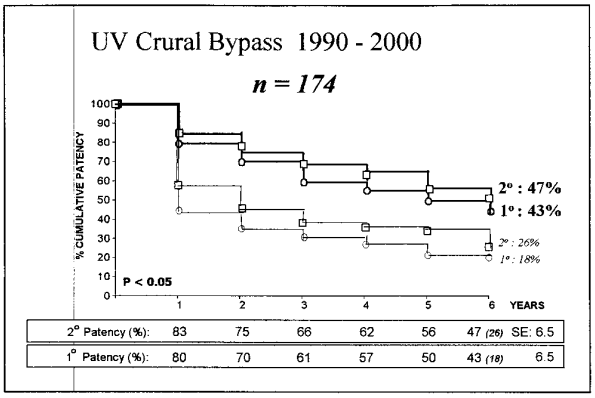

Fig 5. Comparative cumulative graft patency rates for crural reconstuctions with use of umbilical vein graft during decades from 1975 to 1985 *(bold lines)* and from 1990 to 2000 (*light lines* and *italics*). Differences between curves were statistically significant ($P < .05$). *UV,* Umbilical vein graft; *SE,* standard error.

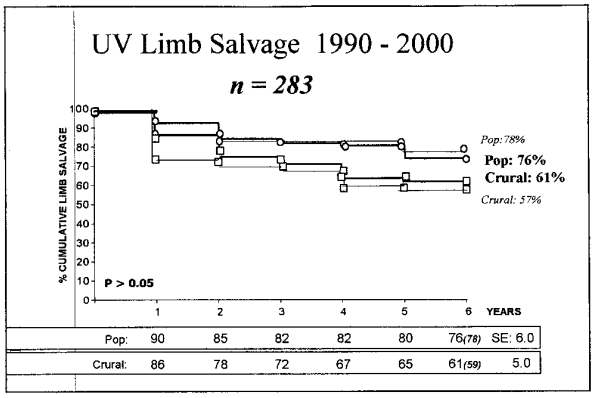

Fig 6. Comparative cumulative limb salvage rates for popliteal and crural reconstuctions with use of umbilical vein graft during decades from 1975 to 1985 *(bold lines)* and from 1990 to 2000 (*light lines* and *italics*). Differences between any curves were not statistically significant. *UV,* Umbilical vein graft; *Pop,* popliteal; *SE,* standard error.

Table II. Secondary cumulative patency and cumulative palliation rates for umbilical vein grafts (1990 to 2000)

	Popliteal		*Crural*		*Total*	
Interval (years)	*No.*	*CPR ± SE*	*No.*	*CPR ± SE*	*No.*	*CAP ± SE*
1	115	89.6 ± 3.0	168	82.5 ± 3.1	249	79.6 ± 2.6
2	86	85.1 ± 3.6	114	74.7 ± 3.6	182	67.8 ± 3.1
3	67	81.0 ± 4.1	86	66.1 ± 4.2	144	52.9 ± 3.4
4	56	77.8 ± 4.5	62	62.6 ± 4.4	98	47.4 ± 3.5
5	44	71.4 ± 5.5	47	56.0 ± 5.1	68	32.8 ± 3.8
6	26	67.5 ± 6.4	25	46.7 ± 6.5	25	25.3 ± 4.2

CPR, Cumulative patency rate; *SE,* standard error; *CAP,* cumulative actual palliation.

improvement over the first decade experience when comparable thrombosis and reoperative rates were 11% and 22%, respectively. Thrombolysis was performed during the decade from 1990 to 2000 in 27 UVg cases, with lysis achieved in 23 cases (85%) and limb salvage in 20 cases (74%). These results compare favorably with the first decade experience in which streptokinase lysis was attempted in 38 cases, with occluded popliteal grafts being patent at discharge in 60% versus only 25% for the crural reconstructions.

Nonthrombotic failure occurred in two crural cases (0.7%) and in no popliteal cases. These results compared favorably with a 5% nonthrombotic failure rate that occurred during the decade from 1975 to 1985 (Table III). We believe that this improvement may be one of the factors responsible for the improved limb salvage rates noted in the current decade.

Aside from thrombotic and nonthrombotic events, other complications included infection, stenosis, dissection, and pseudoaneurysm formation (Table III). Infection occurred in nine cases (3%) and always in patients who had undergone two or more procedures. The removal of the entire graft was necessary in all cases and eventually resulted in limb amputation. Stenosis occurred at the distal anastomosis in three grafts (1%), in the proximal anastomosis in one and in the midportion of another. The latter was inexplicable in that intimal hyperplasia has, to this point, never been noted in the main body of the graft. When intimal hyperplasia does occur, it is at the anastomotic areas and represents pannus ingrowth from the native artery. Presumably, the midgraft stenosis occurred as a result of localized intramural dissection or hematoma. Percutaneous balloon angioplasty was successful in three of the stenosis cases; direct surgery and patching were performed in the remaining two. There was one pseudoaneurysm in this series that needed interposition grafting and one case of dissection that was noted during surgery and also corrected with interposition grafting. Both of these cases may have been the result of flow surface defects. Overall, the comparison of these complications between the two decades showed no change in their low incidence rates.

Most impressive however, were the findings with respect to biodegradation and aneurysm formation. The original series had shown a 2.9% requirement for aneurysm surgery after 5 years with an overall incidence rate of biodegradation of 57% (36% aneurysms, 21% dilatation).[15,22] The current series has to date shown no such events.

Table III. Nonthrombotic complications of umbilical vein grafts (1990 to 2000)

Group	*Popliteal*	*Crural*	*Total*	*Old series (1975 to 1985)*
No. of grafts	109	174	283	907
Failure without thrombosis	0	2	2 (0.7%)	49 (5.0%)
Infection	1	8	9 (3.2%)	39 (4.3%)
Stenosis	2	3	5 (1.8%)	19 (2.1%)
Dissection	0	1	1 (0.4%)	1 (0.4%)
Pseudoaneurysm	1	0	1 (0.4%)	13 (1.4%)
Aneurysm (surgical repair)	0	0	0	26 (2.9%)

DISCUSSION

This series represents a continuation of the first decade of experience with UVg of the author and his colleagues.[15] Beginning in 1990, a number of noteworthy events occurred, the most important of which was the change in the manufacturing process and the improvement in quality control before distribution. With accumulating experience, better patient section, routine use of the dAVF with crural reconstructions, and the reintroduction of the tourniquet have clearly contributed to improved patency and durability of reconstructions with UVg.[16,19,23]

The decrease in the nonthrombotic failure rate in the current decade (1.1% versus 5.0%) is also contributory. Since the first 10-year report, the number of UVg reconstructions performed in our institution has significantly decreased. This represents our commitment to the use of autologous vein. Nevertheless, approximately 20% to 30% of our cases still require alternative graft materials. This number reflects the fact that we are often referred cases from other institutions in which saphenous veins were used and are no longer available. The data presented herein and the results with regard to graft patency and limb salvage rates reflect what we believe to be satisfactory outcomes and support our thesis for the use of the UVg as the primary alternative to autologous vein.

Studies on the comparative performances of alternatives to autologous saphenous vein are distressingly lacking. Those randomized prospective studies that do exist are dated or designflawed or generally have only considered a single alternative, thus failing to respond to the query of a "best" alternative in contradistinction to an "acceptable" alternative.[24,25] The Swedish,[10] Dutch,[11] and English[12] studies published in the 1980s, although they did show superiority of UVg as compared with polytetrafluoroethylene grafts, consisted mostly of bypass grafts in the above-knee position, dealt with the original version of the UVg, and lacked standardization. The recently published study by Johnson and Lee[14] suffers from similar flaws. Our studies, although extensive in detail, have been both retrospective and prospective and they lack randomization but do represent a single group/hospital experience. Clearly, the challenge to the vascular community is to develop a multihospital, randomized prospective study with guidelines that will permit the study of two or more materials (biologic and polymer) in infrageniculate positions. We also believe that adjuncts, such as the dAVF, should be included as arms of these studies.[19,26,27]

The patency rates that were reported in this study for popliteal and crural reconstructions are significantly better than those rates reported in the first decade report.[15] This clear trend of improvement is multifactorial, primarily on the basis of changes in manufacturing, quality control, and improved technical aspects in the performance of these operations. Nonetheless, the results of autologous saphenous vein are still superior as long as there is availability and adequacy. On the other hand, alternative autologous veins, such as arm and lesser saphenous veins, have generally not performed as well as the saphenous vein. Several authors who used autologous vein other than the greater saphenous vein as their preferential alternative material have reported patency rates that ranged from 75% (primary) to 90% (secondary) for popliteal reconstructions and 60% (primary) to 65% (secondary) for infrapopliteal reconstructions at 2 years.[28] Other investigators have reported ranges of 46% to 58% (primary) and 58% to 85% (secondary) at 2 years for all lower limb bypass grafting procedures with arm veins.[29-31] At 5 years, Donaldson, Whittemore, and Mannick[32] reported a non–greater saphenous vein patency rate of 49% for all infrainguinal procedures. In that we achieved 5-year UVg secondary patency rates of 71% for popliteals and 56% for crurals, it is clear that UVg not only provided comparable and subsequent superior patency rates but had the decided advantage of simplicity and decreased operative time as compared with the use of alternative autologous vein. The "all autogenous policy" needs to be revisited.

There has been considerable concern expressed by surgeons regarding the devastating effects of biodegradation when biological grafts are used for revascularization. Most surgeons attribute this to antigenicity of the graft, as has been shown with the bovine heterograft.[9] This is not clear for UVg because the glutaraldehyde molecule is better able to mask histocompatibility antigen sites with effective cross-linking than are other agents that were previously used. The possibility for the leaching of glutaraldehyde over time and, as a consequence, the loss or reversal of cross-linkage sites may be one of the possible mechanisms for delayed biodegradation aside from material fatigue or corrosion.[33] Speer et al[34] have also suggested that leached glutaraldehyde can induce adverse cellular effects that consist in vitro of cytotoxic effects on fibroblasts and in vivo

of foreign body giant cell reaction to glutaraldehyde-tanned sponge bioimplants. In our early series, there was indeed a greater than 50% incidence rate of this phenomenon occurring after 5 years of implantation, but this was associated with a low requirement for operative intervention.[15] Graft replacement was shown to be necessary in only 6% of the cases in which graft patency had been maintained for 5 or more years. In fact, there were few cases of biodegradation with aneurysm during the first 5 years of the follow-up period and, when this did occur, it was in patients with aneurysm disease. In the decade from 1990 to 2000 that was reported herein, we have noted the total absence of biodegradation and aneurysm formation. This is in concert with a rigorous surveillance protocol performed with duplex scan sonography. We attribute this phenomenon to improved manufacturing processes and quality control before distribution. If, in fact, little or no glutaraldehyde is leached, retention of cross-linkages and, as a consequence, graft architecture could account for these new and important observations. It is possible that future biodegradation will still occur, but clearly this will be at an impressively decreased incidence rate and remote from the date of surgery.

The UVg is now in its third decade of clinical use and can be a useful alternative to the saphenous vein if surgeons will recognize the need for appropriate case selection and acquire the techniques requisite for success. This includes the use of tourniquets, dAVF for crural bypass grafting, and postoperative anticoagulation therapy. Surveillance of these grafts is essential and can, with appropriate early intervention, aid in the avoidance of thrombotic events or other forms of failure. Skepticism expressed by some surgeons is in fact rarely on the basis of personal experience but is more so on an emotional response relating to the failure of the original bovine heterograft and other negative experiences with biologic materials. An appreciation of aldehyde chemistry, such as the nature and extent of amine linkages and the potential for the reversal of these bonds, and an understanding of the manufacturing process should lead surgeons to better analyze and appreciate the results currently possible and available with the UVg. We all need to be vigilant against unfounded repetitive activity that masquerades as scholarship and recognize that the greatest "obstacle to discovery" is the "illusion of knowledge".[35]

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DISCUSSION

Dr Thomas M. Bergamini (Louisville, Ky). This report represents one of the largest and longest experience with the use of human umbilical cord vein graft in the world. Dr Dardik and his coauthors deserve tremendous credit for their devotion to the study of this alternative conduit.

Numerous randomized, prospective studies have shown human umbilical cord vein graft to be superior to other alternative conduits for femoropopliteal bypass. This study focuses on femoral crural bypass. The improvement in the results in this study are multifactorial, as they have done several things differently. The manufacturing process has changed, which has led to a decrease in graft dilatation and aneurysm formation with an average follow-up of 3 years. Longer follow-up is necessary as the time interval in which graft dilatations and aneurysms occurred in their prior decade of experience was more than 5 years.

Also, they have had a change in patient selection in the current series, avoiding sequential bypasses and bypasses to the trifurcation vessels.

I have the following two questions for you.

You do state that the more remote the distal anastomosis, the poorer your results. What is an acceptable outflow artery score, including the diameter, patency length, stenosis and pedal arch patency? Is bypass to an inframalleolar vessel at the plantar artery or dorsalis pedis artery acceptable?

Second, We have learned that postoperative surveillance of in situ and reverse saphenous vein bypasses significantly improves graft patency and limb salvage as compared to clinical follow-up alone. Has the institution of a graft surveillance protocol in your current decade of experience improved the long-term graft patency and limb salvage, allowing the detection and correction of the failing grafts as compared to your historical control study that had clinical follow-up only? What is the mechanism of human umbilical cord vein graft failure that you've learned with the institution of your surveillance protocol?

Dr Kurt Wengerter. The first question relates to the question of which outflow tract we use for the bypass graft or which one we avoid. We do not use pedal vessels, that is the main restriction we have. The size of the vessel usually doesn't come into play, although certainly we see more failures with very small diseased vessels. The reason for the fistula is to help the outflow of these vessels. We will go down to the ankle but in general not into the foot.

You asked about the follow-up procedure. We follow these procedures, as we do with vein grafts, but clearly the mechanism of failure is often different from veins. The problems generally do not develop within the graft itself. Most of the problems occur from possible defects at anastomosis or progressive disease occurring in the outflow tract. Most of the problems can be detected at the time of surgery because we always perform duplex scans at that time. However, outflow tract problems are the most common cause of graft failure, aside from the patient's own coagulation tendencies, which may reduce patency of the graft as well.

Dr Harry R. Schanzer (New York, NY). I observed an improvement of about 10% between the first series and the late series that I don't think can be explained by modifications in the graft alone. What are the factors that you think may explain this improvement? I'm sure that you have done distal AV fistula more frequently now. You are doing duplex surveillance at the time of surgery. I don't know if you were doing them before. Can you expand on that?

Dr Wengerter. Well, most of the changes were gradual, and that's why we included the transition period. We have seen improvements in all aspects of patency and limb salvage. We feel that the dAVF is extremely important. It was not used routinely in the first group. When it was used in the first group, it was only used in the very worst cases and it tended to give the appearance that the dAVF was associated with a poorer outcome. In the second group it has been adopted across the board for any outflow artery in the crural system. The outflow volume flow rate increases several fold with the fistula and it's important to make sure the fistula is constructed properly.

Another factor, we believe, is the production of the grafts. Since 1990 we have had a new manufacturer, and we think the quality control is better. We think this is the reason we're not seeing aneurysm formation and dilatation. I've been at Englewood for 5 years now, and I have not seen an aneurysm myself in these grafts. In fact, I didn't see the prior ones because at that time I was at Montefiore not using the graft. But I can attest to the great difference that has occurred. We think that's related to the manufacturing.

Duplex scanning intraoperatively has been done for quite a number of years. We think it's extremely important for giving the surgeon feedback as to his technique and we find periodically problems with the graft that can be fixed, not only at the outflow tract but at the inflow tract as well, which may not be seen on angiograms.

Dr Kenneth C. Grant (Charlottetown, Prince Edward Island, Canada). Long grafts, prosthetic grafts to AV fistulas for limb ischemia as a last resort have seemed to worked well for a short time, and then after a year or 2—sometimes that time is enough—but after a year or 2 they close down, mainly because of the fast flow through the fistula, the hyperplastic response to fast flow. I gather that hasn't been an issue with the umbilical vein graft?

Dr Wengerter. We have not seen the hyperplasia as much as I've seen it in the past with PTFE grafts. Compliance is different with the UV graft; it's much better than PTFE, even long term, and we think that is part of the reason. The fistulas don't all stay open long term, and many of the grafts will stay open even after the fistula is closed. So it's not always 100% dependent on the fistula flow. We have not seen the hyperplastic changes occur as much as we see with arm vein fistulas or with other prosthetic outflow tracts. And we think that's part of the reason for the enhanced patency. We have previously reported annual attrition rates of dAVFs ranging from 13% to 26%.