Meta-analysis of alternate autologous vein bypass grafts to infrapopliteal arteries

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Background: **Several studies have described acceptable results for infrapopliteal bypass surgery that uses an autogenous vein other than the greater saphenous vein but is still no reliable prediction of outcomes. The objective of this study was to use meta-analysis to assess the long-term outcomes after infrapopliteal bypass grafting done with alternate autologous veins.**

Methods: **Studies published from 1982 through 2004 were identified from electronic databases and pertinent original articles. Thirty-two series were selected, all of which had used survival analysis and had reported a 1-year graft patency rate, with at least 15 bypasses. An interval success rate was calculated for each month in each series of grafts by using data from life tables, survival curves, and texts. Monthly success rates were combined across series to obtain a pooled estimate of success for each month. Pooled survival curves were then constructed for graft patency and foot preservation.**

Results: **The 5-year pooled estimates were 46.9% (95% confidence interval [CI] = 35.5%-58.3%) for primary patency, 66.5% (95% CI = 54.9%-78.2%) for secondary patency, and 76.4% (95% CI = 68.0%-84.8%) for foot preservation. These results were far superior to those reported for nonautologous grafts. Intensive duplex surveillance had a favorable impact on graft patency and foot preservation. No publication bias was detected.**

Conclusions: **When the greater saphenous vein is unavailable, alternate autologous veins are preferable to other graft materials in bypass surgery to infrapopliteal arteries. (J Vasc Surg 2005;42:449-55.)**

The preferred conduit for infrapopliteal bypass grafting is the greater saphenous vein, but it remains unclear which alternate graft should be used when this vein is unavailable to the surgeon. Often a policy of using all-autogenous tissue grafts has been adopted, but this implies harvesting veins from distant sites and constructing spliced vein grafts. Because the use of nonautologous grafts has the appeal of reducing operating times and the need for multiple incisions, the plausible superiority of using alternate autologous veins (AAV) needs proof. In the absence of such a proof, nonautologous grafts have been used liberally, particularly in nonteaching hospitals.[1]

An ongoing randomized comparative trial has included 19 AAV grafts and 36 polytetrafluoroethylene (PTFE) grafts to infrapopliteal arteries.[2] Much time will elapse before this trial ends, and the final answer will be restricted to spliced vein grafts and cuffed PTFE grafts. In contrast, a historical series from the same center has included more than 500 AAV grafts.[3] A meta-analysis of the many published series of AAV grafts thus seems attractive, as it can assess graft effectiveness rapidly and may allow informal comparison with meta-analyses of studies on other alternatives.[4,5] The present meta-analysis estimated the long-term outcomes after AAV bypass grafting to infrapopliteal arteries.

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METHODS

Type of graft. AAV grafts consisted of one or more segments of autologous vessels harvested from the upper or lower extremities, except for the single-segment greater saphenous vein. Autologous vessel thus meant an arm vein, the lesser saphenous vein, remnants of the greater saphenous vein, the superficial femoral vein, or the endarterectomized superficial femoral artery.

Study identification. The senior author (M.A.) searched the PubMed database for relevant articles published from 1982 through 2004. The descriptor "infrainguinal bypass" retrieved 697 titles, in which several words were searched, including "autogenous," "autologous," "vein," "arm," "cephalic," "basilic," "saphenous," "composite," and "spliced." After reading the abstracts online, 55 articles were printed for complete reading. A similar strategy identified two additional articles in the OVID database. Finally, the reference list of each printed article was searched for additional titles. Of the 32 articles that finally contributed series for the meta-analysis (APPENDIX, online only), 17 articles[3,6-21] were identified from databases and 15 articles[22-36] were found in the reference lists.

Criteria for inclusion. The articles included in this meta-analysis satisfied the following criteria: (1) a minimum of 15 AAV grafts inserted distally into an infrapopliteal artery, (2) a greater number of infrapopliteal than femoropopliteal bypasses, when these procedures had not been described separately, (3) the use of survival analysis to describe the outcomes, and (4) a minimum follow-up of a year, at least for some grafts. Although authors from three different centers have published more than one study on the subject,[3,8-10,22,23] inclusion of the same bypass more than once was avoided based on the period of each study and on other information from the text.

Outcomes. The outcomes selected for meta-analysis included primary patency (PP), secondary patency (SP), and foot preservation (FP). Although PP and SP reflect the fate of arterial reconstructions for different graft materials better than FP, the latter outcome describes the fate of revascularized limbs, which does not depend solely on graft patency. Patency outcomes have generally been reported as recommended.[37] Primary-assisted patency has been rigorously equal to SP in four articles[11-13,28] but was assumed to be equal to PP in another article that reported a large difference between primary-assisted patency and SP.[14] In four instances,[15,23,26,27] the general expression "cumulative patency" was assumed to represent SP.

Published life tables provided PP data for nine series, SP data for 11 series, and FP data for nine series. Life tables obtained directly from the authors supplied data for all three outcomes in five series. Survival curves that showed numbers at risk for all intervals were used to obtain PP for six series, SP for eight series, and FP for seven series. Survival curves that omitted the numbers at risk described SP in one article and all three outcomes in two articles that reported cumulative estimates and standard errors to one decimal place.

Data from the text were combined with a life table or survival curve for another outcome to generate data for PP in one series, data for SP in two series, and data for FP in two series. Data from the text alone were used to assess PP in two articles, SP in one article, and FP in three articles. Abstracts of papers presented at scientific meetings described PP for two series and SP and FP for another series.

Study quality. An ideal study should contain the reasons for using alternate grafts, the rates of patients requiring these grafts, life tables rather than graphs, the 1-month follow-up interval, an account for loss to follow-up, and the use of PP, SP, and FP. Of particular relevance is a link between predictive variables and each life table. Other relevant items include the rates of primary bypasses and tissue loss, regimens of postoperative antithrombotic therapy, the rate of grafts that enlarged or became infected, and data on further bypasses. Therefore, a perfect study would score 14, with a decrease of one point for each unmet requirement. The quality scores ranged from 3 to 14 (median, 9) for the 32 series (APPENDIX, online only). The scoring system used here has not been previously validated but was in strict accordance to recommended standards for reports dealing with lower extremity ischemia[37] and was used in two previous meta-analyses.[4,5]

Data extraction. Two authors (M.R. and F.C.B.N.) retrieved the data from life tables and from survival curves that showed the number of units at risk for all intervals, whereas the senior author (M.A.) retrieved the data from less complete survival curves and from texts. In 15 of 29 life tables for FP, the number of limbs revascularized to treat claudication was subtracted from the total number of limbs at risk at time zero and from the number of limbs censored at subsequent intervals. This ad hoc procedure assumed a null risk of amputation in the absence of critical ischemia. Fourteen life tables for FP remained unmodified, 10 because all the limbs had critical ischemia and four because of missing data for the clinical symptoms.

Meta-analysis of subgroups. AAV graft series were classified according to the period in which the study was published (before or after December 31, 1996), according to quality score (smaller or greater than 8.5), and according to the inclusion or not of femoropopliteal bypasses. Despite missing data in several articles, subgroups were also formed according to the predominance of single-length (n = 13) or multisegment (n = 11) conduits and according to the use of duplex scanning for postoperative graft surveillance, whether intensive (n = 16) or selective (n = 7). In the analyses of duplex surveillance, only series that described all three outcomes were used and time zero for survival analysis was fixed at 30 days after bypass surgery to compensate for possible differences in early outcomes before surveillance was started.

Meta-analysis comparison of different graft materials. Our meta-analysis was compared at yearly intervals to meta-analyses for five different graft materials by using the 95% confidence intervals (95% CIs), either published or calculated from published pooled estimates and their standard errors. The graft materials compared included PTFE grafts, umbilical cord vein allografts, cryopreserved arterial and venous allografts, and cold-storage vein allografts.[4,5]

Statistical methods. A random-effects meta-analysis combined the monthly hazard rates from single series to yield a pooled estimate of success for each month of follow-up. This was done for PP, SP, and FP. The product of successive monthly pooled estimates of success then yielded a pooled measure of cumulative success for each group or subgroup. Within-study, between-study, and between-interval variances calculated as previously reported reduced the influence of study size and provided less precise pooled estimates.[5] At yearly intervals, a standard error was calculated for the pooled estimate and a 95% CI was determined.[4,5] Nonoverlapping 95% CIs indicated a likely significant difference between AAV grafts and nonautologous grafts.

Sensitivity analysis. In sensitivity analysis, adjustments were made in the original series, some of which were also excluded selectively, publication bias was investigated, and fixed-effects modeling was considered.

Bias was introduced in the meta-analysis because (1) the original studies assumed independence between events and loss to follow-up, (2) some series included a few patients with symptoms of claudication alone, and (3) some series contained bypasses to popliteal or pedal arteries. Based on a published protocol,[4] the following adjustments were made to the original series: (1) the first month of follow-up concentrated the differences in the risk of failure attributable to clinical symptoms and the level of distal anastomosis; (2) a relative risk of graft failure of 0.75 was used for patients with claudication alone and for femoropopliteal bypasses; (3) a relative risk of graft failure of 1.14 was used for pedal bypasses; (4) a percentage of censored units representing losses to follow-up of 22% in the first month, 47% from the second to the 6th month, and 18% from the 7th to the 12th month was applied; and (5) 60% of units considered as lost within the first year of follow-up represented additional failures.

Because femoropopliteal bypasses and the symptoms of claudication alone correlated moderately in the series included in the meta-analysis of FP (Pearson $r = 0.49$), the sensitivity analysis used a relative risk of amputation of 0.85 rather than 0.75 for femoropopliteal bypasses in 15 series for which claudicators were excluded ad hoc. Because femoropopliteal bypasses and secondary bypasses correlated moderately in the series included in the meta-analysis of SP (Pearson $r = 0.54$) and in the series included in the meta-analysis of FP (Pearson $r = 0.46$), the sensitivity analysis for clinical symptoms, level of lower anastomosis, and completeness of follow-up also reduced a possible confounding effect of secondary bypasses.

Studies that reported "cumulative patency," a study in which the reported primary-assisted patency was assumed to represent PP, and studies for which the life tables were retrieved from texts or from survival curves that omitted the number of units at risk were excluded selectively.

RESULTS

Studies included in the meta-analysis. Thirty-two articles described a total of 2618 grafts (APPENDIX, online only). The mean age and the prevalence rates of male gender, arterial hypertension, diabetes, secondary bypasses, and smoking habits were frequently omitted (Table I). The overall prevalence rate was 5.1% for surgery in patients with claudication alone (29 articles). In 18 articles, there were 81.9% femorodistal bypasses, 13.2% popliteal-distal bypasses, and 8.5% of other configurations. The overall prevalence rate was 17.9% for bypasses to a popliteal artery (31 articles), which were placed above the knee (4.6%) and below the knee (13.3%), and 14.6% for pedal bypasses (26 articles). The alternative autologous vessel used included an arm vein in 28 studies, the lesser saphenous vein in 11 studies, the superficial femoral vein in two studies, and the endarterectomized superficial femoral artery in one study.

Main meta-analyses. The 5-year pooled estimate of success was 46.9% (95% CI = 35.5%-58.3%) for PP, 66.5% (95% CI = 54.9%-78.2%) for SP, and 76.4% (95% CI = 68.0%-84.8%) for FP (Table II). The early mortality described in 24 articles ranged from 0% to 14% (median, 2.1%; overall rate, 2.6%), whereas the 1-year cumulative death rate described in 15 articles ranged from 3% to 27% (median, 13.5%; overall rate, 12.8%). Half of the articles described wound complications, but the data were not reported with sufficient detail to allow meta-analysis. Graft infection and late graft degradation were rarely described.

Meta-analysis of subgroups. Meta-analysis revealed differences in pooled estimates that varied from month to month. The average of these differences, which was labeled the mean monthly difference, favored recent series (3.2% for PP, 4.0% for SP, and 5.7% for FP), series of better quality (6.7% for PP, 3.9% for SP, but –1.1% for FP),

Table I. Demographic and surgical variables for alternate autologous vein series

	Available data	*Series with no data*
Grafts	2618	0
Median age (y)	68 (61-74)	10
Males	63% (46%-88%)	14
Hypertension	50% (17%-73%)	20
Diabetes mellitus	48% (19%-85%)	14
Smoking	71% (41%-88%)	16
Heart disease	56% (31%-88%)	20
Second bypass	60% (14%-85%)	14
Claudication	3% (0%-30%)	4
Single vein	62% (0%-100%)	3
Popliteal-to-distal bypass	7% (0%-100%)	14
Pedal bypass	5% (0%-35%)	5
Popliteal bypass	9% (0%-48%)	0
Year of publication	1997 (1982-2004)	0
Year of beginning	1988 (1969-1998)	0
Censored 1 y	29% (0%-68%)	0
Score of quality	9 (3-14)	0

The data are median (range).

Table II. Meta-analysis of alternate autologous vein graft series

Mo	*PP (n = 27)*	*SP (n = 30)*	*FP (n = 29)*
1	92.1 (89.4-94.8)	95.8 (93.9-97.7)	96.7 (94.6-98.7)
3	85.7 (81.9-89.4)	92.1 (89.9-94.4)	94.1 (91.6-96.5)
6	77.6 (73.3-81.8)	88.0 (85.2-90.8)	91.7 (88.9-94.5)
12	67.6 (62.2-73.0)	82.2 (78.4-86.0)	88.4 (84.9-91.8)
24	59.6 (53.1-66.2)	76.7 (71.0-82.3)	84.9 (80.2-89.6)
36	55.8 (48.0-63.6)	73.5 (66.7-80.3)	83.5 (77.2-89.8)
48	50.6 (38.0-63.2)	69.6 (60.8-78.4)	81.2 (73.2-89.3)
60	46.9 (35.5-58.3)	66.5 (54.9-78.2)	76.4 (68.0-84.8)

n, number of series combined; *PP*, primary patency; *SP*, secondary patency; *FP*, foot preservation.
Values are pooled estimates (95% confidence intervals).

predominant single-length graft series (3.0 % for PP, 2.2% for SP, and 1.9% for FP), and series containing some femoropopliteal bypasses (−0.5% for PP, but 4.1% for SP and 4.6% for FP). The comparison between 1296 intensive surveillance grafts and 747 selective surveillance grafts used the same series in assessing all three main outcomes and fixed time zero at 30 days. The mean monthly difference favored intensive surveillance series (11.7% for SP and 7.4% for FP, despite –7.0% for PP). Extensive overlapping was found in all the aforementioned comparisons. A summary of the subgroup meta-analyses is also provided (Table III).

Sensitivity analysis. Adjustments for clinical symptoms, level of distal anastomosis, and completeness of follow-up reduced the 5-year pooled estimates by 4.0% for both PP and SP and by 5.0% for FP. When four studies that reported "cumulative patency" were excluded, the 5-year pooled SP decreased by 1.2%. When a study for which primary-assisted patency was assumed to represent PP was excluded, the 5-year pooled PP remained unchanged. When series for which the life tables were retrieved from texts or from survival curves that omitted the number of

Table III. Subgroup meta-analysis of alternate autologous vein grafts according type of conduit, use of duplex scanning for graft surveillance, and inclusion of femoropopliteal grafts

Outcome/subgroup	*n*	*1 mo*	*1 y*	*2 y*	*3 y*	*4 y*	*5 y*
PP/single-length	14	93.8	70.3	60.9	56.9	50.8	46.1
PP/multisegment	11	88.4	62.9	56.3	52.6	51.5	51.5
SP/single-length	15	97.1	84.2	78.0	75.4	69.7	64.3
SP/multisegment	12	93.3	79.4	74.2	70.5	69.9	69.9
FP/single-length	15	96.9	89.8	86.0	84.7	82.7	75.8
FP/multisegment	11	95.4	86.8	83.9	82.0	78.8	78.8
PP/intensive DS*	16	100.0	69.7	60.0	56.6	54.0	54.0
PP/selective DS*	7	100.0	78.2	70.6	66.4	59.2	53.5
SP/intensive DS*	16	100.0	88.4	83.3	80.4	78.8	78.0
SP/selective DS*	7	100.0	79.6	72.8	68.7	62.2	57.3
FP/intensive DS*	16	100.0	93.1	90.6	88.9	86.3	86.3
FP/selective DS*	7	100.0	88.5	83.0	81.3	78.7	71.5
PP/only infrapop	10	94.0	69.3	58.2	55.2	50.2	50.2
PP/other	17	91.2	66.7	59.8	55.8	50.6	46.3
SP/only infrapop	13	94.6	80.0	73.2	68.9	66.4	65.6
SP/other	17	96.3	83.2	78.2	75.4	70.7	66.2
FP/only infrapop	11	95.6	84.1	80.8	79.7	76.3	76.3
FP/other	18	97.1	90.0	86.5	85.0	83.1	76.2

n, number of series combined; *PP*, primary patency; *SP*, secondary patency; *FP*, foot preservation; *DS*, duplex scanning.
Values are pooled estimated. Overlap of 95% confidence intervals was found in all the comparisons.
*Zero time of follow-up was the 30th postoperative day.

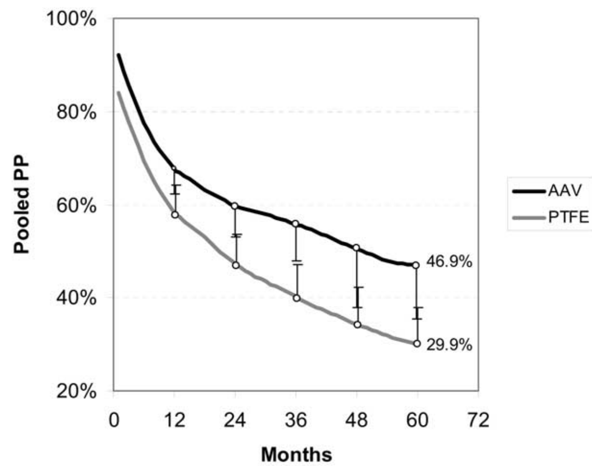

Fig 1. Meta-analysis survival curve of primary patency for alternate autologous veins (AAV) *(black)* and polytetrafluoroethylene (PTFE) *(gray)*. Bars are half the amplitude of 95% confidence intervals.

units at risk were excluded, the 5-year pooled estimate increased by 6.6% for PP, 0.9% for SP, and 1.5% for FP. Therefore, poor specification of the type of graft patency did not introduce bias, and the inclusion of series that reported poor quality survival data avoided overestimation of the results in favor of AAV grafts. When the foregoing adjustments and selective withdrawals were done simultaneously, the 5-year pooled estimate increased by 1.6% for PP, 5.5% for SP, and 3.0% for FP.

For a study size of less than 50 grafts, the 1-year estimate was higher than the 1-year pooled estimate in 7 of 16 series for PP, in 4 of 18 series for SP, and in 4 of 19 series for FP, which did not indicate a bias toward the publication of small series that showed better results.

Fixed-effects meta-analysis showed an absolute increase in the 5-year pooled estimate of 2.6% for PP, 2.0% for SP, and 1.7% for FP and a corresponding absolute decrease in their standard errors of 0.8%, 2.2%, and 1.0%, respectively.

Meta-analysis comparison of different graft materials. A summary of the characteristics of articles included in previous meta-analyses can be found elsewhere.[4,5] In brief, studies of both peripheral allografts and PTFE grafts were more recent than studies of umbilical cord vein allografts. The median quality score ranged from 8.5 to 11.5 for different peripheral allograft series, was 7 for PTFE series, and was only 5.5 for umbilical cord vein allograft series. Femoropopliteal bypasses corresponded to 2.2% of PTFE grafts, 8.4% of peripheral allograft series, and 3.6% of umbilical cord vein allografts. Pedal bypasses corresponded to 1.6% of PTFE grafts and 4.8% of peripheral allografts but were not done with umbilical cord vein allografts.

When AAV grafts were used for reference, there was overlapping of the 95% CIs of the pooled PP for PTFE grafts (Fig 1). Meta-analysis of PP for other graft materials was not possible. The 95% CIs of the pooled SP did not overlap for PTFE grafts, umbilical cord vein grafts, and cryopreserved vein allografts (Fig 2). The 95% CIs of the pooled FP did not overlap for either PTFE grafts or umbilical cord vein grafts (Fig 3), but there were several overlaps for cryopreserved vein allografts.

The 95% CIs of all three pooled outcomes overlapped for cryopreserved arterial allografts and cold-storage vein allografts. For clarity, these outcomes were not displayed graphically. For the same reason, meta-analysis of FP for cryopreserved vein allografts was omitted (Fig 3).

DISCUSSION

Meta-analysis of medical studies as a statistical procedure refines the synthesis of available data, thereby allowing surgical decision making to be done more scientifically. Meta-analysis also enhances patient information and consent and promotes respect for autonomy. The surgical literature is full of uncontrolled series, each of which represents a poor source of scientific evidence. However, the meta-analysis of such series provides a better source of evidence, particularly when randomized trials are rare, as is the case for infrapopliteal revascularization.

This study and two related meta-analyses[4,5] aimed to determine the outcomes after bypass surgery to infrapopliteal arteries for different graft materials. As expected, the AAV graft emerged as the most effective alternative to the standard greater saphenous vein graft. Alternate veins are structurally and functionally similar to the greater saphenous vein, with emphasis on the presence of a living endo-

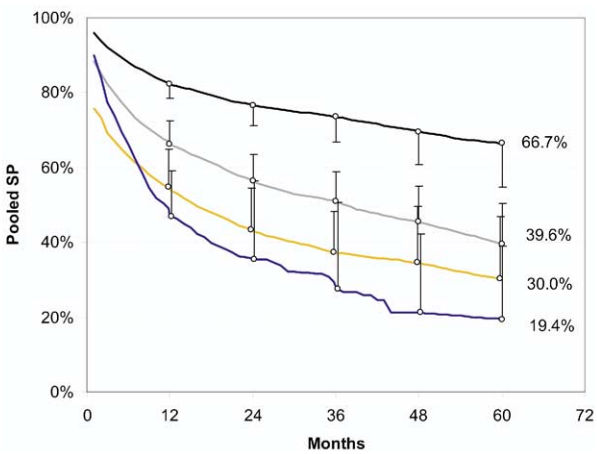

Fig 2. Meta-analysis survival curve of secondary patency (SP) for alternate autologous veins (AAV) *(black)*, polytetrafluoroethylene (PTFE) *(gray)*, umbilical cord vein *(orange)*, and cryopreserved vein *(blue)*. Bars are half the amplitude of 95% confidence intervals.

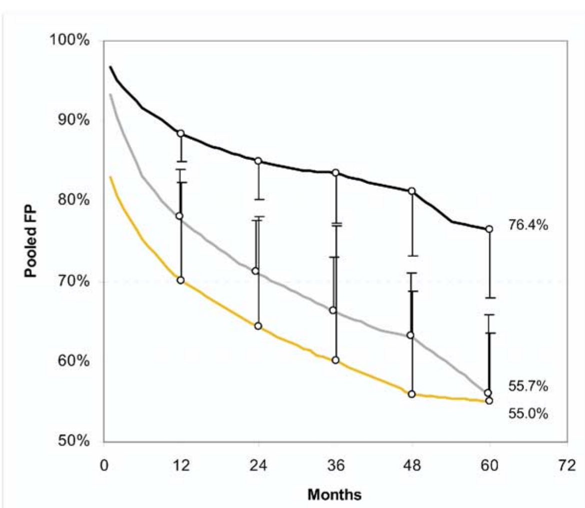

Fig 3. Meta-analysis survival curve of foot preservation (FP) for alternate autologous veins (AAV) (*black*), polytetrafluoroethylene (PTFE) *(gray)*, and umbilical cord vein *(orange)*. Bars are half the amplitude of 95% confidence intervals.

thelial layer. PTFE grafts came next, without challenging AAV grafts in terms of SP (Fig 2) and FP (Fig 3).

When the present meta-analysis and the meta-analysis of PTFE grafts were compared, the difference in PP was greater than 10% at 18 months and beyond, which seems clinically relevant, but the 95% CIs overlapped at most yearly intervals (Fig 1). However, this comparison is unfair because intensive duplex surveillance will create a lower PP curve for AAV than for PTFE, for which intensive surveillance is not usually used. Perhaps selective surveillance AAV grafts would provide a better comparison with PTFE grafts. The difference in SP between these meta-analyses was of high clinical relevance and was likely significant. In the meta-analysis of FP, an ad hoc procedure applied to symptoms of claudication alone avoided bias in favor of AAV grafts, but the difference in favor of these grafts remained impressive and was still significant. Although the patency of PTFE grafts may benefit from the use of adjunctive procedures at the distal anastomosis, a corresponding improvement in FP remains uncertain.[4]

Meta-analyses of SP for peripheral vessel allograft bypass grafts have shown excellent early outcomes followed by poor mid-term outcomes.[5] Mainly because of repeat bypass surgery, the 5-year pooled FP was greater than 60% for three series of cryopreserved artery allografts and ten series of cryopreserved vein allografts, which is a gratifying result. Because the median year of publication for articles included in the meta-analysis was 1995 for the PTFE grafts and 1997 for the cryopreserved allografts, these grafts currently compete each other. Despite the inclusion of patients with more advanced limb ischemia, meta-analysis of three series of cold-storage vein allografts yielded a 5-year pooled FP close to 40%, still an acceptable result if the transmission of viral infection were not a major concern.[5] Peripheral vessel allografts may be useful in overcoming critical ischemia for a short time, when a pedal bypass is indicated or when there is a greater risk of wound dehiscence.

A meta-analysis for 16 series of umbilical cord vein grafts[5] has shown a poor early SP, but the long-term SP has been slightly superior to those obtained for peripheral vessel allografts. The 5-year pooled FP has been an acceptable 55%, which was nearly identical to the 5-year pooled FP of 55.7% described for PTFE grafts. The meta-analysis for umbilical cord vein grafts has mostly reflected historical vascular practice (median publication year, 1986), but superb outcomes from a modern series keep these grafts among the current alternatives for distal bypass surgery.[38] However, these grafts have not been used in very distal bypass grafting.[5]

The marked superiority of AAV grafts over nonautologous alternatives may increase further with statin therapy[39] and a more frequent use of angioscopy or duplex scanning intraoperatively.[18] Intensive postoperative graft surveillance with duplex scanning, which has been in use for more than a decade, and the aggressive treatment of failing grafts sacrifice PP to increase SP in the hope of also relieving the symptoms and increasing FP. However, the appropriateness of intensive surveillance remains controversial because the relief of symptoms is difficult to assess and because intensive-surveillance studies in patients originally presenting with critical ischemia have sometimes omitted FP rates.[18] To avoid the latter problem, the subgroup meta-analysis of graft surveillance was restricted here to studies that described all three outcomes. An absolute risk-reduction of major amputation estimated as 4.6% at 12 months, 7.6% at 36 months, and 14.8% at 60 months (Table III) provided some support for using duplex surveillance intensively after AAV bypass grafting to the infrapopliteal area.

Subgroup meta-analysis according to the period of publication and study quality was done mainly for completeness and revealed a superiority trend that favored more recent series for all three outcomes and better quality studies for both PP and SP, but not for FP. The type of AAV conduit may be a promising predictor of graft patency, but only a few series have actually constituted distinct subgroups of single-segment or multisegment grafts. The initially worse pooled outcomes for predominant multisegment grafts probably reflected technical difficulties, whereas the greater stability in long-term follow-up may be the result of better ultimate conduits.

The applicability of AAV grafts was not addressed, but nonautologous grafts may rarely be necessary, even when a single-length AAV graft is unavailable. Roddy et al[3] described 536 spliced AAV grafts and 130 prosthetic grafts, which corresponds to a ratio of 4:1. Because the proponents of prosthetic grafts have usually reported limited experience with AAV grafts, it remains uncertain whether a complete inventory of the available veins had been done. If nonautologous grafts are rarely needed, provide inferior outcomes, and often require the prolonged use of oral anticoagulants, then the choice of such grafts must be fully justified to be ethically acceptable.

A limitation in the methodology used here concerned the use of statistical inference when comparing two pooled survival curves. It was not possible to calculate the P values or to construct the 95% CIs for the differences observed. Therefore, overlap of the 95% CIs was the only indication of the lack of significant difference. Conversely, nonoverlapping 95% CIs indicated a significant difference. This problem did not affect the main results of this study.

Bias was of small magnitude in this meta-analysis of observational studies. Indeed, sensitivity analysis showed that subjectivism in the assessment of patency outcomes and the acceptance of a few studies with poorly described survival data did not introduce bias. Furthermore, patients with critical ischemia corresponded to 95% of the grafts at risk. In addition, the graft material and the level of distal anastomosis were mostly restricted by design, and the rates of less favorable pedal bypasses and of possibly more favorable femoropopliteal bypasses were equivalent. The overall study quality would have been greatly improved had the authors of the original studies adhered to recommended standards for reporting.[37]

The validity of the inferences from this meta-analysis is strongly supported by internal and external evidence. The studies reviewed adopted similar outcomes, used data of acceptable quality, and reported high response rates. In addition, the study design, particularly the inclusive entry criteria, was compatible with real life and allowed adequate sampling of a hypothetical population of studies. Finally, random-effects modeling avoided overestimation and undue precision of the measured outcomes. In the absence of bias and study invalidity, we conclude that AAV grafts provide better outcomes than nonautologous grafts in bypass surgery to infrapopliteal arteries and should be used preferentially in the absence of a usable greater saphenous vein.

REFERENCES

1. Merrell GA, Gusberg RJ. Infrainguinal bypass conduit: autogenous or synthetic. A national perspective. Vasc Endovascular Surg 2002;36: 247-54.
2. Kreienberg PB, Darling RC 3rd, Chang BB, Champagne BJ, Paty PS, Roddy SP, et al. Early results of a prospective randomized trial of spliced vein versus polytetrafluoroethylene graft with a distal vein cuff for limb-threatening ischemia. J Vasc Surg 2002;35:299-306.
3. Roddy SP, Darling RC 3rd, Ozsvath KJ, Kreienberg PB, Chang BB, Mathew TS, et al. Composite sequential arterial reconstruction for limb salvage. J Vasc Surg 2002;36:325-9.
4. Albers M, Battistella VM, Romiti R, Rodrigues AA, Pereira CA. Meta-analysis of polytetrafluoroethylene bypass grafts to infrapopliteal arteries. J Vasc Surg 2003; 37:1263-9.
5. Albers M, Romiti R, Pereira CA, Antonini M, Wulkan M. Meta-analysis of allograft bypass grafting to infrapopliteal arteries. Eur J Vasc Endovasc Surg 2004;28:462-72.
6. Hölzenbein T, Aslim E, Domenig C, Orner S, Weber D, Kretschmer G. Surgical and non-surgical adjuncts to make arm veins work for distal leg bypass [abstract]. European Society for Vascular Surgery. XVII Annual Meeting, Dublin, 2003. Available at: http://esvs.co.uk/. Accessed August 15, 2003.
7. Osman HY, Shiralker S, Gibbons CP. The search for alternative sources of autologous vein for infrainguinal bypass— is it worth the trouble? Br J Surg 2000;87(suppl 1):41.
8. Chew DK, Owens CD, Belkin M, Donaldson MC, Whittemore AD, Mannick JA, et al. Bypass in the absence of ipsilateral greater saphenous vein: safety and superiority of the contralateral greater saphenous vein. J Vasc Surg 2002;35:1085-92.
9. Chew DK, Conte MS, Donaldson MC, Whittemore AD, Mannick JA, Belkin M. Autogenous composite vein bypass graft for infrainguinal arterial reconstruction. J Vasc Surg 2001;33:259-64.
10. Chang BB, Paty PS, Shah DM, Leather RP. The lesser saphenous vein: an underappreciated source of autogenous vein. J Vasc Surg 1992;15: 152-6.
11. Alexander J, Gutierrez C, Katz S. Non-greater saphenous vein grafting for infrageniculate bypass. Am Surg 2002;68:611-4.
12. Gentile AT, Lee RW, Moneta GL, Taylor LM, Edwards JM, Porter JM. Results of bypass to the popliteal and tibial arteries with alternative sources of autogenous vein. J Vasc Surg 1996;23:272-9.
13. Eugster T, Stierli P, Fischer G, Gürke L. Long-term results of infrainguinal arterial reconstruction with spliced veins are equal to results with non-spliced veins. Eur J Vasc Endovasc Surg 2001;22:152-6.
14. Curi MA, Skelly CL, Woo DH, Desai TR, Katz D, McKinsey JF, et al. Long-term results of infrageniculate bypass grafting using all-autogenous composite vein. Ann Vasc Surg 2002;16:618-23.
15. Schulman ML, Badhey MR. Late results and angiographic evaluation of arm veins as long bypass grafts. Surgery 1982;92:1032-41.
16. Tisi PV, Crow AJ, Shearman CP. Arm vein reconstruction for limb salvage: long-term outcome. Ann R Coll Surg Engl 1996;78:497-500.
17. Halloran BG, Lilly MP, Cohn EJ, Benjamin ME, Flinn WR. Tibial bypass using complex autologous conduit: patency and limb salvage. Ann Vasc Surg 2001;15:634-43.
18. Armstrong PA, Bandyk DF, Wilson JS, Shames ML, Johnson BL, Back MR. Optimizing infrainguinal arm vein bypass patency with duplex ultrasound surveillance and endovascular therapy. J Vasc Surg 2004;40: 724-30.
19. Balshi JD, Cantelmo NL, Menzoian JO, LoGerfo FW. The use of arm veins for infrainguinal bypass in end-stage peripheral vascular disease. Arch Surg 1989;124:1078-81.
20. Presti C, Puech-Leão P, Albers M. Superficial femoral eversion endarterectomy combined with a vein segment as a composite artery-vein bypass graft for infrainguinal arterial reconstruction. J Vasc Surg 1999; 29:413-21.
21. Sesto ME, Sullivan TM, Hertzer NR, Krajewski LP, O'Hara PJ, Beven EG. Cephalic vein grafts for lower extremity revascularization. J Vasc Surg 1992;15:543-9.
22. Harris RW, Andros G, Salles-Cunha SX, Dulawa LB, Oblath RW, Apyan RL. Totally autogenous venovenous composite bypass grafts.

Salvage of the almost irretrievable extremity. Arch Surg 1986;121:1128-32.
23. Harris RW, Andros G, Salles-Cunha SX, Dulawa LB, Oblath RW, Apyan R. Alternative autogenous vein grafts to the inadequate saphenous vein. Surgery 1986;100:822-7.
24. Faries PL, Arora S, Pomposelli FB Jr, Pulling MC, Smakowski P, Rohan DI, et al. The use of arm vein in lower-extremity revascularization: results of 520 procedures performed in eight years. J Vasc Surg 2000; 31:50-9.
25. Hickey NC, Thomson IA, Shearman CP, Simms MH. Aggressive arterial reconstruction for critical lower limb ischaemia. Br J Surg 1991;78:1476-8.
26. Weaver FA, Barlow CR, Edwards WH, Mulherin JL Jr, Jenkins JM. The lesser saphenous vein: autogenous tissue for lower extremity revascularization. J Vasc Surg 1987;5:687-92.
27. Graham JW, Lusby RJ. Infrapopliteal bypass grafting: use of upper limb vein alone and in autogenous composite grafts. Surgery 1982;91: 646-9.
28. Brochado-Neto FC, Albers M, Pereira CA, Gonzalez J, Cinelli M Jr. Prospective comparison of arm veins and greater saphenous veins as infrageniculate bypass grafts. Eur J Vasc Endovasc Surg 2001;22:146-51.
29. Goyal A, Shah PM, Babu SC, Mateo RB. Popliteal-crural bypass through the posterior approach with lesser saphenous vein for limb salvage. J Vasc Surg 2002;36:708-12.
30. Lovell MB, Gray DE, Harris KA, DeRose G, Jamieson WG. The use of arm vein as an alternative conduit for lower-extremity bypass. J Vasc Nurs 1996;14:104-9.
31. Harward TR, Coe D, Flynn TC, Seeger JM. The use of arm vein conduits during infrageniculate arterial bypass. J Vasc Surg 1992;16:420-6.
32. Chalmers RT, Hoballah JJ, Kresowik TF, Sharp WJ, Synn AY, Miller E, et al. The impact of color duplex surveillance on the outcome of lower limb bypass with segments of arm veins. J Vasc Surg 1994;19:279-86.
33. Browning N, Zammit M, Rodriguez D, Sauvage L, Loudenback D, Raghavan A. Use of arm veins for lower extremity arterial bypass - results, anatomical features and technical considerations. S Afr J Surg 2000;38:36-41.
34. Schneider JR, Walsh DB, McDaniel MD, Zwolak RM, Besso SR, Cronenwett JL. Pedal bypass versus tibial bypass with autogenous vein: a comparison of outcome and hemodynamic results. J Vasc Surg 1993; 17:1029-40.
35. Calligaro KD, Syrek JR, Dougherty MJ, Rua I, Raviola CA, DeLaurentis DA. Use of arm and lesser saphenous vein compared with prosthetic grafts for infrapopliteal arterial bypass: are they worth the effort? J Vasc Surg 1997;26:919-24.
36. Ouriel K. The posterior approach to popliteal-crural bypass. J Vasc Surg 1994;19:74-80.
37. Rutherford RB, Baker JD, Ernst C, Johnstone KW, Porter JM, Ahn S. Recommended standards for reports dealing with lower extremity ischemia. J Vasc Surg 1997;26: 517-38.
38. Dardik H, Wengerter K, Qin F, Pangilinan A, Silvestri F, Wolodiger F, et al. Comparative decades of experience with glutaraldehyde-tanned human umbilical cord vein graft for lower limb revascularization: an analysis of 1275 cases. J Vasc Surg 2002;35:64-71.
39. Abbruzzese TA, Havens J, Belkin M, Donaldson MC, Whittemore AD, Liao JK, et al. Statin therapy is associated with improved patency of autogenous infrainguinal bypass grafts. J Vasc Surg 2004;39:1178-85.

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APPENDIX. Main features of 32 alternate autologous vein graft series

Author	*Size*	*IC (%)*	*2nd bypass (%)*	*Popliteal/ pedal (%)*	*Single vein (%)*	*DS*	*Score of quality*	*Outcomes*
Alexander et al[11]	51	22	?	41/0	82	+	9	All 3
Armstrong et al[18]	89	0	85	24/8	74	+	13	All 3
Balshi et al[19]	36	0	65	42/?	72	–	9	All 3
Brochado-Neto et al[28]	35	3	46	31/20	66	–	12	All 3
Browning et al[33]	40	8	73	18/3	42	+	9	All 3
Calligaro et al[35]	45	0	?	0/18	82	+	10	All 3
Chalmers et al[32]	42	2	80	36/0	29	+	11	All 3
Chang et al[10]	69	0	74	12/6	58	+	6	PP FP
Chew et al[9]	136	?	58	0/12	0	+	12	All 3
Chew et al[8]	34	?	?	0/?	100	+	8	All 3
Curi et al[14]	61	5	51	7/8	0	?	9	All 3
Eugster et al[13]	86	16	?	29/?	0	+	6	All 3
Faries et al[24]	520	2	53	27/35	70	–	10	All 3
Gentile et al[12]	133	0	?	0/?	?	+	6	SP FP
Goyal et al[29]	21	0	14	0/0	100	+	13	All 3
Graham and Lusby[27]	37	5	?	0/0	27	–	6	All 3
Halloran et al[17]	61	0	?	0/20	59	+	6	All 3
Harris et al[22]	54	7	39	22/6	0	–	10	SP FP
Harris et al[23]	102	30	?	48/5	100	–	8	All 3
Harward et al[31]	43	7	49	21/0	14	+	13	All 3
Hickey et al[25]	60	0	?	0/0	38	–	4	SP
Hölzenbein et al[6]	120	3	83	23/7	75	?	5	PP
Lovell et al[30]	36	14	64	0/0	?	+	9	All 3
Osman et al[7]	43	?	60	9/9	47	+	8	All 3
Ouriel[36]	21	0	29	0/0	100	?	11	All 3
Presti et al[20]	30	0	17	0/3	0	–	14	All 3
Roddy et al[3]	536	0	?	?/?	0	+	8	All 3
Schneider et al[34]	41	0	?	0/20	?	+	8	All 3
Schulman and Badhey[15]	16	0	?	0/6	100	–	6	SP
Sesto et al[21]	35	17	50	29/0	66	–	9	All 3
Tisi et al[16]	42	5	64	12/0	70	+	7	All 3
Weaver et al[26]	43	?	?	9/0	67	–	3	SP FP

IC, patients with intermittent claudication only; *DS*, intensive duplex surveillance; *?*, not informed; *PP*, primary patency; *SP*, secondary patency; *FP*, foot preservation.