Meta-analysis of femoropopliteal bypass grafts for lower extremity arterial insufficiency

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Background: **In femoropopliteal bypass surgery, the use of saphenous vein grafts is preferable, but synthetic grafts are widely used above the knee. The objective of this meta-analysis was to assess the long-term patency of femoropopliteal bypass grafts classified as above-knee polytetrafluoroethylene, above-knee saphenous vein, or below-knee saphenous vein.**

Methods: **Studies published from 1986 through 2004 were identified from electronic databases and reference lists; 73 articles contributed 1 or more series that used survival analysis, assessed femoropopliteal bypasses in one of the foregoing configurations, reported a 1-year graft patency rate, and included at least 30 bypasses. The series with a predominance of claudicant patients were included in meta-analysis C, and the series in which critical ischemia predominated were included in meta-analysis CI. Pooled survival curves of graft patency were constructed.**

Results: **In meta-analysis C, the pooled primary graft patency was 57.4% for above-knee polytetrafluoroethylene, 77.2% for above-knee vein, and 64.8% for below-knee vein at 5 years; there was a significant difference between above-knee grafts at 3, 4, and 5 years ($P < .05$). The corresponding pooled secondary graft patency was 73.2%, 80.1%, and 79.7%, respectively ($P > .05$). In meta-analysis CI, the pooled primary graft patency was 48.3% for above-knee polytetrafluoroethylene, 69.4% for above-knee vein, and 68.9% for below-knee vein at 5 years; there was a significant difference between above-knee grafts until 4 years ($P < .05$). The corresponding pooled secondary graft patency was 54.0%, 71.9%, and 77.8%, respectively, with a significant difference between above-knee grafts at 2, 3, and 4 years ($P < .05$).**

Conclusions: **The great saphenous vein performs better than polytetrafluoroethylene in femoropopliteal bypass grafting and should be used whenever possible. (J Vasc Surg 2006;44:510-7.)**

The great saphenous vein is considered the most durable conduit for infrainguinal revascularization. A classic randomized trial published in 1986 demonstrated the superiority of vein grafts in below-knee revascularization, whereas the above-knee femoropopliteal polytetrafluoroethylene bypass graft (AK-P) was equivalent to the above-knee femoropopliteal saphenous vein bypass graft (AK-V) for 18 months and was not significantly inferior thereafter.[1] On the basis of these findings and data from uncontrolled surgical series,[2,3] it was argued that an AK-P should be initially preferred to spare the saphenous vein for a future bypass to a below-knee artery in the same limb. However, a vein bypass subsequent to an AP has rarely been performed,[4,5] and such a vein-sparing approach has been unrewarding.[4,5] It is interesting to note that AK-Ps remain in frequent use.[6,7]

Femoropopliteal revascularization deserves re-evaluation for many reasons. First, four recent randomized trials[8–11] have shown the superiority of AK-V over AK-P in the first 12 months of follow-up. Second, it has been suggested that the below-knee saphenous vein bypass graft (BK-V) must be considered as the reference standard of infrainguinal bypasses.[1,12–14] Third, patients with different symptoms must be appraised separately, and standard types of graft patency should be used. Finally, although there is continual development of surgical skills,[15] the competing endovascular alternatives often improve at a much faster rate.[16]

Meta-analysis of uncontrolled surgical series can provide a reliable account of available data because these series are frequent in the literature and often involve a large number of patients.[5] In this meta-analysis, we estimated the long-term outcomes after femoropopliteal bypass performed for claudication or critical ischemia and classified as AK-P, AK-V, or BK-V.

MATERIALS AND METHODS

Study identification. The MEDLINE electronic database was searched by using the expression "femoropopliteal bypass" and the terms "PTFE" and "saphenous" for the period from January 1986 to December 2004. Two complementary databases, EMBASE and LILACS, were searched by using the term "femoropopliteal bypass." The abstracts of articles selected by title were read online to reduce the number of articles for full-text examination. Finally, additional titles were sought in the bibliographies of the retrieved articles. Articles written in English, German, French, Italian, Spanish, or Portuguese were examined.

Inclusion criteria. The articles included satisfied the following requirements: (1) graft patency described with life tables, survival curves, or suitable texts; (2) series of

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AK-Ps, AK-Vs, or BK-Vs; (3) a follow-up of 1 year for at least some grafts; (4) a minimum of 30 bypasses in at least 1 series when an article described 2 or more series; and (5) publication in 1986 or later. The series were included in meta-analysis C when patients with claudication predominated and in meta-analysis CI when critical ischemia predominated.

Exclusion criteria. Various articles were excluded for at least one of the following reasons: (1) clinical symptoms not described, (2) predominance of blind segments of popliteal artery, (3) predominance of composite bypass grafts, (4) predominance of bypasses to the infrapopliteal arteries, (5) repeat inclusion of bypasses, and (6) unreliable or unattainable reconstruction of life tables from graphs or texts. A total of 73 articles[1,2,8–12,14,17–81] provided series for meta-analysis (Appendix I, online only).

Data extraction. Two authors (C.E.P. and M.A.) extracted the data independently and resolved any disagreement by discussion on several occasions. The outcome measures of interest were primary graft patency and secondary graft patency.[82] Of the 73 articles included, 54 described primary or secondary patency, whereas the remaining 19 articles reported primary assisted patency, inappropriate primary patency, or simply cumulative patency. These nonstandard patencies were used subjectively as primary patency for 2 AK-P series in meta-analysis C and arbitrarily as secondary patency in 17 articles that contributed 14 (AK-P, n = 5; AK-V, n = 6; BK-V, n = 3) series to meta-analysis C and 13 (AK-P, n = 2; AK-V, n = 3; BK-V, n = 8) series to meta-analysis CI. The survival data were extracted from life tables, survival curves that showed the number of grafts at risk for at least some intervals, and plain survival curves that omitted the number at risk. The survival data were also extracted from the text and another source, either a life table or a survival curve describing a different outcome, and from the text alone.

Early mortality was investigated for the AK-V and BK-V series combined and for the AK-P series. The effects of runoff, the late use of a vein bypass after AK-Ps, and the percentage of AK-Ps that became infected were also investigated.

Study quality. An ideal study should contain life tables rather than graphs, the 1-month follow-up interval, a 5-year follow-up, losses to follow-up, no flat tails, and a report of primary patency, secondary patency, and foot preservation. Also important are a demographic profile linked to survival analysis, the rates of previous operation and tissue loss, a measurement of runoff, regimens of postoperative anticoagulant therapy, reference to the use of duplex scanning for graft surveillance, and data on further bypasses. Each of the preceding items was graded 1 or 0, so that a perfect study would score 15.

Statistical methods. Random-effects modeling explicitly recognizes that differences exist between outcomes at different centers. This procedure combined monthly hazard rates from single series of AK-Ps, AK-Vs, or BK-Vs to yield a pooled estimate of patency for each graft configuration and each month of follow-up. The product of successive monthly pooled estimates of success then yielded a pooled measure of cumulative patency for each type of graft. Standard errors were calculated for the pooled estimates, and within-study and between-study variances were used to reduce the influence of study size on the pooled estimates (Appendix II, online only). Statistical significance ($P < .05$) was assessed for the differences between the AK-P series and the other graft series at yearly intervals. The statistical method used judges the significance of differences by examining the overlap between confidence intervals, but it does not calculate P values.[83] The pooled estimates were displayed graphically for both meta-analyses (Figs 1-4).

Sensitivity analysis. The effects of excluding series that used nonstandard patencies or included heterogenous clinical symptoms were investigated in both meta-analyses, as also were the effects of excluding AK-P series with a score of study quality higher than 9 for primary patency or higher than 10 for secondary patency in meta-analysis C. A fixed-effects model of meta-analysis, which estimates a single

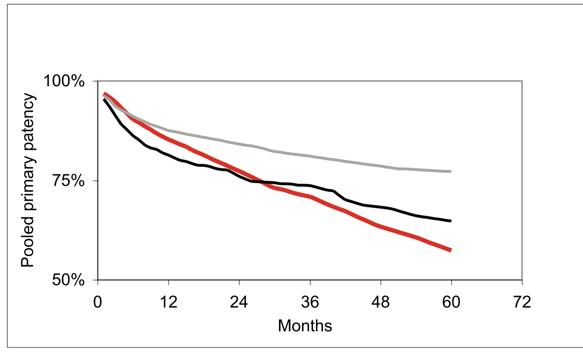

Fig 1. Meta-analysis C of primary patency for above-knee femoropopliteal polytetrafluoroethylene bypass grafts (AK-P; *red line*), above-knee femoropopliteal saphenous vein bypass grafts (AK-V; *gray line*), and below-knee saphenous vein bypass grafts *(black line)*. The *vertical line* indicates when AK-V surpassed AK-P.

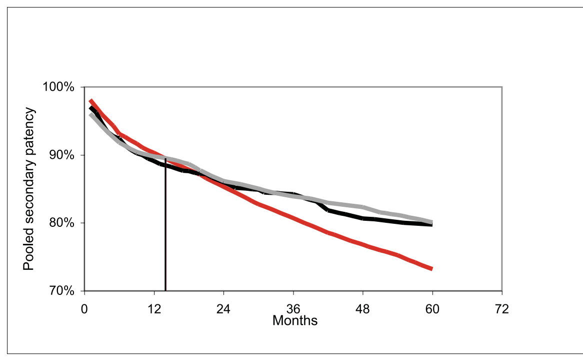

Fig 2. Meta-analysis C of secondary patency for above-knee femoropopliteal polytetrafluoroethylene bypass grafts (AK-P; *red line*), above-knee femoropopliteal saphenous vein bypass grafts (AK-V; *gray line*), and below-knee saphenous vein bypass grafts *(black line)*. The *vertical line* indicates when AK-V surpassed AK-P.

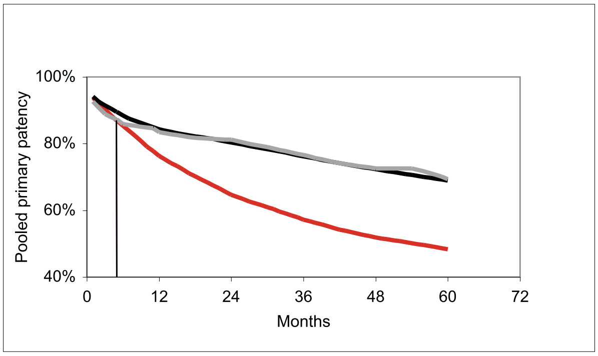

Fig 3. Meta-analysis CI of primary patency for above-knee femoropopliteal polytetrafluoroethylene bypass grafts (AK-P; *red line*), above-knee femoropopliteal saphenous vein bypass grafts (AK-V; *gray line*), and below-knee saphenous vein bypass grafts *(black line)*. The *vertical line* indicates when AK-V surpassed AK-P.

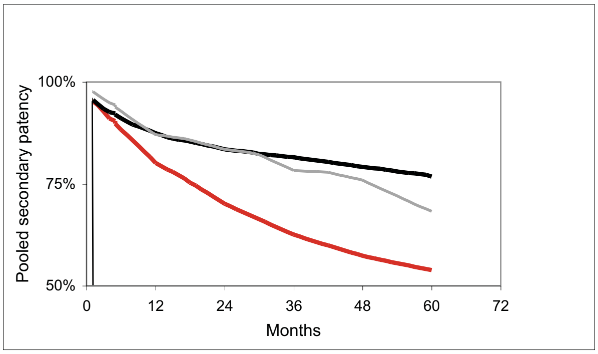

Fig 4. Meta-analysis CI of secondary patency for above-knee femoropopliteal polytetrafluoroethylene bypass grafts (AK-P; *red line*), above-knee femoropopliteal saphenous vein bypass grafts (AK-V; *gray line*), and below-knee saphenous vein bypass grafts *(black line)*. The *vertical line* indicates when AK-V surpassed AK-P.

common effect among studies and assumes no between-study variances, was considered. To adjust for flat tails, one failure was added and then distributed in equal parts to the months in the flat tail. This procedure seemed valid because a null value for a sequence of monthly hazard rates at the end of a survival curve, which determines the flat tail, likely introduces bias. Changes in the pooled outcomes and in the statistical inferences were examined. Funnel plots to detect publication bias were not used because of the small number of series in some meta-analyses.

RESULTS

Characteristics of the original studies. The study design was retrospective in 49 articles and prospective in the remaining 24. The latter included 6 randomized trials comparing AK-Ps and AK-Vs and 18 nonrandomized studies. In the follow-up, the number of articles that contributed at least 1 series was 67 (92%) at 2 years, 65 (89%) at 3 years, 50 (68%) at 4 years, and 39 (53%) at 5 years. With regard to the use of postoperative duplex scanning for graft surveillance, 21 studies used this tool, either routinely (AK-P, n = 4; AK-V, n = 3; BK-V, n = 6) or selectively (AK-P, n = 6; AK-V, n = 4; BK-V, n = 6); 37 studies did not use this tool; and 15 articles did not mention this technology. The proportion of claudicant patients or an interval containing this datum was often reported, but other clinical variables were frequently omitted. AK-P series scored the highest for quality in meta-analysis C (Table I).

The early mortality rate was 2.0% for 3405 procedures in 30 vein graft series and was 1.9% for 3357 procedures in 23 AK-P series; it was 1.5% for 15 series in meta-analysis C and 2.0% for 38 series in meta-analysis CI. The effects of runoff on graft patency were described in 15 articles, but good runoff was associated with a higher patency rate in only 12 of these. The percentage of late vein bypasses after an AK-P was 6.5% in 13 studies, but the rate of use of a spared saphenous vein, described in only 6 of these studies, was 5.1% after 648 AK-Ps. Graft infection occurred in 1.4% of 1063 AK-Ps, but only 11 studies reported this event.

Graft patency in meta-analysis C. In a graphical display of pooled survival curves for primary patency, AK-V occupied the top position, whereas BK-V occupied the lowest position until 27 months after bypass. Thereafter, AK-P performed the worst (Fig 1). The difference in the pooled primary patency between AK-P and AK-V was significant at 3 years and beyond, but the difference between AK-P and BK-V was not significant at any interval (Table II). When secondary patency was analyzed, AK-P, AK-V, and BK-V were equivalent until 19 months after bypass. Beyond this time, AK-P occupied the lowest position (Fig 2), but the differences between AK-P and the vein grafts were not significant (Table II).

When series that did not use standard patencies were excluded, the difference between the pooled estimates of primary patency at 5 years remained unchanged in AK-P vs AK-V and increased by 7.7% in AK-P vs BK-V. In the former comparison, the statistical significance became restricted to one interval. When secondary patency was considered, there was an increase of 0.5% in AK-P vs AK-V, with AK-V surpassing AK-P 4 months earlier, and a decrease of 1.1% in AK-P vs BK-V at 5 years, with no change in the statistical inferences.

When bypasses for critical ischemia were excluded, the 5-year difference in AK-P vs AK-V decreased by 8.9% for primary patency and increased by 6.9% for secondary patency, the 5-year difference in AK-P vs BK-V decreased by 2.7% for primary patency and 7.7% for secondary patency, and the significant differences in AK-P vs AK-V were eliminated. When AK-P series with the highest scores of quality were excluded, the 5-year pooled estimate decreased by 0.8% for primary patency and 0.9% for secondary patency.

Graft patency in meta-analysis CI. AK-P occupied the lowest position from 5 months onward, whereas AK-V and BK-V occupied similar upper positions for primary patency (Fig 3). The difference in the pooled primary patency between AK-P and AK-V was significant up to 4 years, whereas the difference between AK-P and BK-V was

Table I. Meta-analysis characteristics

Variable	*Graft*	*Series/grafts*	*Standard patency*	*Year (median)*	*Grafts for claudication (%)*	*Quality (median)*
Meta-analysis C						
Primary patency	AK-P	20/1713	20	1996	82-91	9
	AK-V	9/580	9	1998	86	7
	BK-V	6/1338	4	1996	66	7
Secondary patency	AK-P	13/1187	11	1997	82-93	10
	AK-V	9/576	6	1997	90	7
	BK-V	9/1750	5	1995	71	8
Meta-analysis CI						
Primary patency	AK-P	22/2431	18	1992	35-37	7
	AK-V	11/703	10	1995	13-15	7
	BK-V	17/2441	14	1994	1-4	7
Secondary patency	AK-P	13/2101	9	1992	28-30	9
	AK-V	9/663	4	1994	9-18	6
	BK-V	23/3194	16	1992	9-15	7

AK-P, Above-knee femoropopliteal polytetrafluoroethylene bypass grafts; *AK-V,* above-knee femoropopliteal saphenous vein bypass grafts; *BK-V,* below-knee saphenous vein bypass grafts.

Table II. Meta-analysis pooled estimates of graft patency

Variable	*Years* 1	2	3	4	5
Meta-analysis C					
Primary patency					
AK-P	85.3(1.9)	77.4(2.0)	70.9(2.4)	63.3(2.7)	57.4(3.3)
AK-V	87.5(4.4)	84.1(3.4)	81.1(3.5)*	78.6(5.0)*	77.2(6.4)*
BK-V	81.4(4.5)	76.0(3.9)	73.8(4.6)	68.3(6.5)	64.8(7.2)
Secondary patency					
AK-P	90.3(2.7)	85.3(3.1)	83.9(4.3)	76.8(5.4)	73.2(6.3)
AK-V	89.8(2.2)	86.2(3.2)	83.9(4.3)	82.3(5.6)	80.1(6.4)
BK-V	89.1(2.0)	86.0(2.7)	84.2(4.9)	80.7(7.2)	79.7(7.7)
Meta-analysis CI					
Primary patency					
AK-P	76.3(1.9)	64.7(2.0)	57.2(2.8)	51.8(3.0)	48.3(3.6)
AK-V	83.4(3.1)*	81.2(4.1)*	76.6(5.0)*	72.6(5.4)*	69.4(9.1)
BK-V	84.3(2.3)*	80.4(2.9)*	76.2(3.5)*	72.3(3.3)*	68.9(4.7)*
Secondary patency					
AK-P	80.1(1.6)	70.1(2.2)	62.6(2.6)	57.4(3.1)	54.0(3.4)
AK-V	87.2(3.6)	83.7(3.2)*	79.1(5.1)*	76.9(6.3)*	71.9(8.7)
BK-V	87.4(2.0)*	83.5(2.3)*	81.8(2.6)*	79.7(3.3)*	77.8(4.5)*

AK-P, Above-knee femoropopliteal polytetrafluoroethylene bypass grafts; *AK-V,* above-knee femoropopliteal saphenous vein bypass grafts; *BK-V,* below-knee saphenous vein bypass grafts.
*$P < .05$ compared with AK-P series.

significant at all yearly intervals (Table II). When secondary patency was analyzed, AK-P occupied the lowest position, whereas BK-V and AK-V performed equally well during the entire follow-up (Fig 4). The difference in the pooled secondary patency between AK-P and AK-V was significant from 2 to 5 years, whereas the difference between AK-P and BK-V was significant at all yearly intervals (Table II).

When series that did not use standard patencies were excluded, the difference between the pooled estimates of primary patency at 5 years increased by 2.0% in AK-P vs AK-V and by 1.3% in AK-P vs BK-V, whereas for secondary patency the corresponding increases were 7.6% and 1.4%. There was no change in the statistical inferences.

When bypasses for claudication were excluded, the 5-year difference in AK-P vs AK-V increased by 0.7% for secondary patency, whereas the 5-year difference in AK-P vs BK-V decreased by 1.3% for primary patency and increased 5.0% for secondary patency, with few changes in the statistical inferences.

Other sensitivity analyses. In meta-analysis C, the fixed-effects model increased the pooled primary and secondary patency by 1.9% and 3.7% for AK-P, by 1.2% and 1.0% for AK-V, and by 0.8% and 1.9% for BK-V, respectively, at 5 years. These changes favored AK-Ps slightly, but the difference between AK-P and AK-V became significant for primary patency also at 2 years as a consequence of decreased standard errors. The adjustments for flat tails decreased the 5-year pooled primary patency by 0.6% for AK-P, 2.7% for AK-V, and 1.7% for BK-V. For secondary patency, the corresponding decreases were 0.2%, 2.0%, and 0.8%, respectively. There was no change in the statistical inferences.

In meta-analysis CI, the fixed-effects model increased the pooled primary and secondary patency by 1.2% and 1.1% for AK-Ps, by 5.7% and 1.7% for AK-Vs, and by 1.1% and 2.5% for BK-Vs, respectively, at 5 years. The difference between AK-Vs and AK-Ps became significant for primary and secondary patency at all yearly intervals. The adjustments for flat tails decreased the 5-year pooled primary patency by 0.6% for AK-P and BK-V and by 3.4% for AK-V. The significance was abolished at 12 and 60 months and was maintained at all other intervals in AK-P vs AK-V. The corresponding adjustments for secondary patency increased the 5-year pooled secondary patency by 0.3% for AK-P and by 0.2% for BK-V but decreased this outcome by 1.6% for AK-V, with no change in the statistical inferences.

DISCUSSION

The small differences in primary and secondary patency in AK-Vs in meta-analyses C and CI indicated that only a few redo procedures were performed for this particular type of bypass, probably because only three AK-V studies used duplex scanning for graft surveillance routinely. In addition, graft patencies for AK-Ps were considerably lower in meta-analysis CI than in meta-analysis C, but this was not the case for AK-Vs and BK-Vs. Perhaps more severe atherosclerosis in critical ischemia is more unfavorable to AK-P grafts.

Meta-analysis C showed that AK-V tended to be superior to AK-P, and this became apparent for primary patency at 5 months. The validity of the vein-sparing approach in claudicant patients was denied, but this was less certain for secondary patency (Fig 2), possibly because of the use of standard patencies in only four of nine AK-V series (Table I). Clearly, the small number of series and the lower proportion of claudicant patients in the BK-V series biased the comparison of AK-P vs BK-V, particularly for primary patency, but the highest scores of study quality for AK-Ps had no influence on the results. It is interesting to note that AK-P series were published more frequently than AK-V series; this reflects the preference for AK-Ps. Apart from a sincere belief in the similarity between AK-P and AK-V and in the value of not using the saphenous vein, other reasons for such a preference include the reduced operative time and, perhaps, the influence of commercial marketing activities.

In meta-analysis CI, which dealt with critical ischemia, the difference between the vein graft series and the AK-P series was readily apparent and significant at most yearly intervals. The paucity of AK-V series was evident and possibly reflected a more extensive popliteal involvement above the knee than below the knee, a better opportunity for using BK-V grafts in situ, or both. The validity of the vein-sparing approach in terms of graft patency was denied even more emphatically than for claudicant patients. This was so despite a larger proportion of claudicant patients in the AK-P series. Because patients with critical ischemia deserve the best operation on the first occasion,[26] an AK-P should not be recommended in the presence of a usable saphenous vein.

The vein-sparing approach is also unwarranted for reasons other than graft patency. Indeed, the mechanisms of graft failure differ. There is more sudden thrombosis in AK-P and greater myointimal hyperplasia in vein grafts[36]—this is better identified by using a postoperative duplex surveillance program—as well as a greater need for urgent reoperation or a repeat bypass after AK-Ps.[84] This analysis showed that short-term graft failure was more frequent for AK-Ps than previously believed and that, in the treatment of such failure, thrombectomy or thrombolysis has been used more often than a new bypass but has not been highly successful.[2,14,22,29,34–37] Notably, the ultimate limb loss in claudicant patients has been two times greater after AK-Ps than after AK-Vs,[56] and graft infection of AK-Ps may not be as rare as the frequency of 1.4% suggested in this study. Indeed, Pedersen et al[85] reported a graft infection rate of 12% in 141 AK-Ps for claudication.

Apart from the inconveniences surrounding AK-Ps, sparing a saphenous vein is unreasonable because the rate of use of a saved vein in a late bypass has been consistently low,[9,11,18–22,34–37] alternative autologous veins are often available for secondary bypass,[86] and a failing vein graft can be treated with no further bypass.[64,65] Hence, a smaller number of graft failures, together with less severe consequences of failed or complicated grafts, strengthen the argument for the use of a saphenous vein in primary femoropopliteal bypass.

Despite traditional preferences, uncertainty remains about the best synthetic graft for above-knee bypasses and the best configuration of vein grafts. Umbilical cord vein grafts performed significantly better than AK-Ps in two randomized trials,[8,22] whereas Johansen and Watson[15] reported a superb 5-year cumulative primary patency rate of 84% for Dacron grafts (DuPont, Wilmington, Del) in a cohort of 92 good-risk patients with claudication. Only a few reports have suggested BK-V as the standard femoropopliteal bypass with the reversed saphenous vein,[3,12,13] but BK-V has emerged as the best-suited anatomic configuration for in situ saphenous vein bypasses.[14] The current meta-analyses failed to show any reliable trend favoring AK-Vs or BK-Vs but revealed that BK-Vs were performed much more often than AK-Vs.

The superiority of vein grafts over angioplasty has not been challenged in the treatment of femoropopliteal disease for claudication, but the same cannot be said for synthetic grafts. Hunink et al[87] determined a 5-year primary patency of 73% for vein grafts, 49% for polytetrafluoroethylene grafts, and 45% for angioplasty. In the treatment of critical limb ischemia, there seems to be even less room for AK-Ps. Indeed, another meta-analysis yielded a 3-year pooled primary patency of 63%,[16] whereas the corresponding figure for AK-Ps was 62.6% in meta-analysis CI described previously. Hence, it may be possible to choose between an endovascular procedure and a synthetic graft for suitable patients who have no usable vein.

Early mortality rates were described infrequently in the studies examined. These rates, which cannot be ignored by the surgeon, must be disclosed to the patient and are useful in choosing between angioplasty and open bypass, but not in choosing between an AK-P and a vein graft, because the same rate occurs in AK-P and vein graft series. Because AK-Ps and vein grafts have the same risk of early mortality and because in meta-analysis CI AK-V and BK-V performed significantly better than AK-Ps at 1 year, an AK-P should not be used in patients with critical ischemia simply because of a short life expectancy. Meta-analysis C did not show significant differences between AK-P and vein graft series in the early years of follow-up, but a short life expectancy is an uncommon feature of claudicant patients.

In strong support of the inferences from this meta-analysis, the study design was compatible with real life; allowed an adequate sampling of hypothetical populations of studies; reduced the confounding effect of clinical symptoms, graft material, and level of distal anastomosis; and provided pooled survival curves that consistently decreased over time. Furthermore, the studies reviewed in this meta-analysis adopted similar outcomes, used data of acceptable quality, and reported high response rates. Finally, sensitivity analysis showed that outcomes were robust in favor of vein grafts.

Most of the limitations in this study were attributable to the nonrestrictive criteria of inclusion that were adopted and to the imperfect state of the existing literature. Articles were often retrospective, did not separate clinical symptoms appropriately, reported outcomes selectively, described AK-Vs and BK-Vs together, did not use standard patencies, described a short follow-up time, omitted losses to follow-up and their effect on graft patency, showed a flat tail in the survival curve, or did not mention the postoperative use of duplex scans. Not all of these problems could be handled satisfactorily in this analysis.

This meta-analysis provided observational evidence on femoropopliteal bypass surgery for which the randomized evidence is scarce. AK-Vs and BK-Vs performed better than AK-Ps and should be used whenever possible to reduce the gap between the best practice and the true practice.[6] However, the absence of a suitable saphenous vein remains an acceptable indication for an AK-P, at least until the potentials of other alternatives are fully established.

AUTHOR CONTRIBUTIONS

Conception and design: CEP, MA, MR, FCB-N, CABP
Analysis and interpretation: CEP, MA, CABP
Data collection: CEP, MA
Writing the article: CEP, MA, MR, FCB-N, CABP
Critical revision of the article: MR, FCB-N
Final approval of the article: CEP, MA, MR, FCB-N, CABP
Statistical analysis: MA, CABP
Overall responsibility: MA

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Appendix I (online only). Articles included in the meta-analyses

Author	Year	AK-P PP	AK-P SP	AK-V PP	AK-V SP	BK-V PP	BK-V SP	Meta-analysis
Aalders[25]	1992	+*	+	−	−	−	−	C
AbuRahma[10]	1999	+*	+	+*	+*	−	−	C
Achermann[30]	1998	+	−	+	−	−	−	C
Allen[19]	1996	+*	+	−	−	+*	+*	C
Archie[26]	1994	+*	−	+*	−	+*	−	CI
Ballotta[11]	2003	−	+*	−	+	−	−	C
Bandyk[65]	1987	−	−	−	−	+*	+*	CI
Bastounis[46]	1999	−	−	−	−	+	−	CI
Blankensteijn[56]	1988	−	−	+*	+*	−	−	C
Böhmig[66]	1995	−	−	−	−	−	+	C/CI
Bourke[48]	1992	−	−	−	−	+*	+*	CI
Budd[33]	1990	+*	−	+*	−	+*	−	CI
Chapleau[60]	1991	−	−	−	−	−	+	C
Chikiar[68]	2003	+*	−	+*	−	−	−	CI
Curi[41]	2002	+*	+*	+*	+*	−	−	CI
D'Addato[55]	1992	−	+	−	−	−	−	CI
Davies[34]	1991	+*	+	−	−	−	−	CI
Deutsch[69]	1999	+*	−	−	−	−	−	C
El-Kayali[37]	2003	+*	−	−	−	−	−	CI
Enzler[63]	1991	−	−	−	−	−	+*	CI
Erasmi[27]	1996	+	+	−	−	−	−	C
Falco[70]	1995	−	−	−	−	−	+*	CI
Florenes[59]	1993	−	−	−	−	−	+*	C
Franks[71]	1992	−	−	−	−	−	+	C/CI
Green[28]	2000	+	+	−	−	−	−	C
Griffiths[42]	2004	+	−	−	−	−	−	CI
Gupta[24]	1991	+*	−	−	−	−	−	CI
Hagmüller[72]	1990	+	−	−	−	−	−	C/CI
Hamann[73]	1998	+*	−	+*	−	−	−	C/CI
Harris[74]	1987	−	−	−	+	−	−	CI
Jamsen[75]	2001	−	−	−	−	+*	−	CI
Jensen[52]	1992	−	−	−	−	+	+	CI
John[36]	1993	+	−	+	−	−	−	CI
Johnson[8]	2000	−	+	−	+*	−	−	C/CI
Kavanagh[21]	1998	+	+	−	−	−	−	CI
Kent[44]	1988	−	−	+	−	+	−	C
Klinkert[9]	2003	+	+	+*	+*	−	−	C
Kretschmer[76]	1992	−	−	−	−	−	+	CI
Kumar[43]	1995	+	+	+	+	−	−	C
Lang[77]	2001	+	+	−	−	−	−	CI
Laurendeau[35]	1989	+	+	−	−	−	−	CI
Lawson[47]	1999	−	−	−	−	+*	+*	C
Lu[40]	2002	+*	−	−	−	−	−	C
Lundell[64]	1995	−	−	−	−	+	+	CI
Macaulay[80]	1996	−	−	−	−	+*	+*	CI
Maini[51]	1996	−	−	−	−	+*	+*	CI
McLoughlin[81]	1989	+*	−	−	−	−	−	CI
Mills[50]	1991	−	−	−	−	+	+*	CI
Miyazaki[17]	2002	+	+	−	−	−	−	C
Najmaldin[61]	1987	−	−	−	−	−	+*	CI
Neale[31]	1994	−	−	−	+*	−	+	CI
Okadome[67]	1990	−	−	−	+	−	−	C
Parker[57]	1988	−	−	−	+	−	+*	CI
Patterson[20]	1990	+	+	−	−	−	−	CI
Plecha[45]	1996	−	−	−	−	+*	+*	CI
Post[38]	2001	+*	−	−	−	−	−	C
Prendiville[2]	1990	+*	+	−	−	−	−	C/CI
Rafferty[23]	1987	+	+	+	+	+	+	C/CI
Raptis[18]	1995	+	−	−	−	−	−	C
Rosenthal[22]	1990	+	+	−	−	−	−	C
Sala[32]	2003	+	+	+	+	−	−	CI
Schulman[49]	1987	−	−	−	−	+	+	CI
Stierli[78]	2001	−	−	+*	−	−	−	C

Appendix I (online only). Articles included in the meta-analyses. Continued.

Author	*Year*	*AK-P*		*AK-V*		*BK-V*		*Meta-analysis*
		PP	*SP*	*PP*	*SP*	*PP*	*SP*	
Stonebridge[54]	1997	−	+	−	−	−	−	CI
Strayhorn[62]	1988	−	−	−	−	−	+	CI
Taylor[12]	1990	−	−	−	−	+	+*	CI
Veith[1]	1986	−	+	−	+*	−	+*	CI
Veterans Administration[53]	1988	−	−	−	−	+	+	CI
Watelet[58]	1987	−	−	−	+*	−	+	CI
Whittemore[29]	1989	+	−	−	−	−	−	C/CI
Wilson[39]	1995	+*	−	+*	−	−	−	CI
Woratyla[14]	1997	+	+	−	−	+	+	C/CI
Z'graggen[79]	1990	−	+*	−	+*	−	−	CI

AK-P, Above-knee femoropopliteal polytetrafluoroethylene bypass grafts; *AK-V,* above-knee femoropopliteal saphenous vein bypass grafts; *BK-V,* below-knee saphenous vein bypass grafts; *PP,* primary patency; *SP,* secondary patency; −, not included in meta-analysis; +, included in meta-analysis.
*Flat tail present.

Appendix II (Online Only): Statistical Notes

The strategy. We constructed a strategy to combine survival data because different grids of time intervals had been used in the series reviewed. In the first step, we redistributed in equal quantities at 1-month intervals grafts censored at intervals greater than 1 month. Next, we obtained the numbers of failed grafts for intervals of 1 month by using the grafts at risk at the start of an interval, the redistributed censored units, and the interval hazard rates. We then calculated the Kaplan-Meier success rates for each series and each month of follow-up and used these rates as treatment effects. This approach assumed constant hazard rates within long time intervals and the midpoint of such intervals as the survival time for censored units, as is usual in actuarial survival analysis.

In the second step, we calculated a within-series variance (s^2) for each monthly success rate in each series; next, we calculated a between-series variance (τ^2) for each month. To obtain pooled measures of treatment effect for each month of follow-up, we used in the third step random-effects modeling, which assumes that included studies are a random sample of the universe of studies. Finally, the product of successive monthly pooled measures of treatment effect allowed us to obtain pooled measures of cumulative success and to calculate approximate standard errors.

The statistical problem. Because this meta-analysis dealt with uncontrolled studies, our primary problem was one of parameter estimation, not hypothesis testing. Consequently, we estimated pooled measures and calculated their standard errors for AK-P, AK-V, and BK-V at yearly intervals. From these quantities, it was possible to calculate the overlap of two 95% confidence intervals and use this result to declare statistical significance ($P < .05$) or negate it ($P < .05$) for the comparison of AK-P vs AK-V and AK-P vs BK-V at yearly intervals.[86]

Interval success rate. For each series *i* and each month *j* of follow-up, an interval success rate, λ_{ij}, was determined as follows:

$$\lambda_{ij} = 1 - f_{ij}/n_{ij},$$

where f_{ij} is the number of failed grafts and n_{ij} is the number of grafts at risk.

Within-series variance. The within-series variance, $s_{ij}{}^2$, was obtained as follows:

$$s_{ij}^2 = n_{ij}\,(n_{ij} + 2)^2/\left[(f_{ij} + 1)(n_{ij} - f_{ij} + 1)\right].$$

Between-series variance. For each month *j*, the between-series variance, $\tau_j{}^2$, was calculated as follows:

$$\tau_j^2 = \Sigma\left[n_i(\lambda_i - m_j)^2\right]/\left[(k_j - 1)/k_j\,\Sigma n_i\right],$$

where, in the target month *j*, λ_i is the success rate in study *i*, m_j is the average for λ_i, n_i is the number of units at risk, and k_j is the number of series available.

Weighting and combining the $\boldsymbol{\lambda_{ij}}$. Let w_{ij} be the weight attributed to each λ_{ij}. When using random-effects modeling, it follows that

$$W_{ij} = 1/\left(s_{ij}^2 + \tau_j^2\right).$$

A summary effect estimate, L_j, was obtained for interval graft patency in month *j* as follows:

$$L_j = \Sigma(\lambda_i w_i)/\Sigma w_i,$$

where λ_i is the success rate in the target month *j* and w_i is the weight attributed to λ_i.

Such estimators L_j will be consistent and approximately normal and are derived on the basis of the fact that the estimators for each series are approximately normal with an estimable variance. Finally, the product of successive L_j yielded G_j, the summary estimate for cumulated success at month *j*.

Variance and confidence interval for $\boldsymbol{G_j}$. After they were properly corrected, Kaplan-Meier estimates and their respective variances in the single series were used to obtain the variance of G_j. This was performed by again using random-effects modeling in a way similar to that of obtaining L_j. The difference was that Peto within-series variances in study *i* at month *j* and $\tau_j{}^2$ were summed up to weigh the Kaplan-Meier estimates at month *j*. A summary Kaplan-Meier estimate, K_j, and its variance, $V_{\{Kj\}}$, were thus obtained for month *j*. Because K_j and G_j differed a little, the variance of G_j, $V_{\{Gj\}}$, was obtained as follows:

$$V_{\{G_j\}} = V_{\{K_j\}}\left[L_j(1 - L_j^2)\right]/\left[K_j\,(1 - K_j^2)\right].$$

The standard error for G_j was the square root of $V_{\{Gj\}}$.