

Risk factors for failed healing in amputation for vascular disease

A prospective, consecutive study of 177 cases

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We examined factors which may lower the mean amputation age and factors which may serve as predictors of success or failure of amputations in the lower extremities for vascular disease in 177 consecutive amputees. Smoking lowered the mean amputation age by 9 years and diabetes by 3 years. Preoperative absence of gangrene in the ischemic limb pre-

dicted a higher risk of failure compared to patients with gangrene. Also preoperative hemoglobin > 120 g/L gave a higher risk of failure. Failure to heal was not correlated with age, sex, diabetes, level of amputation, previous vascular surgery, smoking, preoperative blood pressure, serum creatinine, erythrocyte sedimentation rate, blood glucose or temperature.

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Healing after transtibial amputation may be expected in not less than 75 percent (Kacy et al. 1982, Keagy et al. 1986, Harris et al. 1988). Primary amputation at a more proximal level would increase the success rate, but at the expense of decreased mobility in most patients.

As an aid in the assessment of tissue viability and in amputation level selection, different types of laboratory measurements have been studied (Holstein et al. 1977, Malone et al. 1981, Burgess et al. 1982). Although it is important to further develop the optimal test for amputation level selection, one must not forget to try to promote healing or even postpone amputation by correction of risk factors and by strict attention to the pre- and perioperative management. Perioperative antibiotics have substantially reduced the number of postoperative infections and healing complications (Huizinga et al. 1983, Møller and Krebs 1985, Sonnehlm et al. 1985, Friis 1987). Other correctable factors that affect the frequency of wound complications are the surgical technique (Falstie-Jensen and Christensen 1990), the preoperative hemoglobin and hematocrit values (Bailey et al. 1979, Kacy et al. 1982, Hansen et al. 1988) and cigarette smoking (Hughson et al. 1978b, Liedberg and Persson 1983, Lind et al. 1991).

The present study was a part of a prospective study of different preoperative variables which may serve as predictors of success or failure of healing after lower extremity amputations.

Patients and methods

All major amputations in the lower extremities due to arterial occlusive disease were studied prospectively and consecutively in Malmöhus County, Sweden, during 1 year and were followed for 6 months after the primary amputation. A total of 177 amputees were included. During the same period, 302 lower extremity arterial operations were performed. 40 percent were diabetic, and 52 percent men. The mean age at amputation was 77 (43-95) years. Selection of level was made by the attending orthopedic surgeon, mainly on the basis of clinical symptoms and signs and in 64 percent it was supported by Doppler-derived systolic-pressure measurements. Smoking habits were classified with respect to number of cigarettes per day or length of time since cessation. Temperature, hemoglobin (Hb), serum creatinine, blood glucose, erythrocyte sedimentation rate (ESR), and blood pressure were determined before amputation. Preoperative extension of gangrene and subjective level of rest pain were recorded. Sagittal technique was used in 87 percent, and a complete circular plaster was used in 93 percent of all transtibial amputations. 84 percent were treated with perioperative intravenous antibiotics.

For comparison of categories, chi-square test and Fischer's exact test were used. Mann-Whitney's u-test was used for evaluating factors which may affect the amputation age. For the simultaneous analysis of risk factors, Multivariate Polychotomous Logistic Regression analysis (Koch and Edwards 1988) was used by

Table 1. Preoperative gangrene levels and number of non-healed or reamputated at 6 months. Fraction in parentheses

Gangrene	Number	Non-healed or reamputated
None	13	7 (0.54)
Toes/forefoot	61	8 (0.13)
Foot	32	6 (0.19)
Above ankle	34	8 (0.24)
Other	37	8 (0.22)
Total	177	37 (0.21)

means of a recent revision of the BMDP computer software package (BMDP 1990).

Results

Preoperative laboratory parameters

Hemoglobin > 120 g/L gave 35 percent failures (22/62), while hemoglobin 120 g/L or lower gave 13 percent failures, (P 0.0004). Hemoglobin > 120 g/L in primary transtibial amputations resulted in 37 percent failures (18/49), while hemoglobin 120 g/L or lower gave 16 percent failures (14/86, P 0.007). Only 6 percent (2/31) of amputees with hemoglobin values of 100 g/L or lower failed to heal. There was no difference in hemoglobin values between smokers and non-smokers. Neither blood glucose, temperature, serum creatinine, erythrocyte sedimentation rate nor blood pressure had any influence on healing.

Smoking habits

Excluding 5 patients with unknown smoking habits, 26 percent were smokers, 24 percent former smokers and 50 percent had never smoked; 87 percent of all smokers were men. 11 percent of the women and 36 percent of the men had stopped smoking \geq 1 year before amputation. The mean age at amputation among heavy smokers (> 15 cigarettes daily) was 59 years versus 74 years in moderate smokers. Among amputees aged 75 or older, 15 percent were smokers (18/118), while 58 percent were smokers among amputees younger than 65 years (14/24, P 0.0001).

6 months after amputation, smokers had a failure rate of 31 percent and those who had never smoked had a failure rate of 18 percent. The difference was not significant (P 0.08).

Vascular surgery

67 of the amputees had been operated on by a vascular surgeon at the amputated side. 33 thromboembolectomies, 11 percutaneous transluminal angioplasties (PTA), 16 bypasses and in 7 cases other types of vascular surgery were recorded as the latest vascular surgery before amputation.

The mean amputation age

Smoking lowered the amputation age by 8.6 years (P 0.0001) and diabetes by 3.2 years (P 0.041). Male sex and previous smoking lowered the amputation age by about 1 year each.

Rest pain and gangrene

Before amputation 125 patients had severe, 40 patients moderate, and 3 no rest pain; in 9 cases rest pain was not recorded. Smokers and non-diabetics had a higher frequency of severe preoperative rest pain than non-smokers (P 0.009) and diabetics (P 0.02), respectively.

13 amputees had no preoperative gangrene, and 164 had different degrees of gangrene before amputation (Table 1). Of those with no preoperative gangrene, 12 had severe rest pain, 9 were women, 2 were diabetics, 5 were smokers, and 5 were thromboembolctomized 0-30 days before amputation. All were seen by a vascular surgeon prior to amputation. 9 were amputated at the transtibial level and 9 received perioperative antibiotics. The other leg was normal in all 13.

At a follow-up of amputees without preoperative gangrene only 2 had healed stumps, 1 was not healed, 6 reamputated (including 1 dead), and 4 dead without reamputation. 30 of those with gangrene before amputation failed to heal. In Fischer's exact test, the absence of gangrene before amputation indicated a higher failure rate than among those with preoperative gangrene (P 0.007).

Follow-up at 6 months

One third of the amputees had died within 6 months. Among the 109 alive amputees, 85 had healed stumps (78 percent), 10 were not healed (9 percent), and 14 were revised or reamputated (13 percent). Among the deceased, a further 13 had been reamputated on before death. A total of 37 amputees were thus classified as failures, of which 32 were primary transtibial amputations, 1 knee disarticulation, and 4 transfemoral amputations.

Table 2. Relative risks for failure to heal after amputation in relation to other risk factors (Polychotomous Logistic Regression analysis, adjusted for sex and age)

Risk factors	Relative risk of failure (95 percent confidence interval)
Diabetes	0.5 (0.1-1.8)
Smoker	2.1 (0.3-13)
Ex smoker	1.1 (0.2-5.8)
No preoperative gangrene	37 (2.7-500)
Hemoglobin > 120 g/l	6.3 (1.7-23)
Transtibial amputation level	1.4 (0.3-6.4)
No antibiotics	3.1 (0.4-27)
Bypass surgery	1.1 (0.1-13)
PTA	1.8 (0.2-14)
Thromboembolectomy	0.4 (0.02-10)

Multivariate analysis

Absence of preoperative gangrene as well as hemoglobin > 120 g/L increased the risk of failure to heal among transtibial amputees as well as among all the major amputations as a group (Table 2). Smokers had a 2.1 higher relative risk of failure compared to those who had never been smokers, and those who did not receive perioperative antibiotics had a 3.1 higher risk of failure compared to those who did. These differences were, however, not significant. Previous vascular surgery did not influence the healing rate.

Discussion

Hughson et al. (1978a) found that smoking outranks all other risk factors for peripheral vascular disease. Liedberg and Persson (1983) showed that smoking lowered the age at amputation; in the present material smoking lowered the mean age at amputation by 8 years, and previous smoking lowered the amputation age by only 1 year. The age difference between former smokers and those who had never smoked thus was not significant, but continuing smokers were markedly younger at amputation than those who had never smoked. This implies that even a late stop in smoking is valuable.

The main indications for lower extremity amputation are progressive gangrene with or without septicemia and intractable pain not responding to other treatment; most of our patients had both gangrene and severe rest pain, and none had neither rest pain nor gangrene. Absence of gangrene before amputation resulted in a higher failure rate than when gangrene was present. Amputation when no gangrene was present is thus, paradoxically enough, not a good but a

bad prognostic factor for healing after amputation. To our knowledge this has not been shown before. Although statistical analysis shows that absence of gangrene is a prognostic risk factor for failure to heal, it does not justify a definite change in the treatment until other investigations support our findings. We do, however, suggest that a patient with severe rest pain, but without gangrene, where no vascular operation is possible, should be treated conservatively until a level of demarcation has emerged. If ischemia is evident also in the thigh, however, renal failure may be induced, if expectation is prolonged.

Hemoglobin > 130 g/L has been reported to be an important preoperative risk factor in digital, metatarsal and transmetatarsal amputations in diabetics (Bailey et al. 1979). Kacy et al. (1982) reported a higher preoperative hematocrit in complicated transtibial amputations among diabetics with cellulitis. Hansen et al. (1988) found gradually increasing rates of complication and reamputation with increasing levels of preoperative hemoglobin and hematocrit in arteriosclerotic amputations, while no such association was found in diabetics. Tripses and Pollak (1981), on the other hand, found no difference in stump complications or reamputations in more or less anemic patients, and Lepäntalo et al. (1987) found no difference in pre- or postoperative hemoglobin in the failure and success group among below-knee amputations. Falstie-Jensen and Christensen (1990) and Weiss et al. (1990) were not able to show that the level of hematocrit or hemoglobin was a valuable predictor of stump failure. Lind et al. (1991) suggested that the majority of patients with low levels of hemoglobin are non-smokers and that their postoperative complications thereby are reduced. Apart from Falstie-Jensen and Christensen (1990), who did not evaluate smoking habits, multivariate analysis has not before been performed with this question at issue. In the present material a preoperative hemoglobin > 120 g/L resulted in a marked increase in healing complications both in chi-square and polychotomous logistic regression analysis.

The mechanism behind the association between hemoglobin > 120 g/L and complications in the healing of amputations is probably due to a compromised microcirculation secondary to increased whole blood viscosity at high hematocrit values which, in turn, in many cases probably is secondary to dehydration. It has been described that hemodilution by replacing blood with starch or dextran induces a fall in oxygen-carrying capacity, together with a reduction in blood viscosity, and the latter effect must outweigh the former for enhancement of oxygen supply (Jan and Chien 1977, Messmer et al. 1982). Lowering of the hematocrit by normovolemic hemodilution has been shown to increase leg blood flow and pain-free walking distance

in patients with stable intermittent claudication (Yates et al. 1979, Ernst et al. 1987). Although we do not know of any study describing the effects of reducing blood viscosity among amputees, we believe it is of great importance to rehydrate dehydrated patients with critical ischemia, not only to optimize preparation before surgery, but also to reduce blood viscosity and thereby increase leg blood flow. Whether further reduction of blood viscosity is necessary after rehydration remains to be studied. Not only is rehydration important but also the correction of malnutrition. Dickhaut et al. (1984) demonstrated that, in Symes amputations, malnutrition, described as an albumin level of less than 3.5 g/dL, or a total lymphocyte count of less than 1500 cells/mm³, makes wound healing almost impossible. It would be of interest to investigate if a preoperative correction of the nutritive status of the amputee may favorably affect wound healing or even postpone amputation.

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