Prospective 2-Years Follow-up Quality of Life Study after Infrageniculate Bypass Surgery for Limb Salvage: Lasting Improvements Only in Non-diabetic Patients

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Quality of life; Critical limb ischaemia; Infrageniculate bypass; Diabetes; Peripheral arterial disease

Abstract  Objectives: To assess health-related quality of life (HRQoL) up to 24 months after successful infrageniculate bypass surgery for limb-threatening ischaemia.
Methods: 89 patients with infrageniculate bypass surgery for limb-salvage were studied. HRQoL was assessed using the Short Form (SF)-36v1 questionnaire before, 6, 12, and 24 months after revascularisation.
Results: 47 patients (53%) with intact limb and functioning graft were assessed after 24 months, 27 patients (30%) died, further 7 required secondary amputation, 3 suffered irreparable graft occlusion, and 4 were lost to follow-up. The 24-months HRQoL-values were significantly improved in 4 domains: physical functioning ($p < 0.01$), bodily pain ($p < 0.01$), mental health ($p < 0.04$), and social functioning ($p = 0.01$). Except for baseline-values, HRQoL remained inferior in diabetics compared to non-diabetics throughout follow-up. Maximum improvement of HRQoL was delayed in diabetics (12 months vs. 6 months) and less pronounced. After 24 months non-diabetic patients maintained improvement in 5 domains and diabetic patients only in bodily pain.
Conclusions: Improvement in HRQoL is sustained for more than 12 months after successful infrageniculate bypass surgery. Therefore, an aggressive approach towards revascularisation seems to be justified from the patient’s perspective. However, this benefit in quality of life is less in diabetic patients, despite similar limb-salvage rates.

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Introduction

Infrainguinal bypass surgery is a well established treatment for patients with critical limb ischaemia (CLI), and some specialized centres attempt some type of revascularisation in as many as 90% of patients with limb-threatening ischaemia. On the other hand, frequent adverse effects such as delayed wound healing, prolonged recovery from surgery, readmissions, and the need for repeated endovascular and surgical treatment for maintenance of graft patency, raise question about the appropriateness of femoro-distal bypass grafting in this problematic group of patients with severe co-morbidities and limited life expectancy. Therefore, it has repeatedly been pointed out that traditional outcome measures, such as patency rates, alone are not sufficient to judge the true value of infrainguinal bypass surgery. Rather, more patient-based measures, such as functional outcome and health-related quality of life (HRQoL), should be taken into account as well.

Meanwhile, there is a great body of evidence that successful infrainguinal bypass surgery can be expected to improve the severely impaired quality of life in patients with CLI. While this improvement has well been documented for the first 6 to 12 months after revascularisation, durability of this benefit beyond the first year still remains unclear. The few long-term assessments of health status and functional outcome after revascularisation for limb-salvage indicate that the surviving patients are likely to achieve limb salvage, but retain physical disabilities with limited functional status and quality of life. To our knowledge as yet there is no prospective, intermediate or long-term assessment of HRQoL in patients with infrageniculate bypass surgery for limb-threatening ischaemia.

Previously we reported that early quality of life improvement after successful infrageniculate bypass surgery is clearly less in patients with diabetes mellitus than in non-diabetic patients. Delayed recovery from surgery and problematic wound healing were suspected to be reasons for this impaired benefit in the diabetic group. Unclear is as yet, whether this adverse influence on HRQoL remains throughout further follow-up.

Therefore, aim of this prospective study was to assess the intermediate-term changes of HRQoL up to 24 months after successful infrageniculate bypass surgery for limb-threatening ischaemia, and to evaluate the influence of diabetes on quality of life.

Materials and Methods

In part, the study methods have been reported previously. All patients with CLI scheduled for infrageniculate bypass surgery at the Zentralklinikum Augsburg/Germany between July 2002 and April 2004 were eligible for the study. The patients were asked for their consent to be surveyed, and to complete the Short Form (SF)-36 (Version 1) questionnaire for baseline assessment of their HRQoL before bypass surgery. Patients unwilling to give consent or unable to complete the Short Form (SF)-36 questionnaire were excluded from the study.

Patients with successful revascularisation, defined as functioning graft and intact limb, were reassessed after follow-up periods of 6, 12, and 24 months, respectively. A limb was considered intact, if major amputation could be avoided and there was no foreseeable need for secondary amputation in the near future. Standardized follow-up included a physical examination and duplex scanning of the infrageniculate bypass. Again, all patients were asked to complete the SF-36 questionnaire. In addition, final HRQoL-assessment after 2 years included patients with failed arterial reconstruction, i.e. secondary amputation or irremediable graft occlusion, as well. However, these data were analyzed separately. In a subgroup-analysis, HRQoL-scores of patients with diabetes (diabetic group) and without diabetes (non-diabetic group) were compared.

The SF-36 questionnaire has been recommended as the most appropriate generic quality of life assessment tool for peripheral arterial disease. This instrument is a self-assessment measure, containing 35 questions that cover eight dimensions of health-related quality of life: physical functioning, role-physical, bodily pain, social functioning, mental health, role-emotional, vitality, and general health perceptions. An additional item addresses the change in general health status over time. A high score indicates good health status from the patient’s perspective.

Data were collected and analysed using SPSS (Version 10.0) statistical software (SPSS, Munich, Germany). Non-parametric Wilcoxon matched pairs test was used to compare baseline and follow-up results, and the Mann-Whitney U-test compared subgroups of the sample. Cumulative patency rates, limb salvage rate, patient survival rate, and amputation-free survival rate were calculated by the Kaplan-Meier method using the log-rank test for comparison. A p-value <0.05 was considered to be statistically significant.

| Table 1 Patient demographics, risk factors, and co-morbid diseases (n = 89) |
|-----------------------------|---------------------|---------------------|
| Demographics                |                     |                     |
| Age                         | 71 (IQR, 64–77.5)   | years               |
| Male                        | 64 (72%)            |                     |
| Risk factors                |                     |                     |
| Diabetes                    | 53 (60%)            |                     |
| Hypertension                | 80 (90%)            |                     |
| Hyperlipidaemia             | 48 (54%)            |                     |
| Smoking                     |                     |                     |
| Never                       | 32 (36%)            |                     |
| Former                      | 31 (35%)            |                     |
| Current                     | 26 (29%)            |                     |
| Co-morbid diseases          |                     |                     |
| CABG                        | 11 (12%)            |                     |
| MI                          | 18 (20%)            |                     |
| CHF                         | 8 (9%)              |                     |
| TIA                         | 2 (2%)              |                     |
| Stroke                      | 16 (18%)            |                     |
| ESRD                        | 1 (1%)              |                     |

CABG, coronary artery bypass grafting; MI, myocardial infarction; CHF, congestive heart failure; TIA, transient ischaemic attack; ESRD, end-stage renal disease.
Results

Of 111 patients scheduled for infrageniculate bypass surgery 22 refused to participate in the study, mainly due to language barriers. These latter patients were revascularised as planned, but were not considered for the study.

The baseline SF-36 questionnaire was completed by 89 patients (80%), who compromised our study group. Patient demographics and co-morbid diseases are given in Table 1. Indications for arterial reconstruction were presence of rest pain in 16 patients (18%) (diabetic group, 11%), non-healing ulceration in 32 (36%) (diabetic group, 36%), and gangrene in 41 (46%) (diabetic group, 53%).

Distal graft sites were the popliteal artery below knee in 46 (52%), tibial/peroneal vessels in 39 (44%), and pedal arteries in 4 patients. The use of prosthetic grafts (ePTFE 18%, composite 9%) was limited to popliteal and proximal tibial reconstructions. Outflow vessels were similarly distributed in diabetic and non-diabetic patients with infrapopliteal reconstructions in 55% and 52%, respectively.

During follow-up 27 patients (30%) died. Forty-seven patients (53%) presented with patent grafts and intact limbs at 24-months outcome assessment. Of these patients 12 (26%) underwent minor amputation (4 non-diabetic; 8 diabetic). By the time of final follow-up 29 patients (62%; 15 non-diabetic and 14 diabetic) had no PAD-specific

Table 2  Outcomes 12 months and 24 months after infrageniculate bypass surgery for all patients and for the subgroups non-diabetic and diabetic patients

<table>
<thead>
<tr>
<th>Outcome rates</th>
<th>Follow-up 12 Months</th>
<th>Follow-up 24 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary patency</td>
<td>85%</td>
<td>82%</td>
</tr>
<tr>
<td>Assisted primary patency</td>
<td>86%</td>
<td>86%</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Limb salvage</td>
<td>82%</td>
<td>81%</td>
</tr>
<tr>
<td>Patient survival</td>
<td>77%</td>
<td>65%</td>
</tr>
<tr>
<td>Amputation-free survival</td>
<td>69%</td>
<td>60%</td>
</tr>
</tbody>
</table>

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Figure 1  HRQoL-values (physical functioning, role-physical, bodily pain, general health perceptions) before (baseline), 6, 12, and 24 months after successful infrageniculate bypass surgery (n = 47; mean values with corresponding 95% confidence intervals of SF-36 domains) (*p ≤ 0.01; **p ≤ 0.001; vs. baseline).
complaints, 12 patients (26%) presented with claudication (6 non-diabetic; 6 diabetic) and 6 patients with CLI: 2 patients with rest pain (all diabetic group) and 4 patients with tissue loss (2 persistent lesions in diabetic patients, and 2 new lesions in non-diabetic patients). Seven patients (8%) required secondary amputation due to non-healing wounds and persisting rest pain. Four (5%) patients suffered irremediable graft occlusion, but were not amputated. One patient with secondary amputation and one with untreated graft occlusion refused to complete the SF-36 questionnaire at final HRQoL-assessment. In total 4 (5%) patients were lost to follow-up. The technical outcomes of bypass surgery are presented in Table 2. In both, the diabetic and the non-diabetic group, similar outcome rates were obtained in terms of clinical outcome (Table 2).

Twenty-four months after successful revascularisation HRQoL was significantly improved in 4 domains of the SF-36 compared to baseline-values: physical functioning ($p < 0.01$), pain ($p < 0.01$), mental health ($p = 0.04$), and social functioning ($p = 0.01$) (Figs. 1 and 2). Likewise, a trend toward improvement was observed in the domains role-physical, role-emotional, and vitality (Figs. 1 and 2).

The time-course of postoperative HRQoL-values revealed that the initial improvement after 6 months was most pronounced, followed by a continuous decline during the following 18 months in all but one domain, physical functioning (Figs. 1 and 2). However, only in general health perceptions the poor baseline level was reached again by the end of the follow-up period.

After 24 months, all patients with patent reconstruction and intact limb judged their general health status as being improved or at least similar compared to their situation prior to surgery: "much better" 19 (40%), "better" 14 (30), and unchanged 14 (30%).

Subgroup-analysis, comparing the diabetic and the non-diabetic group, revealed that the overall benefit in HRQoL can be attributed mainly to an improvement in the non-diabetic group (Figs. 3 and 4). Prior to bypass surgery, both groups did not differ significantly except for the domain role-emotional ($p = 0.04$). During the complete follow-up period, HRQoL-values in the non-diabetic group were superior to those of diabetic patients. While the non-diabetic group reached a peak in HRQoL after 6 months, improvement was delayed in the diabetic group with a maximum after 12 months in most domains (Figs. 3 and 4). At final follow-up examination, HRQoL-values of non-diabetic patients were still significantly improved in all domains of physical health (physical functioning, role-physical, and bodily pain), as well as in mental health and social functioning (Table 3). The diabetic subgroup sustained significant

Figure 2  HRQoL-values (mental health, role-emotional, social functioning, vitality) before (baseline), 6, 12, and 24 months after successful infrageniculate bypass surgery ($n = 47$; mean values with corresponding 95% confidence intervals of SF-36 domains) ($^*p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$; vs. baseline).
improvement only in the domain bodily pain, whereas general health perceptions were judged even worse than before surgery (Table 3).

The small group of patients with secondary amputation self-assessed their HRQoL as being improved compared to the preoperative situation, especially in the physical health domains physical functioning and bodily pain (Table 3). Asked whether they would give consent to bypass surgery in the same preoperative situation once again, 4 patients agreed and 1 patient denied (1 undecided). In patients with non-treated graft occlusion \( n = 3 \) quality of life was even further impaired compared to baseline-values, except for the domains bodily pain and mental health which remained nearly unchanged.

**Discussion**

Chronic critical limb ischaemia has a progressively detrimental impact on quality of life. In recent years, it has well been documented that successful infrainguinal bypass surgery can improve this impaired HRQoL in patients with limb-threatening ischaemia, at least for the first year after revascularisation. Beyond that, the present prospective study revealed that this benefit in HRQoL is sustained for a time period exceeding the first 12 months after surgery. An early significant improvement of HRQoL 6 to 12 months after surgery, well in line with previous reports, was followed by a slight decline during the further observation period. Nevertheless, lasting improvement could be sustained in 7 out of 8 domains of HRQoL up to 24 months after successful revascularisation. Likewise, the majority of patients felt general health status being better than before surgery.

Previous reports on quality of life after bypass surgery were in their majority limited to a 12 months follow-up period, and only a few retrospective studies assessed functional outcome or HRQoL with an observation period exceeding the first year. The surviving patients were likely to retain their limb after successful revascularisation, but their functional capabilities were impaired, often necessitating significant care, and their overall quality of life was poor compared to healthy controls.

The only prospective long-term HRQoL-study by Wann-Hansson et al. reported a decline of physical mobility following an initial first year improvement of quality of life. This development of quality of life values is analogous to the results obtained in the present study, although different tools for HRQoL-assessment were applied: the Nottingham Health Profile (NHP) and the SF-36,
respectively. However, in the Swedish study, the qualifying procedures included endovascular reconstructions as well as different types of open surgery, and only 36% patients from the CLI-group could be included in the 4-year follow-up assessment.23

In contrast to previous reports,8,11,12,14,17,20,23 this study focuses on a homogenous group of patients with below-knee bypasses for limb-threatening ischaemia. In these patients, the benefit in quality of life seems particularly questionable due to the high susceptibility of these reconstructions to failure and the increased incidence of ischaemic lesions and severe co-morbidities. Nevertheless, even in this problematic group of patients, self-assessed quality of life was substantially improved by successful revascularisation.

In terms of graft patency and limb salvage, equally good results can be achieved in diabetic and non-diabetic patients after successful arterial reconstruction.30–32 On the other hand, diabetes proved to be associated with prolonged wound healing,6 increased likelihood for loss of ambulation,5,20 lower patient survival rates,31,33 and impaired quality of life at least within the first year after revascularisation.11,15,20,34 In the present study, technical outcome was similar in diabetic and non-diabetic patients as well. However, in the diabetic group, postoperative improvement of quality of life was delayed, less pronounced, and never reached the HRQoL-level observed in the non-diabetic group. As the SF-36 is a generic health status questionnaire, changes in general health status attributable to numerous co-morbid diseases may adversely affect responses despite functioning reconstruction and intact limb.7 In diabetic patients, severe co-morbidities and the progressive nature of these conditions continuously reduce general health status. This may explain why these patients encounter less improvement, and why their limited benefit in quality of life is not sustained over a longer period of time, despite functioning graft and limb salvage.

As there is no control group without revascularisation, no information is available on how untreated CLI-patients would have done with respect to their quality of life during the same follow-up period. Two years after infrageniculate bypass surgery, HRQoL was superior or at least the same as before surgery in all patients with successful revascularisation. With exception for the domain general health perceptions, this observation was true even for the diabetic group. There is every reason to believe that without revascularisation HRQoL would continuously deteriorate in patients with CLI.24 Therefore, maintenance of preoperative baseline level alone might very well be regarded as

Figure 4  Comparison of non-diabetic (n = 21) (—) and diabetic (n = 26) (······) patients (mental health, role-emotional, social functioning, vitality) before (baseline), 6, 12, and 24 months after successful infrageniculate bypass surgery (mean values with corresponding 95% confidence intervals of SF-36 domains) (*p < 0.05; **p ≤ 0.01; ***p ≤ 0.001).
Two-years Quality of Life after Bypass Surgery

It was not the primary aim of the present study to evaluate HRQoL in patients with failed revascularisation. Surprisingly, however, analysis of the small group of patients with secondary amputation revealed there was no significant difference in quality of life between patients with successful revascularisation and those with secondary amputation—the latter group even improved in the domains of physical health compared to their baseline scores. Unexpectedly good results in mobility and “activities of daily living” despite secondary amputation have been reported by Johnson and co-workers previously as well. However, as there were few survivors with secondary amputation in our study, and other working groups reported contrary observations with negative impact of secondary amputation on quality of life, these data do not justify the conclusion that quality of life of secondary amputees equates that of patients with successful revascularisation two years after surgery.

A limitation of this study is the selection bias due to the abbreviated survival of the study population. Furthermore, especially patients with an unfavourable clinical outcome may have refused to participate in the study any further. This could result in an optimistic bias. While the limited survival rate remains a general problem in longitudinal studies on patients with CLI, including the present study, the number of patients lost to follow up was, however, rather small with only 4 patients after 24 months. Therefore, the completed data sets can be expected to represent the group of patients with functioning grafts and intact limbs sufficiently.

In conclusion, infrageniculate bypass surgery has a lasting positive effect on self-assessed quality of life in patients with CLI. Therefore, an aggressive approach towards bypass surgery for limb-salvage seems to be justified from the patient’s perspective. This seems especially true for patients without diabetes, who feel a gain in quality of life for at least 2 years after successful revascularisation. Diabetic patients tend to benefit as well, albeit to a lesser extent. Considering the dismal prognosis CLI has for both life and limb, this should not deter clinicians from attempting revascularisation in the presence of diabetes, as quality of life may at least be preserved for a limited period of time. Hence, these findings may be of use when counselling diabetic patients to provide them with a realistic picture of what they may expect to encounter following infrageniculate bypass surgery.

References


