

Quality of life after infrainguinal bypass grafting surgery

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Purpose: The purpose of this study was to compare quality of life in patients with and without various ischemic complications after infrainguinal bypass grafting surgery for occlusive vascular disease.

Methods: A sample of patients (n = 746) randomized in the Dutch BOA study (n = 2645), a multicenter trial that compared the effectiveness of oral anticoagulant therapy with aspirin in the prevention of infrainguinal bypass graft occlusions, was entered in this study. On the basis of clinical outcomes of the trial, the patients were grouped as follows: patients with patent grafts (n = 409); patients with nontreated graft occlusions, subdivided into an asymptomatic group (n = 32) and a symptomatic group (n = 65); patients with subsequent revascularizations (n = 194); patients with amputations (n = 36); and patients with failed secondary revascularizations followed by secondary amputation (n = 38). In case an outcome event occurred, the patients were regrouped accordingly. Every half year, the patients completed a Short Form-36 and a EuroQol questionnaire. A multilevel model was used for repeated measure analysis.

Results: The mean follow-up time was 21 months. The quality of life in patients with nontreated asymptomatic occlusions was roughly similar to the quality of life in patients with patent grafts. Patients with symptomatic nontreated occlusions had the lowest outcome with regard to pain as compared with the other groups. Furthermore, physical and social functioning was lower for these patients than for patients with patent grafts. Revascularizations, successful or not, negatively affected pain, social functioning, and physical and emotional role. After successful revascularization, some improvement was observed in pain, physical and social functioning, and general and mental health as compared with the group with nontreated symptomatic occlusions. Amputation deteriorated physical functioning strikingly, especially after failed secondary revascularization. These patients also had the lowest scores of all the groups in the dimensions of social functioning, physical and emotional role, and mental health. EuroQol score showed deterioration of quality of life after all events, except for asymptomatic occlusions. The same patterns emerged if we stratified our analysis according to the indication for the initial operation: claudication or limb salvage. Quality of life was constant over time in all the groups in the observed period.

Conclusion: Quality of life in patients with asymptomatic occluded grafts is similar to quality of life in patients with patent grafts. Revascularization of symptomatic occluded grafts improves quality of life to a certain extent. Amputation, in particular after failed secondary revascularization, seemed to be the lowest possible outcome. The results of the Short Form-36 and EuroQol measurements were in line with the clinical expectations. The association of disease severity with scores on the instruments supports the construct validity of these outcome measures for an objective assessment of quality of life in controlled studies. (*J Vasc Surg* 1999;29:913-9.)

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The outcome of infrainguinal bypass grafting surgery is usually assessed by means of graft patency and limb salvage. To stimulate standard methods of reporting, guidelines have been developed.¹ From the point of view of the patients, functional health status is the most important outcome. So far, only few studies have added measures of health-related quality of life to the traditional parameters. Many quality of life instruments have been developed for both clinical and economic appraisal. The clinical instruments measure quality of life from a patient's point of view. The instruments used for economic appraisal typically value the health state for a societal point of view: the health state of a patient is valued by the general public. Both kinds of instruments have to be validated before the scores can be interpreted. The clinical instruments compare the scores of the patients with the scores of the other patient groups and the "normal" score of the general population. The health states measured with the economic instruments have to be valued by the general public in large population surveys.

Review of the literature revealed only a few studies with many different instruments: the Spitzer QL-Index,^{2,3} the Short Form-36 (SF-36),⁴ the Rosser Scale,⁵ the Visual Analogue Scale (VAS),⁶ the mobility scale,⁶ the hospital anxiety and depression score,^{6,7} the Barthel independent activities of daily living index,⁶ the Frenchay activities index,⁶ the environment score,⁶ and the social functioning scale.⁷ Most of the studies indicated an improved quality of life after successful bypass grafting surgery and limb salvage.²⁻⁷ Only one study, in which the RAND-36-Item Health Survey (which is comparable to the SF-36) was used,⁸ did not show a difference in quality of life in 17 patients with patent bypass grafts as compared with four patients with amputated limbs. Interpretation of the data from these studies is complicated by the variety of instruments used and limited by the small numbers of patients in the subgroups studied. The SF-36 and the EuroQol are valid, reliable, and widely used generic questionnaires for measuring quality of life.⁹⁻¹³ Their use has been recommended for quality of life assessment in patients with vascular disease.¹⁴⁻¹⁶

The purpose of this study was to assess quality of life by means of the SF-36 and EuroQol in patients with and without various further ischemic complications after infrainguinal bypass grafting surgery for occlusive vascular disease.

METHODS

Patients. Between April 1995 and March 1998, 2645 patients were randomized in the Dutch BOA study (*Bypass, Oral anticoagulants, or Aspirin study*),¹⁷

a multicenter trial that compared the effectiveness of oral anticoagulant therapy with aspirin in the prevention of occlusions after infrainguinal bypass grafting surgery. Clinical outcome events in the trial were graft occlusion, vascular intervention, amputation, myocardial infarction, cerebrovascular accident, and death. We performed a substudy on quality of life in patients with different postoperative outcomes. The study was approved by the Ethics Committees of all the participating hospitals and by the Dutch Health Insurance Council. All the patients who were enrolled in the study gave informed written consent.

From November 1995, a sample of 409 consecutive patients who were included in the trial and who had had patent grafts and no other outcome event at the time of the first follow-up examination 3 months after surgery were included in the present quality of life study. Furthermore, all the patients with clinical outcome events in the trial from November 1995 until the last follow-up examination in April 1998 were included in the quality of life study (n = 337). On the basis of clinical outcomes within the trial, the 746 patients were grouped as follows: patients with patent grafts and no other outcome events; patients with nontreated graft occlusions, subdivided into an occluded asymptomatic group (ie, no claudication in the concerning leg in patients who initially underwent operation for claudication and no pain at rest or ulceration in patients who initially underwent operation for limb salvage) and an occluded symptomatic group (ie, claudication or critical ischemia in the concerning leg); and patients with treated graft failures, subdivided into patients with subsequent revascularizations, patients with primary amputations after initial bypass grafting surgery, and patients with secondary amputations after failed secondary revascularizations. Patients underwent analysis in their initial group until an outcome event eventually occurred. In case an outcome event occurred, the patients were regrouped and underwent analysis from those concerning follow-up examinations in the new groups accordingly. For example, if a patient was in the patent graft group during the first and second follow-up examinations and underwent an amputation during the third follow-up period, this patient underwent analysis twice in the patent graft group and from the third follow-up examination on in the amputation group. For a comparison of quality of life of patients with other severe vascular events, we also entered patients with myocardial infarctions and cerebrovascular accidents after the initial operation. These patients had no other clinical outcome events.

Quality of life measurement. Quality of life was

Table I. Number of patients, indications for initial surgery, and completed questionnaires in each group

| <i>Group</i> | <i>No. of patients</i> | <i>Claudication* (%)</i> | <i>No. of questionnaires</i> | <i>No. of questionnaires per patient</i> |
|--------------------------|------------------------|--------------------------|------------------------------|--|
| Patent graft | 409 | 48 | 1612 | 3.9 |
| Asymptomatic occlusion | 32 | 47 | 96 | 3 |
| Symptomatic occlusion | 65 | 62 | 243 | 3.7 |
| Revascularization | 194 | 49 | 712 | 3.7 |
| Primary amputation | 36 | 6 | 124 | 3.4 |
| Secondary amputation | 38 | 18 | 126 | 3.3 |
| Myocardial infarction | 16 | 31 | 58 | 3.6 |
| Cerebrovascular accident | 25 | 52 | 82 | 3.3 |

*Indication for bypass grafting surgery at baseline; in the remaining patients the indication was limb salvage.

measured with the EuroQol and the SF-36 quality of life questionnaires. The EuroQol instrument consists of a questionnaire that classifies the patient into one of 243 health states (five dimensions, each with three levels: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). This concise questionnaire generates a single numeric index of health status between 0 (worst health) and 100 (best health) that enables calculation of “quality-adjusted life years.”¹⁸⁻²⁰ The societal value of quality of life is obtained.²¹ This societal perspective is the preferred perspective in an economic evaluation of health care. The EuroQol also contains a VAS on which patients rate their own health between 0 and 100. This value represents the patients’ perspective and is considered as the clinical perspective of quality of life. The EuroQol generates two overall values (utilities) for the quality of life (one from societal and one from the patients’ perspective) and is recommended for use in combination with other more detailed generic measures, such as the SF-36.^{9,11} The SF-36 contains 36 questions that cover the following eight dimensions of health: pain, physical functioning, social functioning, physical role, emotional role, mental health, general health, and vitality. It produces a health profile with scores between 0 and 100 for each dimension. A high score indicates good health status from the patient’s perspective.

Every 6 months, the patients were asked to complete the EuroQol and the SF-36 quality of life questionnaires. The questionnaires were sent by mail to all the patients. Incomplete questionnaires were returned to the patients for completion. If necessary, the missing questions were completed with a telephone call. Because the inclusion of the patients in this study continued until the moment of analysis (May 1998), the first patients included completed more questionnaires than those patients who were included last.

Statistical analysis. In longitudinal studies of quality of life, the usual statistical test applied is a

repeated measure analysis. However, this test is not suitable when the number of observations varies with patients and when the same patients undergo analysis in different groups, which was the case in the present study. Therefore, we used a relatively new statistical method called multilevel modeling that allows repeated measures analysis with an unequal number of observations per patient.²² A pivotal assumption for multilevel models is that the number of observations is independent of the outcome (ie, quality of life). In the design of the study, this condition is fulfilled because the number of observations is determined by the inclusion of patients over time, independent of the quality of life of the patients.

The recognition that quality of life must be seen as a multidimensional phenomenon and the large number of relevant clinical groups led to multiple comparisons of results. This large number of comparisons complicated the formal statistical testing of the results. We therefore chose to present the results in an explorative fashion as mean values, with the corresponding unbiased 95% confidence intervals as calculated with the multilevel model, which then was interpreted with caution. This presentation was also in line with the observational nature of the quality of life measurement.

RESULTS

The mean age of the 746 patients who were included in the study was 70 years, with most patients being men (64%). In 341 patients (46%), the indication for surgery at study entry was intermittent claudication, and 405 patients (54%) underwent operation for critical ischemia.

The mean follow-up period was 21 months. The number of patients in each group and the proportion of patients who underwent operation for claudication are given in the two left columns of Table I. The number of questionnaires that were completed

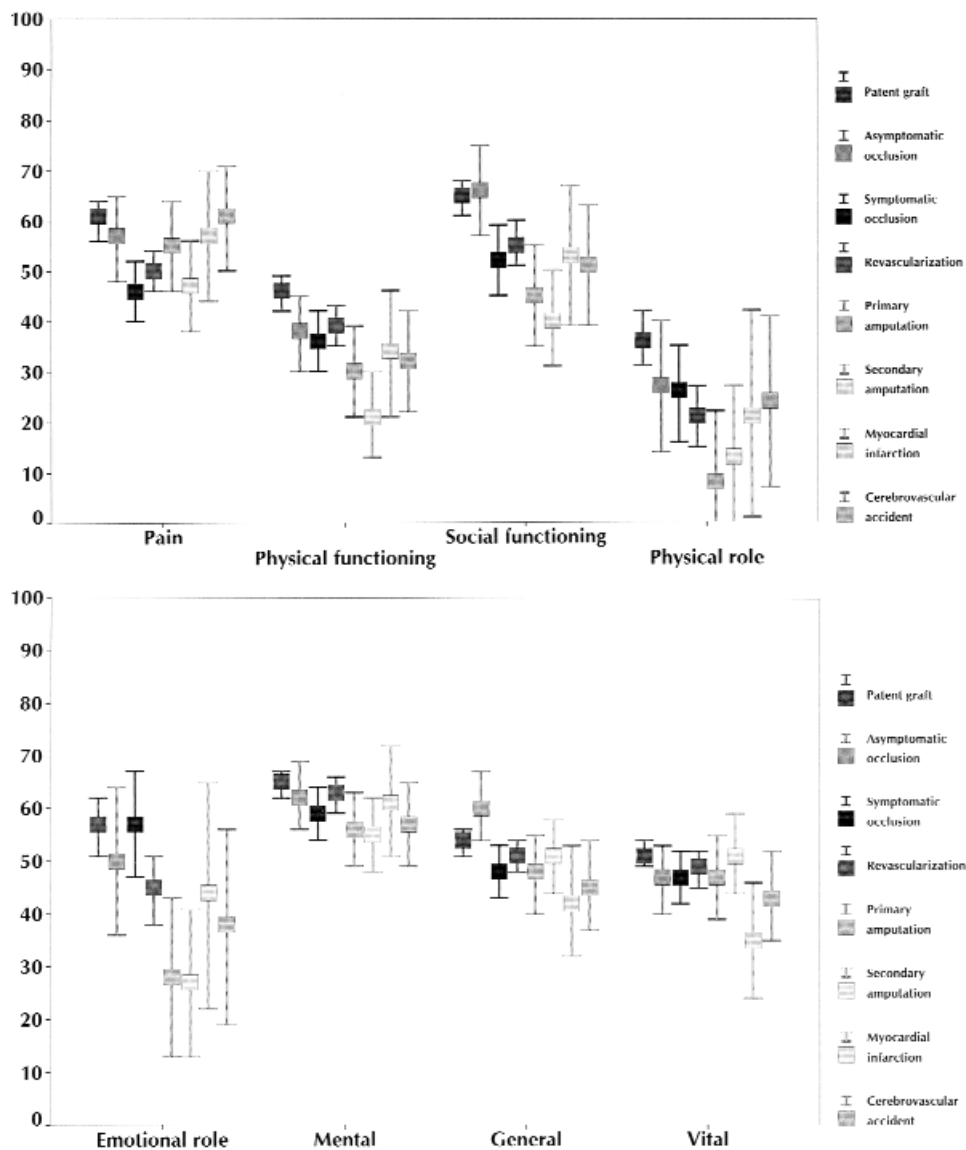


Fig 1. Mean values (squares) with corresponding 95% confidence intervals of SF-36 domains for each of the clinical outcome groups.

by each group is presented in the right part of Table I. Because of the occurrence of a clinical outcome, patients entered subsequent groups 69 times.

The number of missing values was small: only 64 patients (8.6%) of those included did not complete one or more questionnaires. The following reasons were mentioned: not interested (n = 22), too emotional (n = 21; 8 patients because of amputation), unable because of dementia (n = 5), unable because of stroke (n = 2), other (n = 3), and unknown (n = 11).

Quality of life results, subdivided over eight

dimensions of the SF-36, are shown in Fig 1. Quality of life in patients with nontreated asymptomatic occlusions was roughly similar to quality of life in patients with patent grafts, with a tendency for lower values in the physical domains for the first group. The patients with clinically symptomatic nontreated occlusions had the lowest scores with regard to pain. Furthermore, their physical and social functioning appeared to be less than that in patients with patent grafts. After secondary revascularizations, successful or not, the scores for pain, social functioning, and

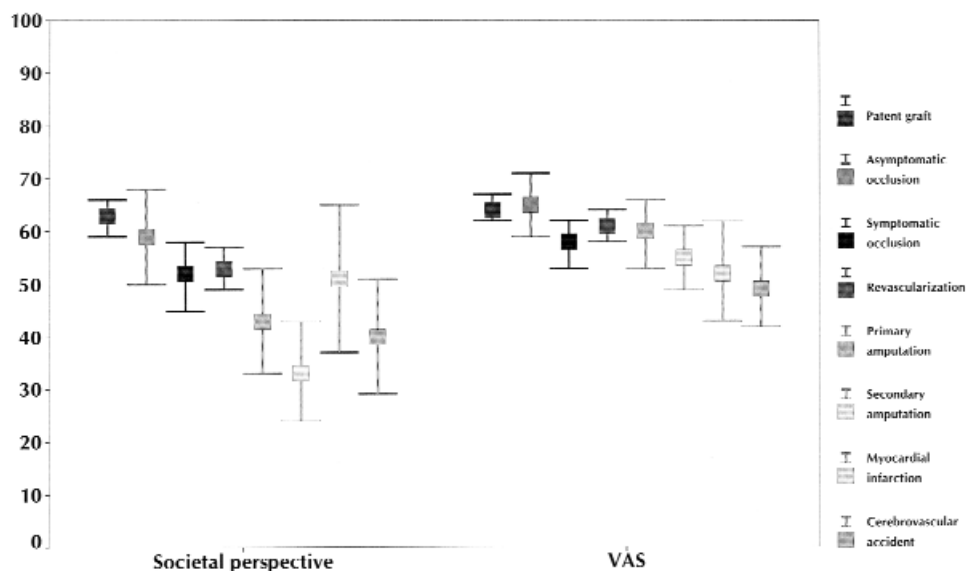


Fig 2. Mean values (squares) with corresponding 95% confidence intervals of EuroQol for each of the clinical outcome groups. VAS, visual analogue scale.

physical and emotional role were lower than those scores in patients with patent grafts or with asymptomatic occlusions. However, after successful revascularization, some improvement was observed in pain, physical and social functioning, and general and mental health as compared with the group with non-treated symptomatic occlusions. In patients after amputation, low scores in the physical functioning domain were reported, especially after failed secondary revascularization. These patients also had the lowest scores of all the groups in the dimensions of social functioning, physical and emotional role, and mental health. A difference in the extent of disease was seen between the latter two groups. In the primary amputation group, 16 of the 36 cases were transmetatarsal or Syme's amputations, whereas in the secondary amputation group, there was only one transmetatarsal amputation and 37 below-knee, through-knee, and above-knee amputations (with χ^2 test, $P = .00002$; Table II). After myocardial infarction and stroke, general health and vitality most clearly were deteriorated.

The results of the EuroQol scores are presented in Fig 2. Both unidimensional measures of quality of life confirmed the findings of the multidimensional measures from the SF-36. Quality of life of patients with asymptomatic occlusions did not essentially differ from quality of life of patients with patent grafts. However, quality of life was lower after the other outcomes. The quality of life as valued by the patients themselves on the VAS was higher than the values

Table II. Levels of amputations

| Amputation level | Primary amputation group (n = 36) | Secondary amputation group (n = 38) |
|------------------|-----------------------------------|-------------------------------------|
| Transmetatarsal | 15 (41.7%) | 1 (2.6%) |
| Syme's | 1 (2.8%) | 0 |
| Below knee | 12 (33.3%) | 25 (65.8%) |
| Through knee | 4 (11.1%) | 3 (7.9%) |
| Above knee | 4 (11.1%) | 9 (23.7%) |

that were given to health status by the general public (ie, the societal value).

Quality of life in all groups, in all domains of the SF-36, and in the societal perspective of the EuroQol was lower for patients who initially underwent operation for limb salvage as compared with those who underwent operation for claudication. On the contrary, the VAS scores of patients with asymptomatic occlusions were higher in the patients who entered the study with critical ischemia as compared with the patients with claudication at baseline. In all groups and in all domains of SF-36 and in EuroQol, quality of life was essentially constant over time after the initial procedure.

DISCUSSION

This study was conducted to describe the observational differences of quality of life after graft occlusion, reoperations, and amputations in patients who had undergone infrainguinal bypass grafting surgery. In most domains of the SF-36 and EuroQol, the

patients with patent grafts had the highest quality of life. Quality of life in patients with clinically asymptomatic graft occlusions was nearly similar as compared with quality of life in patients with patent grafts. Patients with symptomatic occlusions, on the other hand, had a lower quality of life as compared with patients with patent grafts, particularly with regard to pain. After revascularization of symptomatic occluded grafts, a tendency toward improved quality of life was observed: improvement was seen in six of the eight domains of SF-36 and in the EuroQol score. Amputation deteriorated quality of life in all domains, except for pain, which makes an attempt for revascularization, particularly in patients with critical ischemia, worth the effort. Failed revascularization that resulted in secondary amputation, however, had a dramatic impact on the deterioration of quality of life. The differences between the studied groups stratified for indication for initial operation at study entry revealed approximately the same results as for the reported overall groups of patients, except for the VAS score in the patients with patent grafts and with asymptomatic occlusion.

Quality of life of the patients for vascular surgery was in all domains far lower than in the healthy population, which had scores from a minimum of 61 (general) to a maximum of 84 (physical functioning).¹³ This implies that the measured quality of life is a result of vascular disease and is not easily explained with comorbid factors.

In this prospective study, the number of patients in the groups with ischemic complications was relatively small, which resulted in wide confidence intervals. These intervals should be interpreted with caution when multiple comparisons of results are made. The mean scores are observational values of quality of life.

Missing data that may have been related to poor quality of life possibly induced bias. The number of patients who failed to complete one or more questionnaires was low in this group of elderly patients (8.6%). These patients were equally distributed over the various groups.

The aim of this observational study was to measure quality of life in patients with different clinical outcomes after infrainguinal bypass grafting surgery. Therefore, possible differences in comorbid conditions between the studied groups were not considered. However, the influence of the most important risk factor on the quality of life, indication for the initial operation, was assessed. The similarity of quality of life between all patients with patent grafts and with asymptomatic occluded grafts was stratified in the analysis for indication for initial operation not

consistent in the VAS score. The VAS score represented the subjective value of quality of life from the perspective of a patient. It therefore seems likely that the better quality of life in patients who underwent operation for limb salvage is caused by coping mechanisms as a result of achieved limb salvage. The similarity in all other domains between patients in the patent graft and asymptomatic occlusion groups might be explained by effects of conservative treatment, such as walking exercises.

The lower quality of life in patients with symptomatic occlusions cannot be explained by a difference in severity of disease at study entry because 62% of the patients with symptomatic occlusions underwent operation for claudication, in contrast with the group with asymptomatic occlusions, in which the indication for surgery was claudication in only 47%. The differences in quality of life between the patients with asymptomatic and symptomatic occlusions and also in the primary and secondary amputation groups may be explained by the difference in the severity of the disease between the groups at the time of measuring quality of life. Because transmetatarsal amputations produce less disability than do higher amputations, it is likely that these patients contributed to the higher score of quality of life in the primary amputation group. The association of disease severity with scores on the instruments used can be considered as convergence validity, which supports the construct validity of the SF-36 and EuroQol in this population.²³ The good relation between symptoms as a result of graft occlusion as assessed by the clinician and functional health status as experienced by the patient affirms the good responsiveness of the SF-36 and EuroQol score to increasing limb ischemia as also seen in studies by Chetter et al.^{15,24}

Results of infrainguinal bypass grafting surgery are usually reported as graft patency, sometimes supplemented by change of ankle pressure, clinical description, and walking distance, with the latter two giving some information about pain and physical functioning. However, functional health status concerns more than these two clinical measures reported from the doctor's perspective. To compare quality of life in different categories of patients and to compare results of different studies, it is recommendable to use standard instruments, such as SF-36 and EuroQol. In addition to the SF-36, we used EuroQol because it permits one to measure the societal perspective of quality of life. This is the preferred perspective in the future cost-effectiveness analyses.¹⁹ The results on the two EuroQol scores indicate that quality of life as valued by the patients themselves was higher than that assessed by the gener-

al public. This is a common finding and usually is interpreted as a result of coping mechanisms. The inclusion of coping effects in the patients' value of quality of life is one of the reasons not to use these values but societal values for economic appraisal.²⁰

The occurrence of failure of an arterial reconstruction triggers a complex process of decision making, which is influenced and directed by clinical symptoms, risk factors, anatomic situations, and technical aspects of surgery and experience, and results in a choice of treatment. Besides improvement of clinical symptoms and limb salvage, a satisfactory quality of life should be the goal of treatment. Knowledge of functional health prospects in various categories of patients is therefore indispensable. This study showed similar quality of life in patients with asymptomatic occluded grafts as compared with patients with patent grafts. Revascularization of symptomatic occluded grafts improves quality of life to a certain extent. Amputation, however, in particular after failed secondary revascularization, seems to be the lowest possible outcome. As far as quality of life is concerned, this sequence of events has to be avoided by optimal patient selection.

The low quality of life and the extensive use of resources necessary for management of patients for vascular surgery, especially after failed bypass grafting surgery, justify profound decision analytic research. The multilevel model is a suitable tool for analyzing these type of data with various numbers of observations over time and with patients measured in various groups because they incorporate only repeated measure models but allow for skipped measurements. The good responsiveness of the SF-36 and EuroQol to events in patients for vascular surgery pleads for widespread use of these instruments as valid and objective outcome measures besides the traditional clinical outcomes in controlled studies.

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