Objective: Patient- and society-oriented measures of outcome have a critical role in determining the effectiveness of any treatment in patients with critical limb ischaemia (CLI). In particular, the impact of an intervention on patient’s dependency and functional performance is relevant but is largely unknown.

The aim of the study was to investigate whether the limitations encountered in the activities of daily living (ADLs) measured with the Katz Index (KI) in patients with CLI were changed by the treatment.

Methods: During the period 2006–2008, 248 consecutive patients undergoing repair for CLI were investigated with an ADL questionnaire for assessing KI before and after a mean of 16.19 months from treatment. Changes in KI were stratified by type of treatment and outcome.

Results: There were 165 males and 83 females, mean age 73.3 ± 8.3 years; 125 patients showed tissue loss and 123 rest pain alone, 98 received surgical bypass and 150 endovascular repair. Pre-operative KI mean was 10.42. At the post-operative assessment, there was significant worsening in patients’ functional outcome (mean KI decreased to 9.78) despite relief of pain (81.5%), tissue healing (72%), good vessel patency (83.8%) and low amputation rate (9.7%). Deterioration of KI was not significantly higher in patients undergoing endovascular repair. Patients receiving major amputation started with worse pre-operative functional score (KI mean 9.42) and did further deteriorate (KI mean 7.71) after demolition surgery. However, patients who received successful revascularisation showed deterioration in the dependence index.

Conclusions: Successful vascular treatment is not associated with improved functional ability in patients with CLI, especially when already highly dependent in their activities. Large
Critical limb ischaemia (CLI) is a disease process with tremendous cardiovascular burden. The care of patients with CLI is not straightforward because many of them have significant co-morbidities including diabetes, renal disease and advanced age that further contribute to the overall morbidity, mortality, dependency and poor life satisfaction. Furthermore, CLI is associated with significant reduction in health-related quality of life and, of more relevance, in functional independency with reported patients’ perception status comparable to or worse than patients with recent myocardial infarction or cancer. The decision to perform a revascularisation procedure (whether by surgical bypass or endovascular treatment) versus amputation or treat with medical therapy alone remains a challenge.

To be effective, any intervention for CLI needs to be measured within the global functional perception of health and dependency.

Many standardised health measurement scales failed to reliably consider the functional ability in patients with CLI. Furthermore, the results of different studies using either general health-quality instruments (e.g., Short Form 36 Health Survey (SF-36)) or more specific questionnaires (e.g., Vascular Quality of Life Questionnaire, VascuQol) did not provide reliable information and comparable data and did not assess impact of revascularisation on functional dependency.1,2 Currently, there are no quality of life instruments that have been standardised in a large patient population requiring treatment for CLI and the Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC) claimed that specific instruments capable of detecting improvement in functional outcome in this patient population must be developed.3

The Katz Index of Independence in Activities of Daily Living (ADL), commonly referred to as the Katz ADL, is one of the most employed general instruments to assess functional status as a measurement of the patients’ ability to perform activities of daily living independently.4,5 This instrument, largely validated in the elderly/geriatric population is simple, quick, easy to understand and complete also for elderly patients, stroke populations and patients with disabilities. Furthermore, it can be useful for recording data retrospectively.

The purpose of this study was to document outcome of functional status using a general ADL instrument after revascularisation for CLI.

Methods

For the purpose of this study, all patients who provided informed consent and underwent planned elective infragenual lower-extremity revascularisation between January 2006 and December 2008 for an indication of CLI were investigated. Consecutive patients without a history of primary amputation and who survived after the revascularisation procedure were included. Criteria for inclusion were CLI defined as ischaemic rest pain and/or gangrene or non-healing ischaemic ulceration corresponding to categories 4, 5 and 6 of the Society of Vascular Surgery/International Society for Cardiovascular Surgery (SVS/ISCVS) standards6 and according to the TASC guidelines.3 In the presence of diabetic patients, CLI was diagnosed by clinical findings in combination with signs of diminished perfusion, transcutaneous oxygenation (tcPO2) findings and radiologic/ultrasound diagnostics.

All revascularisation procedures, either by endovascular or open surgery, were included for the analysis, regardless of the specific inflow site, outflow site and conduit or stent material/configuration. The included lesions were according to the TASC classification type B, C or D for vascular anatomy.3

Risk factors and co-morbidities

Risk factors and co-morbidities were registered prospectively during the admission intake. Co-morbidities examined included coronary artery disease (history of myocardial infarction or angina), chronic obstructive pulmonary disease (COPD), hypertension (history of hypertension or blood pressure >140/90 mmHg on the pre-operative evaluation), history of tobacco use (never; <1 year or current), hyperlipidaemia (total cholesterol level higher than 200 mg/dl or when the patient took lipid-lowering drugs for history of high cholesterol levels), diabetes mellitus (insulin dependent or controlled by oral medications or diet) and renal disease (normal, creatinine ≤1.5 mg/dl renal insufficiency, serum creatinine >1.5 mg/dl or dialysis dependent). Procedure details were also evaluated.

All patients received planned revascularisation and unplanned re-interventions. Revascularisation procedures were divided into percutaneous endovascular and bypass graft (BG) repairs. Endovascular procedures were carried out by conventional balloon dilatation of the target lesion with or without stent placement, and were performed under local anaesthesia with or without sedation. BG procedures were performed according to standard vascular techniques using preferably an autologous vein for crural BG. The choice of revascularisation was left to the surgeon’s discretion, according to extension and type of lesions.

Follow-up data

Vital status and patency was confirmed during follow-up visits scheduled at 1 month and every 6 months after the revascularisation. Follow-up data included vital status, patency of the graft or target artery, amputation status and symptoms (asymptomatic, claudication, rest pain or tissue loss). The BG or endovascular target vessel patency was determined by duplex ultrasound examination. ‘Patency’ was defined as patency across the same limb segment by one or more additional procedures (preserving or not the original graft). The decision to re-intervene and the type of re-intervention were driven by the SVS/ISCVS and TASC reporting standards.3,6

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Functional status

The functional status was evaluated according to the functional independence measure assessed with Katz ADL. This was determined before and after the revascularisation procedure by a physician trained in peripheral vascular diseases through telephone interviews to all identified survivors. The mean follow-up time from revascularisation to telephone survey was of 16.19 ± 10.75 months (range 6–36) after repair.

The Katz ADL is the instrument to assess functional status as a measurement of the patient’s ability to perform activities of daily living independently. The Index ranks adequacy of performance in the six functions of bathing, dressing, toileting, transferring, continence and feeding. In more than 30 years since the instrument was developed, it has been modified and simplified, and different approaches to scoring have been used. However, it has consistently demonstrated its utility in evaluating functional status in the elderly population. In this study, patients were scored from 0 to 2 (from the worse to the best) for independence in each of the six functions, according to the following scale:

- Score 0: the patient is unable to do any part of the activity;
- Score 1: the patient is able to complete the activity with difficulty, which may or will lead to requirement for assistance; and
- Score 2: the patient is able to complete the activity without assistance.

A detailed description of the ADL questionnaire is reported in Appendix.

In addition to the six functions of the ADL questionnaire, patients were specifically questioned about presence of rest pain and healing status of foot ulcers. Standardised questions (regarding ulcer healing, pain, ambulation and each of the KI-specific functions) were systematically asked during the interview.

Statistical analysis

The data of functional outcome were presented as mean ± standard error. For the purpose of comparison between predefined groups, t-test and analysis of variance (ANOVA) were used.

Cumulative patency and limb salvage rates were calculated using the life-table method.

Pre-operative, intra-operative and post-operative variables (listed in Table 1) were examined with univariate and multiple regression analysis for their influence on functional outcome changes after revascularisation. In particular, four predefined groups of patients were investigated for functional outcome changes according to: presence of non-healing ulcer at baseline; type of revascularisation procedure (endovascular or open BG); graft/target vessel patency; and limb salvage status.

Independent associations of variables with functional outcome were analysed with multiple regression and logistic regression analyses. For logistic regression a change of ±2 in the KI score was assumed as a clinically relevant outcome measure.

Revascularisation procedures (endovascular and BG) were analysed by intention-to-treat.

A value of p < 0.05 was considered statistically significant. Statistical analyses were performed through a computerised software package, Statistical Package for Social Sciences (SPSS) 16.0 for Windows.

Results

Cohort characteristics

Between January 2006 and December 2008, 370 consecutive patients were admitted for treatment of CLI at a single vascular centre. Thirty-five patients were judged with no-option CLI and received primary major amputation. Of the remaining vascularised patients, 57 died early after revascularisation and could not be assessed for post-operative function, and 30 were not available to respond to questionnaires. A total of 248 patients with KI measured before and after treatment represent the study population. There were 165 males and 83 females; mean age was 73.3 ± 8.3 years (range 47–91).

Demographic and co-morbidities are shown in Table 1. Almost half the patients at baseline had non-healing ulcer or tissue loss (n = 125) and half showed rest pain with foot integrity (n = 123).

There were 150 primary endovascular procedures and 98 primary BGs.

Outcome and patency rate

After a mean of 16.9 ± 10.75 months from revascularisation, 24 (9.7%) major amputations occurred. Patients were specifically investigated for the persistence of pain and non-healing ulcer: 46 (18.5%) patients were still rested-pain; in 90 (72%), ulcer healing occurred, while in 35, tissue loss persisted.

Secondary procedures were performed in 59 patients: in 48, after endovascular repair (32%) and, in 11, after BG (11.2%), p = 0.003. In seven, two or more re-interventions were performed.

According to life-table analysis at 24 months, cumulative limb salvage rate was 90% and patency rate was 82%.

Cumulative patency rates at 24 months were significantly higher after BG than after endovascular approach: 90% versus 77% (p = 0.035), after BG versus endovascular repair, respectively.

Functional outcome

At baseline, mean KI score was 10.42 ± 2.45. Baseline and post-operative mean KI scores are shown in Table 1.

Baseline KI scores were worse in patients who underwent amputation (9.42 ± 2.70) and in those with persistent rest pain (9.46 ± 2.89) or persisting non-healing ulcer (9.77 ± 2.78) after revascularisation (Table 1).

At post-operative assessment, mean KI significantly deteriorated to 9.78 ± 3.04 (difference –0.64; p = 0.0001). KI deterioration was detected in each of the specific score functions, but was not significant for transfer (difference –0.06 ± 0.49; p = 0.055). For eating: difference –0.12; for
dressing: difference −0.14, for bathing: difference −0.15 and for continence: difference −0.04 (Fig. 1).

Factors associated with changes in post-operative KI are shown in Table 2. Significant KI deterioration with respect to baseline was found for patients receiving endovascular repair (difference −0.84; \( p = 0.049 \)); for patients who had undergone amputation (difference −1.71; \( p = 0.006 \)) and for patients with persisting rest pain (difference −1.54; \( p = 0.001 \)). Statistical significance for endovascular repair was lost when patients with re-interventions were censored from the analysis (\( p = 0.14 \)).

At multiple regression analysis (Table 3), independent predictors of KI change after repair were non-healing ulcer at baseline (\( p = 0.048 \); estimate −0.81; 95% confidence interval (CI) −1.61 to −0.01), need of major amputation (\( p = 0.017 \); estimate −1.52; 95% CI −2.77 to −0.27), healing ulcer after repair (\( p = 0.003 \); estimate 1.22; 95% CI 0.41−2.02) and persistence of rest pain after repair (\( p = 0.01 \); score difference: −0.87; 95% CI −1.56 to −0.22).

Multiple logistic regression analysis using a clinical relevant deterioration of −2 KI score change from baseline as dependent variable confirmed the occurrence of major amputation (\( p = 0.02 \); odds ratio (OR) 11.66; 95% CI 1.48−91.94) and persistence of rest pain after revascularisation (\( p < 0.0001 \); OR 5.82; 95% CI 2.31−14.69) as independent predictors.

**Subgroup analysis**

Changes in KI were analysed in subgroup analyses by presence of non-healing ulcer/tissue loss at baseline, type of repair (endovascular vs. BG), patency and requirement of amputation (Table 1).

Deterioration was significant in each of the analysed subgroups: for patients with non-healing ulcer/tissue loss at baseline (\( p < 0.0001 \)) and for those with foot integrity at baseline (\( p = 0.004 \)); for patients with vessel patency (\( p = 0.0001 \)) and those with patency loss (\( p = 0.012 \)); for patients undergoing amputation (\( p = 0.013 \)) and those with limb salvage (\( p < 0.0001 \)).

In the analysis by treatment type, for patients receiving endovascular treatment, KI changed from 10.21 ± 2.51 to 9.37 ± 3.10, difference −0.84 (\( p < 0.0001 \)). For patients receiving BG, KI changed from 10.72 ± 2.33 to 10.40 ± 2.83, difference −0.32 (\( p = 0.048 \)). After censoring patients with re-interventions, these figures became: for endovascular group, KI changed from 10.39 ± 2.44 to 9.51 ± 3.13, difference −0.88, (\( p < 0.0001 \)); for the BG group, KI changed from 10.90 ± 2.29 to 10.44 ± 2.86, difference −0.45 (\( p = 0.008 \)).

**Discussion**

CLI is a chronic, evolving disease with inevitable progressive degeneration and is associated with high rate of hospitalisation and death and poor patient health perception. Most CLI patients have a tremendous disease burden, with poor baseline function, loss of functional status and ability to live independently.\(^{10,11}\) Impaired functional status in patients with CLI is strongly associated with multiple co-morbidities resulting in increased risk of death and complications during revascularisation procedures.\(^{2,7–9}\) Furthermore, the poorer the baseline functional outcome the worse the functional improvement, even after successful revascularisation has been performed\(^ {8–10} \).
patient functional independence does not improve at the same rate as the leg after successful revascularisation. In our study, at the post-operative assessment, there was no improvement in CLI patients’ functional outcome (mean KI decreased by $-0.64$; $p = 0.0001$) regardless of successful revascularisation and vessel patency. Deterioration of KI was strongly associated with more advanced disease stages predisposing unsuccessful treatment as in patients with baseline non-healing ulcer ($p = 0.048$), in those requiring major amputation ($p = 0.017$) and in those with persisting non-healing ulcer ($p = 0.003$) or persisting rest pain after repair ($p = 0.010$). Nevertheless, patients who received successful revascularisation did not improve but showed deterioration in the dependence index (from $10.54 \pm 2.40$ to $10.00 \pm 2.94$, difference $-0.54$; $p = 0.0001$). These data suggest that functional impairment is difficult to reverse despite the treatment applied to recover the advanced ischaemia of the limb.\textsuperscript{2,7,8,10} The best treatment to manage patients with CLI should be the prevention of the advanced disease.

![Figure 1](image)

**Figure 1** Katz index pre and post revascularisation by specific function.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Factors associated with changes in post-operative Katz Index score.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Katz Index score mean variation</td>
</tr>
<tr>
<td>Male</td>
<td>$-0.6$</td>
</tr>
<tr>
<td>Diabetes</td>
<td>$-0.84$</td>
</tr>
<tr>
<td>Hypertension</td>
<td>$-0.66$</td>
</tr>
<tr>
<td>CAD\textsuperscript{a}</td>
<td>$-0.58$</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>$-0.66$</td>
</tr>
<tr>
<td>COPD\textsuperscript{b}</td>
<td>$-0.86$</td>
</tr>
<tr>
<td>Renal failure</td>
<td>$-1.08$</td>
</tr>
<tr>
<td>Smoking</td>
<td>$-0.6$</td>
</tr>
<tr>
<td>Pre-operative non-healing ulcers</td>
<td>$-0.74$</td>
</tr>
<tr>
<td>Endovascular procedures</td>
<td>$-0.84$</td>
</tr>
<tr>
<td>By-pass grafts</td>
<td>$-0.33$</td>
</tr>
<tr>
<td>Patency</td>
<td>$-0.55$</td>
</tr>
<tr>
<td>Major amputation</td>
<td>$-1.71$</td>
</tr>
<tr>
<td>Post-operative healing ulcers</td>
<td>$-0.31$</td>
</tr>
<tr>
<td>Post-operative rest pain</td>
<td>$-1.54$</td>
</tr>
</tbody>
</table>

\textsuperscript{a} CAD (coronary artery disease).

\textsuperscript{b} COPD (Chronic obstructive pulmonary disease).
Use of a less-invasive approach of revascularisation did not translate into a more positive influence on functional outcome in patients with CLI. Conversely, in our study, despite the higher preference for an endovascular first approach (n = 150 endovascular vs. n = 98 BG), there was a trend towards higher functional deterioration after endovascular treatment with respect to bypass surgery (post-operative KI score difference from baseline: −0.84 vs. −0.32; p = 0.049). The higher number of failures and re-interventions might have likely affected the results after the endovascular approach (n = 48/150 vs. n = 11/98, in endovascular vs. BG groups, p = 0.003). Indeed, after censoring patients with re-intervention, the difference in KI deterioration between endovascular and BG treatment became not significant (p = 0.14). Major surgery may provide a better impact on functional outcome and may be preferred above weeks of hospitalisation to undergo repeated revascularisation attempts after first endovascular approach. Accordingly, the randomised trial Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) recently showed a slight (even though transient and non-significant) gain in quality of life perception in patients with severe CLI assigned to bypass with respect to those assigned to balloon angioplasty.12

In our experience, a number of patients (57/335) could not be interviewed for functioning after a mean of 16.2 months from repair due to the high mortality rate from all causes inherent to CLI disease. Ultimately, amputation is often the only resolute option left to a subset of patients with CLI, multiple co-morbidities and prohibitive mortality whichever the treatment. However, even though limited in numbers (amputation rate was 10% at 24 months), our results demonstrated a detrimental effect of major amputation after the attempt of revascularisation on functional status in most patients with CLI. Nevertheless, patients undergoing amputation started from poorer baseline functional score, as an expression of more advanced disease (KI 9.42 vs. 10.52, in amputation vs. limb salvage patients). Recent studies analysed the quality of life of patients with no-option CLI (CLI without therapeutic options) and suggested an exceptionally poor, far-behind-generalpopulation health perception score in them.1 Our results can suggest that even in CLI with options for therapy, the indication to treat might not be worthwhile given the irreversible deterioration of functional status of most CLI patients, persisting also after a successful revascularisation procedure. Due to the poor and frequently irreversible functional performance, the need for aggressive interventional/surgical procedures and, thus, the need for the development of new revascularisation strategies in patients with advanced CLI might be questionable. A number of new therapies such as administration of growth factors or bone-marrow-derived stem cells that are currently being evaluated in trials are most likely to provide illusive and not definite solutions in patients with advanced CLI.

Prevention strategies are indeed consistently needed. There is the need to implement patient care plans, pharmacology strategies and patient-education programmes to early and aggressively address risk factors associated with poor outcome and worse functional ability in peripheral vascular disease. A number of studies have investigated factors associated with poor outcome in patients with CLI.1,7,9 Several variables, including co-morbidities such as diabetes and renal failure, foot lesion complexity/extent, technical complexity of revascularisation and nutritional status, have been identified, most of which can be pursued with aggressive early preventive strategies. Indeed, patients with CLI characterise extremely compound and multitasked entities. To address this complexity, we used a generic geriatric health scale such as the Katz ADL to provide an all-through evaluation of the functional ability of patients with CLI.4,5 Even though the KI ranks performance of six functions, some of which might seem minimally affected by CLI, we did not intend to measure which specific daily living function was affected by CLI but, more likely, whether the overall functional disability of dependent patients with CLI could be reversed with effective CLI revascularisation, as this issue has a relevant burden on social health and costs. Functional assessment is a comprehensive evaluation of the physical and cognitive abilities required to maintain independence and functioning (“the ability to function in the arena of everyday living”). Therefore, we did not intentionally use a specific

| Table 3 Factors associated with changes in post-operative Katz Index score (multiple regression analysis). |
|----------------|----------------|----------------|
| Contract estimate | 95% confidence interval | p |
| Male | 0.18 | −0.37 | 0.72 | 0.52 |
| Diabetes | −0.27 | −0.77 | 0.23 | 0.28 |
| CADa | 0.19 | −0.30 | 0.69 | 0.44 |
| COPDc | −0.16 | −0.85 | 0.54 | 0.65 |
| Renal failure | −0.53 | −1.16 | 0.09 | 0.09 |
| Smoking | −0.25 | −0.79 | 0.30 | 0.37 |
| Pre-operative non-healing ulcers | −0.81 | −1.61 | −0.01 | 0.048 |
| Endovascular procedures | −0.42 | −0.94 | 0.11 | 0.12 |
| Patency | −0.57 | −1.58 | 0.43 | 0.26 |
| Major amputation | −1.52 | −2.78 | −0.27 | 0.017 |
| Post-operative healing ulcers | 1.22 | 0.41 | 2.02 | 0.003 |
| Post-operative rest pain | −0.89 | −1.56 | −0.22 | 0.01 |

a CAD (coronary artery disease).

b COPD (Chronic obstructive pulmonary disease).
opportunities for patient health improvement. Although the Katz ADL’s ability in measuring small increments of change seen in the revascularisation of older adults is limited (with respect to specific health-quality questionnaires), little changes cannot reflect improvements in function and dependency in CLI patients. Similarly, the simple assessments of wound healing, pain relief or vessel patency are all incomplete measurements of successful treatment of CLI patients as a whole. In driving appropriate indications for treatment of CLI, any invasive treatment should be balanced by expected gain (or prevention of loss) in health. A comprehensive patient assessment including functional dependency is important to evaluate the true impact of the successful treatment of CLI on social health.

The Katz ADL is also very useful in creating a common language regarding patient function for all problems and has been validated in geriatric populations with chronic disabilities such as after stroke or cancer.\(^1\,4\)\(^{13}\) The social and health burden of CLI in developed countries is comparable to that of stroke as a similar high rate of disabilities is provided while no effective treatment is available after the occurrence of the disease, the best treatment option being the prevention. It is of relevance that dependency recovery might be more consistent after stroke than after CLI where patient functional ability remains exceptionally poor over time, confirming that CLI is a marker of a poor, irreversible condition with high functional dependency and limited opportunities for patient health improvement.

**Limitations**

There are two primary limitations in this study design. First, although the data analysed in this study were prospectively collected, questionnaires to assess functional outcome were administered by telephone interviews and were reviewed retrospectively. Nevertheless, the reliability of our results was compensated for by low dropout rates. Other studies prospectively analysing quality of life are biased by higher rate of non-responders and those lost to follow-up. As it is likely that the worse patients are those who are non-responders and non-compliant with follow-up, results from these studies might be overestimated.

Second, the patients were from a singe centre and the size was limited to provide detailed information for subgroups. Finally, there was no analysis of costs.

**Conclusions**

Most patients with CLI cannot adequately gain functional advantages from revascularisation because of competing co-morbidities. The successful lower-extremity bypass or endovascular procedure does not translate into subsequent functional dependency recovery.

In evaluating indications and benefits of invasive treatments in CLI, functional outcome should be also considered. For patients with poorer functional status at baseline, primary major amputation might be an option. Bypass and endovascular procedure may be effective when the impairment in CLI is not severe and the procedure can be performed with minimal complications. Otherwise, large nationwide preventive strategies of medical optimisation, monitored risk factors and patient-education programmes are more cost-effective tools to address the enormous social health impact associated with CLI.

**Conflict of Interest**

None.

**Financial Disclosure**

None.

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**Appendix. Supplementary data**

Supplementary data associated with this article can be found in the on-line version, at doi:10.1016/j.ejvs.2010.10.014.

**References**