

# Is amputation in the elderly patient with critical limb ischemia acceptable in the long term?

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**Purpose:** Despite high amputation rates, data on patient-reported outcomes is scarce in the elderly population with critical limb ischemia. The aim of this study was to provide mortality rates and long-term changes of the following patient-reported outcomes in elderly critical limb ischemia amputees: quality of life (QoL), health status (HS), and symptoms of depression.

**Patients and methods:** In this prospective observational cohort study, amputated critical limb ischemia patients  $\geq 70$  years were included. The follow-up period was two years. Within the follow-up period patients completed the following questionnaires: the World Health Organization Quality Of Life -abbreviated version of the WHOQOL 100 (WHOQOL-BREF), the 12-Item Short Form Health Survey, and the Center for Epidemiological Studies Depression Scale.

**Results :** A total of 49 elderly patients with critical limb ischemia had undergone major limb amputation within two years after inclusion. In these patients, the one-year mortality rate was 39% and the two-year mortality rate was 55%. The physical QoL was the only domain of the WHOQOL-BREF that improved significantly across time after amputation ( $p \leq 0.001$ ). In the long-term, there was no difference in the ability to enjoy life ( $p = 0.380$ ) or the satisfaction in performing daily living activities ( $p = 0.231$ ) compared to the scores of the general elderly population. After amputation, the physical HS domain ( $p \leq 0.001$ ) and the mental HS domain ( $p = 0.002$ ) improved. In the first year, amputees experienced less symptoms of depression ( $p = 0.004$ ).

**Conclusion:** Elderly critical limb ischemia amputees are a fragile population with high mortality rates. Their QoL and HS increased after major limb amputation as compared to the baseline situation and they experienced less symptoms of depression. Moreover, our results show that, in the long-term, major limb amputation in the elderly patients with critical limb ischemia shows an acceptable QoL, which, in some aspects, is comparable to the QoL of their peers. These results can improve the shared-decision making process that does not delay the timing of major limb amputation.

**Keywords:** amputation, critical limb ischemia, frail elderly, health status, quality of life

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## Introduction

Critical limb ischemia is the most severe stage of peripheral arterial disease (PAD) and is characterized by ischemic rest pain and/or tissue loss. In patients with critical limb ischemia, the main goal of treatment is to salvage the affected limb.<sup>1,2</sup> The success of treatment for critical limb ischemia is measured by amputation free survival (AFS).<sup>2</sup> In order to achieve this desired outcome, patients with critical limb ischemia are aggressively revascularized by endovascular or surgical procedures, if possible.<sup>1,2</sup> However, despite these efforts, amputation rates remain high. One year

after the onset of critical limb ischemia, 25% of patients will have to undergo a major limb amputation<sup>2,3</sup> and approximately 35–67% of critical limb ischemia patients undergoes major limb amputation within four years.<sup>4</sup> Moreover, early post-operative mortality rates range from 4% to 22% after major limb amputation from any cause.<sup>5</sup> Early mortality rates of up to 20% are reported in critical limb ischemia amputees.<sup>6,7</sup>

Because of high amputation and mortality rates functional status and mobility success have been studied.<sup>8,9</sup> Norvell et al and Taylor et al report that successful outcome is associated with mobility capacity.<sup>8,9</sup> However, mobility is often impaired in elderly patients with critical limb ischemia. This raises the question whether an assessment of objective functioning, which is expected to be impaired, can be considered a good patient-reported outcome of treatment success. Other patient-reported outcomes (PROs), such as quality of life (QoL) and health status (HS), are increasingly relevant in critical limb ischemia patients.<sup>10–12</sup> QoL and HS are supplementary, in the sense that HS questionnaires, like the SF-12, focus on physical, psychological, and social objective functioning and QoL questionnaires measure the patients' own satisfaction or evaluation of functioning.<sup>11,13,14</sup>

Furthermore, little is known about the QoL and HS of critical limb ischemia amputees.<sup>15</sup> The lack of literature on long-term results is due to high mortality rates. Besides, the absolute number of amputees per hospital is low. Additionally, reports on changes in other mental health disorders, like depression, after major limb amputation for critical limb ischemia patients, is lacking in literature.<sup>16</sup>

Therefore, the aim of this prospective observational cohort study was to provide short-term and long-term changes of the following patient-reported outcomes in elderly critical limb ischemia amputee patients: QoL, HS, and symptoms of depression. The scores of specified World Health Organization Quality Of Life -abbreviated version of the WHOQOL 100 (WHOQOL-BREF) questions of the elderly sample in the current study were compared to the normal scores in the general elderly population. In addition, the thirty-days, six-month, one-year and two-year mortality rates of elderly critical limb ischemia patients after major limb amputation will be addressed.

## Methods

In this prospective observational cohort study, patients with critical limb ischemia aged 70 years and older undergoing a major limb amputation, were included between January 2012 and February 2016.<sup>17</sup> Exclusion criteria

were a diagnosis of malignancy, lack of Dutch language skills, or cognitive impairment. This study was conducted in accordance with the Declaration of Helsinki. Based on the criteria of the Central Committee on Research Involving Human Subjects, a formal written waiver for ethical approval was not required. The institutional medical ethical committee (AMOA) approved this. All patients included signed an informed consent.

At a weekly multidisciplinary vascular conference, a panel of experts placed the patients into one of four treatment groups: surgical revascularisation, endovascular revascularisation, conservative therapy, or major limb amputation. During follow-up, secondary major limb amputation was recorded. The follow-up period was two years after inclusion.

Within this follow-up period patients completed the following self-report questionnaires at six specified times: WHOQOL-BREF, the 12-Item Short Form Health Survey (SF-12), and the Center for Epidemiological Studies Depression Scale (CES-D). Patients who underwent major limb amputation during the 2-year follow-up period were selected for this study. Questionnaires were gathered that were completed six months, one year, and between one-and-a-half years and two years after major limb amputation.

## WHOQOL-BREF

In the elderly, the validated WHOQOL-BREF questionnaire was utilized to measure QoL.<sup>18,19</sup> This patient-completed measurement of health-related QoL is the short version of the WHOQOL-100 and contains 26 items with a 5-point Likert type response scale. These 26 questions are grouped into four domains (physical health, psychological health, social relationships, and environment) and a general QoL facet. The WHOQOL-BREF is reliable and valid instrument for measuring quality of life in the Dutch adult population.<sup>10,18,20</sup>

## SF-12

The SF-12 is a reliable and valid instrument for measuring HS of the elderly population.<sup>21</sup> The SF-12 is a shortened version of the RAND 36-Item Short Form Health Survey.<sup>22</sup> The questionnaire consists of 12 questions with three to five response levels, which are completed by patients. It determines HS, which can be divided into the Physical Component Summary (PCS) scale and the Mental Component Summary (MCS) scale.<sup>10,22,23</sup>

## CES-D

Symptoms of depression were measured by means of the CES-D questionnaire.<sup>24,25</sup> In this study, the abbreviated 16-item version was applied, which is both widely used and easy in use, especially in the elderly population.<sup>25</sup> In this questionnaire, patients were presented with 16 symptoms of depression and asked if they experienced any of them. If they had experienced any of the sixteen symptoms, the frequency and duration within the past week was asked to be noted. A CES-D cut off score of  $\geq 12$  specified patients with symptoms of depression.<sup>26</sup>

## Statistical analysis

Statistical analyses were done using a computerized software package: SPSS version 23 (IBM, Chicago IL, USA). Continuous and normally distributed variables were expressed in terms of means and standard deviations. Continuous and non-normally distributed variables were expressed in terms of medians and interquartile ranges. The Shapiro-Wilk test was used to assess whether continuous variables were normally distributed. Categorical variables were expressed in terms of frequencies and percentages. Item-level missing data was imputed according to the guidelines of the particular questionnaire. Scale-level missing data was directly handled through maximum likelihood estimation, as implemented in the mixed modeling procedure. Linear mixed models were used to assess the change of QoL, HS, and symptoms of depression at three specified times. Within mixed modeling, custom hypothesis tests were used to assess differences between baseline and follow-up measurements. Lastly, one sample *t*-tests were used to compare the mean QoL estimates to corresponding estimates in the general elderly population.<sup>27</sup> A *p*-value of less than 0.05 was considered significant.

## Results

A total of 387 patients of 70 years or older were diagnosed with critical limb ischemia during the inclusion period of which 388 patients were excluded based on the criteria previously stated. Two years after inclusion in this study, a total of 49 elderly critical limb ischemia patients had undergone major limb amputation of the affected limb. These patients were selected from a cohort initially treated with surgical revascularisation (n=12), endovascular revascularisation (n=21), conservative therapy (n=11), or primary major limb amputation (n=5). In Table 1, the patient characteristics of all amputees are presented.

**Table 1** Patient characteristics

	<b>Amputees n=49 (100%)</b>
Sex (male)	31 (64)
Median Age (IQR)	82 (75;84)
Living situation	
– Independent*	23 (47)
– Home care	17 (35)
– Nursing facility	6 (12)
– Missing	3 (6)
Civil status	
– Single	8 (16)
– Married or living with partner*	22 (45)
– Divorced	2 (4)
– Widowed*	14 (29)
– Missing	3 (6)
Educational level	
– Low	20 (41)
– Middle	20 (41)
– High	6 (12)
– Missing	3 (6)
Currently smoking	10 (20)
Cardiac comorbidity	41 (84)
Neurologic comorbidity	17 (35)
Pulmonary comorbidity	36 (74)
Renal impairment	29 (59)
Arthrosis	9 (18)
Diabetes mellitus	27 (55)
Hypertension	31 (63)
Rutherford classification*	
– Rutherford-class 4	8 (16)
– Rutherford-class 5/6	41 (84)
ASA classification	
– ASA 2	9 (19)
– ASA 3	35 (71)
– ASA 4	5 (10)
Initially selected therapy	
– Endovascular revascularization	21 (43)
– Surgical revascularization	12 (24)
– Conservative therapy	11 (23)
– Primary amputation	5 (10)
Previous minor amputation	13 (27)
Type of amputation	
– Above knee amputation	15 (31)
– Through knee amputation	4 (8)
– Below knee amputation	30 (61)

**Notes:** Data are presented as n (%), unless otherwise specified. \*Significant difference between age groups ( $p < 0.05$ ).

**Abbreviations:** n, number of patients; IQR, interquartile range; ASA, American Society of Anesthesiologists.

## Clinical outcome & mortality

Place of discharge is shown in Table 2. A small proportion of patients (n=9, 18%) were able to go home after major limb amputation. To the best of our knowledge, 17 amputees (35%) used a prosthesis at some point after major limb amputation. The thirty-day mortality rate was 16%. After 6 months, 31% of the amputees had deceased. The one-year mortality rate was 39% and the two-year mortality rate increased to 55%.

## Patient-reported outcome

Table 3 gives an overview of the median time between amputation and the conduction of the CES-D, the WHOQOL-BREF and the SF-12. As presented in Table 4, the physical QoL was the only domain of the WHOQOL-BREF that significantly improved in time, after amputation. This improvement occurred at the 6-month measurement compared with the baseline measurement (11.29 vs 14.44;  $p \leq 0.001$ , 95% CI 1.61; 4.29) and remained significant after 1.5–2 years (11.29 vs 14.75;  $p \leq 0.001$ , 95% CI 2.49; 4.96). There were no significant differences in time for the overall, psychological, environmental, and social domains of the WHOQOL-BREF. The SF-12 also showed improvement in their physical HS domain, after 6 months compared with the baseline measurement (29.73 vs 34.97;  $p = 0.015$ , 95% CI 0.91; 7.82). This improvement remained significant after 1.5–2 years compared with the baseline measurement (29.73 vs 35.72;  $p \leq 0.001$ , 95% CI 3.02; 9.10). The mental

HS domain only showed a significant improvement after 1.5–2 years compared with the baseline measurement (38.64 vs 44.46;  $p = 0.002$ , 95% CI 3.88; 12.59). Amputee patients experienced less symptoms of depression after 6 months (8.69 vs 4.45;  $p = 0.004$ , 95% CI -5.91; -1.22) and after 12 months (8.69 vs 4.56;  $p = 0.004$ , 95% CI -6.62; -1.40), compared with their baseline measurement.

Table 5 compares the scores of specified WHOQOL-BREF questions at baseline and after amputation to normal scores in the general elderly population.<sup>27</sup> While at baseline the current elderly sample showed significantly higher pain scores than the general elderly population (mean  $\Delta = 0.769$ ;  $p < 0.001$ ; 95% CI 0.47; 1.06), the pain scores significantly improved and reached a level significantly lower than the normal values of the elderly, both in the short-term (mean  $\Delta = -0.603$ ;  $p = 0.022$ ; 95% CI -1.11; -0.10) and in the long-term (mean  $\Delta = -0.824$ ;  $p = 0.024$ ; 95% CI -1.51; -0.13). Elderly critical limb ischemia amputees were able to accept their bodily appearance less, compared to the corresponding elderly. However, their scores did not differ from their pre-amputation scores. Overall, amputees rated their own quality of life significantly lower than the corresponding elderly in the long-term (mean  $\Delta = -0.605$ ;  $p = 0.003$ , 95% CI -0.96; -0.25). However in the long-term, there was no difference in the ability to enjoy life (mean  $\Delta = 0.145$ ;  $p = 0.380$ ; 95% CI -0.21; 0.50), the amount of energy the elderly had (mean  $\Delta = -0.545$ ;  $p = 0.052$ ; 95% CI -1.10; 0.01), or the satisfaction in performing daily living activities (mean  $\Delta = -0.265$ ;  $p = 0.231$ ; 95% CI -0.73; 0.20).

**Table 2** Patient discharge

	Amputees n=49 (100%)
Discharge to	
– Home	9 (18)
– Nursing facility	16 (33)
– Inpatient rehabilitation	18 (37)
– Decease before discharge	3 (6)
– Missing	3 (6)

**Notes:** Data are presented as n and (%).

**Table 3** Time to conduction of the questionnaires

	n	Median time	IQR
Baseline	49		
Half year	23	167	148–185
1 year	16	357	336.5–362.75
1.5–2 years	11	697	651–726

**Note:** Data presented as median.

**Abbreviations:** n, number of patients; IQR, interquartile range.

## Discussion

PROs have become a very important outcome of treatment in the elderly critical limb ischemia patients.<sup>10–12</sup> Considering that a quarter of critical limb ischemia patients undergo major limb amputation during the first year after disease onset, there is a surprising lack of PROs in the vascular amputees.<sup>15</sup> Compared to other multicenter studies, we assessed a relatively large number of critical limb ischemia amputee patients, aged 70 and older, on PROs and clinical outcomes in a prospective observational cohort two-center study. A selection of questions from the WHOQOL-BREF questionnaire, relevant for amputees, was compared to the corresponding values of their elderly peers.<sup>27</sup>

The main finding was that physical QoL and physical HS significantly improved after amputation in elderly critical limb ischemia patients. Mental HS also improved but

**Table 4** Patient-reported outcomes for amputees (n=49)

	n	Mean	SD	p-value	95% CI
<b>WHOQOL-BREF overall QoL</b>					
Baseline	49	3.18	0.85		
Half year	23	3.47	0.59	0.342	-0.1796; 0.4947
1 year	16	3.63	0.56	0.121	-0.0843; 0.6814
1.5–2 years	11	3.55	0.42	0.198	-0.1439; 0.6368
<b>WHOQOL-BREF physical health</b>					
Baseline	49	11.29	2.67		
Half year	23	14.44	2.33	≤ <b>0.001</b>	1.6123; 4.2901
1 year	16	14.46	2.34	≤ <b>0.001</b>	1.6320; 4.1622
1.5–2 years	11	14.75	1.86	≤ <b>0.001</b>	2.4949; 4.9603
<b>WHOQOL-BREF Psychological health</b>					
Baseline	49	14.00	2.36		
Half year	23	14.89	1.90	0.162	-0.2052; 1.1654
1 year	16	15.17	1.57	0.199	-0.3819; 1.7532
1.5–2 years	11	14.73	1.28	0.269	-0.3395; 1.1448
<b>WHOQOL-BREF social relationships</b>					
Baseline	49	15.99	2.23		
Half year	23	16.17	2.00	0.897	-0.7205; 0.8220
1 year	15	16.36	1.55	0.978	-0.9858; 0.9587
1.5–2 years	11	15.76	1.59	0.163	-1.7996; 0.3037
<b>WHOQOL-BREF environment</b>					
Baseline	49	15.57	2.07		
Half year	23	14.96	1.45	0.067	-1.3431; 0.0463
1 year	16	15.34	1.42	0.702	-0.8126; 0.5473
1.5–2 years	11	15.36	0.74	0.125	-1.0256; 0.1248
<b>SF-physical</b>					
Baseline	48	29.73	9.36		
Half year	23	34.98	6.54	<b>0.015</b>	0.9095; 7.8204
1 year	16	34.97	5.40	<b>0.022</b>	0.6319; 7.7767
1.5–2 years	11	35.72	4.77	≤ <b>0.001</b>	3.0249; 9.1026
<b>SF-mental</b>					
Baseline	48	38.64	11.37		
Half year	23	43.21	6.97	0.063	-0.2088; 7.69,795
1 year	16	43.66	8.55	0.262	-2.4686; 8.7032
1.5–2 years	11	44.46	9.07	<b>0.002</b>	3.8787; 12.5862
<b>CESD</b>					
Baseline	48	8.69	7.05		
Half year	22	4.45	4.72	<b>0.004</b>	-5.9119; -1.2185
1 year	16	4.56	3.44	<b>0.004</b>	-6.6151; -1.3993
1.5–2 years	11	5.00	4.90	0.050	-6.3459; 0.0027

**Notes:** Data presented as mean. A p-value<0.05 is considered significant and is characterized by bold text.

**Abbreviations:** n, number of patients; SD, standard deviation; CI, confidence interval; WHOQOL-BREF, World Health Organization Quality Of Life -abbreviated version of the WHOQOL 100; CESD, Center for Epidemiologic Studies Depression.

only in the long-term. This study also demonstrated that critical limb ischemia patients experienced less symptoms of depression after amputation compared to baseline. Mortality rates were also analysed. The one-year mortality rate was 39% and two-year was 55%.

Reduced physical functioning and QoL characterize critical limb ischemia patients.<sup>2</sup> Therefore, one of the goals of the treatment of critical limb ischemia is to improve their physical function and QoL.<sup>2,28</sup> Primary major limb amputation, without an attempt at

**Table 5** WHOQOL-BREF compared to normal values for elderly

	n	Value	Value of general elderly population <sup>27</sup>	Mean difference	p-value	95% CI
<b>Item 1.</b> How would you rate your quality of life?						
Very poor (1) – poor (2) – neither poor nor good (3) – good (4) – very good (5)						
Baseline	49	3.33	4.06	-0.733	<b>&lt;0.001</b>	-1.01; -0.46
Half year	22	3.27		-0.787	<b>&lt;0.001</b>	-1.10; -0.48
1 year	17	3.65		-0.413	<b>0.027</b>	-0.77; -0.05
1.5–2 years	11	3.45		-0.605	<b>0.003</b>	-0.96; -0.25
<b>Item 3.</b> To what extent do you feel that physical pain prevents you from doing what you need to do?						
Not at all (1) – a little (2) – a moderate amount (3) – very much (4) – an extreme amount (5)						
Baseline	48	3.23	<b>2.46</b>	0.769	<b>&lt;0.001</b>	0.47; 1.06
Half year	21	1.86		-0.603	<b>0.022</b>	-1.11; -0.10
1 year	16	1.56		-0.898	<b>0.002</b>	-1.41; -0.38
1.5–2 years	11	1.64		-0.824	<b>0.024</b>	-1.51; -0.13
<b>Item 5.</b> How much do you enjoy life?						
Not at all (1) – a little (2) – a moderate amount (3) – very much (4) – an extreme amount (5)						
Baseline	49	3.10	3.31	-0.208	0.083	-0.44; 0.03
Half year	22	3.48		0.166	0.360	-0.20; 0.54
1 year	17	3.35		0.043	0.852	-0.44; 0.52
1.5–2 years	11	3.45		0.145	0.380	-0.21; 0.50
<b>Item 10.</b> Do you have enough energy for everyday life?						
Not at all (1) – a little (2) – moderately (3) – mostly (4) – completely (5)						
Baseline	49	3.29	4.09	-0.804	<b>&lt;0.001</b>	-1.10; -0.51
Half year	22	3.64		-0.454	<b>&lt;0.001</b>	-0.67; -0.24
1 year	17	3.41		-0.678	<b>&lt;0.001</b>	-1.00; -0.36
1.5–2 years	11	3.55		-0.545	0.052	-1.10; 0.01
<b>Item 11.</b> Are you able to accept you bodily appearance?						
Not at all (1) – a little (2) – moderately (3) – mostly (4) – completely (5)						
Baseline	48	3.77	4.36	-0.589	<b>&lt;0.001</b>	-0.89; -0.29
Half year	22	3.86		-0.496	<b>0.007</b>	-0.84; -0.15
1 year	17	3.88		-0.478	<b>&lt;0.001</b>	-0.65; -0.31
1.5–2 years	11	3.73		-0.633	<b>0.024</b>	-1.16; -0.10
<b>Item 16.</b> How satisfied are you with your ability to perform daily living activities?						
Very dissatisfied (1) – dissatisfied (2) – neither satisfied nor dissatisfied (3) – satisfied (4) – very satisfied (5)						
Baseline	49	2.88	3.81	-0.932	<b>&lt;0.001</b>	-1.24; -0.63
Half year	22	3.18		-0.628	<b>0.006</b>	-1.05; -0.20
1 year	17	3.24		-0.575	<b>0.018</b>	-1.04; -0.11
1.5–2 years	11	3.55		-0.265	0.231	-0.73; 0.20
<b>Item 18.</b> How satisfied are you with yourself?						
Very dissatisfied (1) – dissatisfied (2) – neither satisfied nor dissatisfied (3) – satisfied (4) – very satisfied (5)						
Baseline	49	3.57	3.97	-0.399	<b>0.002</b>	-0.65; -0.15
Half year	22	3.82		-0.152	0.240	-0.41; 0.11
1 year	17	3.82		-0.146	0.270	-0.42; 0.13
1.5–2 years	11	3.73		-0.243	0.116	-0.56; 0.07

(Continued)

**Table 5** (Continued).

	n	Value	Value of general elderly population <sup>27</sup>	Mean difference	p-value	95% CI
<b>Item 25.</b> How well are you able to get around?						
Very poor (1) – poor (2) – neither poor nor good (3) – good (4) – very good (5)						
Baseline	47	2.49	3.70	-1.211	<b>&lt;0.001</b>	-1.56; -0.87
Half year	22	3.32		-0.382	0.058	-0.78; 0.01
1 year	17	3.53		-0.171	0.433	-0.62; 0.28
1.5–2 years	11	3.36		-0.366	0.255	-0.96; 0.28

**Notes:** Data presented as mean; The value of the general elderly population is based on reference 27. One sample t-tests were used to compare the mean QoL estimates to corresponding estimates in the general elderly population. A p-value of <0.05 is considered significant and is characterized by bold text.

**Abbreviations:** n, number of patients; CI, confidence interval; QoL, quality of life; WHOQOL-BREF, World Health Organization Quality Of Life -abbreviated version of the WHOQOL 100.

revascularization, is not often performed because we believe that these treatment goals cannot be achieved with major limb amputation. Still, a large proportion of critical limb ischemia patients must undergo secondary major limb amputation at some point in the course of their disease because of inadequate perfusion. Our cohort shows that improved physical QoL and physical HS are possible in the long-term. Moreover, the ability to enjoy life, the amount of energy elderly patients had, and/or the satisfaction in performing daily living activities is comparable to that of the Dutch elderly. Understandably, critical limb ischemia amputee patients report less pain symptoms than their peers. Still, these patients rate a poorer QoL and poorer acceptance of bodily appearance in these specific questions of the WHOQOL-BREF questionnaire. However, their scores of the acceptance of bodily appearance did not differ from their pre-amputation scores. In terms of personalized medicine and shared-decision making, it is important to understand the changes in the several domains of the questionnaires in comparison with the normal elderly population.

Suckow et al stated that QoL assessment in critical limb ischemia patients should incorporate patient preference.<sup>15</sup> In this study, the WHOQOL-BREF questionnaire was used. Though a consensus still has to be reached on a specific QoL measure for critical limb ischemia amputee patients, the WHOQOL-BREF has the benefit of taking patients' evaluation or satisfaction with functioning into consideration.<sup>14,27</sup> Therefore, we argue that the WHOQOL-BREF is an appropriate instrument to measure QoL in critical limb ischemia amputee patients. In this study, QoL did not deteriorate after major limb amputation. Even more so, patients indicated they were

significantly more satisfied with their physical QoL after amputation compared with before amputation.

Other questionnaires, such as the SF-36, lack discriminatory power in critical limb ischemia patients characterized by their many comorbidities.<sup>15,29,30</sup> Since the SF-12 is an abbreviated version of the SF-36; our results of HS improvement, after major limb amputation, should be interpreted with care. Still, the scores on the physical and mental HS scale did not deteriorate after major limb amputation. These results are in line with the amputee placebo group of Peeters et al in their study investigating the effect on HS of bone marrow derived mononuclear cell administration in critical limb ischemia patients without treatment options.<sup>31</sup>

The prevalence of depression in PAD patients has a range between 3% and 48%.<sup>32</sup> Arya et al and McDermott et al stated that depression in PAD patients leads to a significantly higher risk of mortality.<sup>16,33</sup> Moreover, Arya et al described an increased amputation rate in PAD patients with symptoms of depression.<sup>16</sup> A review on depression in amputees, from varying etiologies, concluded that depression rates are relatively high up to 2 years after major limb amputation.<sup>34</sup> However, little is known about depression after major limb amputation due to critical limb ischemia in the elderly alone.<sup>35</sup> Our study demonstrated that critical limb ischemia patients experienced less symptoms of depression after major limb amputation. A possible explanation for the decrease in scores of symptoms of depression can be the relief of ischemic rest pain in the limb after major limb amputation in the elderly critical limb ischemia patients. So, from a mood-disorder point of view, improved outcome is possible with major limb amputation. Therefore, screening for symptoms of

depression is important to complement the shared-decision making process in elderly critical limb ischemia patients.

In patients undergoing major limb amputation, from any cause, mortality rates are extremely high. The 30-day mortality rates and the in-hospital mortality rates range between 4% and 22%.<sup>5</sup> After 1 year, mortality rates in critical limb ischemia patients are even higher; up to 44% in patients aged 70 or older.<sup>7,36–39</sup> Within 2 years' time, 1 in 2 patients will have deceased after major limb amputation.<sup>7,38,39</sup> Our results are in line with these previously mentioned studies. The 30-day mortality rate was 16%, one-year was 39% and two-year was 55%. These high mortality rates raise the question of what outcome is more important to achieve after major limb amputation. Along this line, one should consider patients who may benefit from having an earlier major limb amputation. Shared-decision making concerning this topic is important, since each patient may value his/her limb salvage differently.

Clearly, this study has limitations. First, the sample size of critical limb ischemia amputee patients decreases over time. Due to high mortality rates in this particular patient population, the sample size can be considered fairly large for a two-center study and also compared to other studies. However, attrition due to mortality could have biased our conclusions. Secondly, symptoms of depression were measured by self-report questionnaires. Self-report questionnaires are not yet part of standard care. The gold standard in diagnosing depression is the use of diagnostic interviews.<sup>40,41</sup> However, if one wants to assess symptoms of depression quickly in routine care, the CES-D questionnaire is a frequently used and accurate instrument in elderly patients.<sup>42</sup> Third, because there was no control group to compare the amputees to, any changes in QoL, HS and depression following amputation can be confounded by other factors not related to the intervention, such as spontaneous recovery.

## Conclusion

Elderly critical limb ischemia amputee patients are a fragile population with high short and long-term mortality rates. In this study, we concluded that QoL and HS did not diminish after major limb amputation, neither in the short-term or the long-term. Moreover, our results show that major limb amputation in the elderly critical limb ischemia patients in the long term gives an acceptable QoL, which, in some aspects, is comparable to the QoL of their peers. Individual treatment goal setting plays an important role when undergoing hospital care, especially in elderly

patients. In order to accomplish a good shared-decision making process that does not delay the timing of major limb amputation, patients and family should not only be informed about the mortality rates but also about the fact that QoL and HS does not seem to diminish in critical limb ischemia amputees, aged 70 and older, in the long-term.

## Disclosure

The authors report no conflicts of interest in this work.

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