Statistical or Clinical Improvement? Determining the Minimally Important Difference for the Vascular Quality of Life Questionnaire in Patients with Critical Limb Ischemia CME

F.A. Frans [a,b,*], P.T. Nieuwkerk [c], R. Met [a], S. Bipat [b], D.A. Legemate [a], J.A. Reekers [b], M.J.W. Koelemay [a]

[a] Department of Vascular Surgery, Academic Medical Center, Amsterdam, The Netherlands
[b] Department of Radiology, Academic Medical Center, Amsterdam, The Netherlands
[c] Department of Medical Psychology, Academic Medical Center, Amsterdam, The Netherlands

WHAT THIS PAPER ADDS

Although patient-reported outcome measures are frequently recorded in patients with peripheral arterial disease (PAD) to determine the statistical significance of change in quality of life as a measure of effectiveness of treatment, the interpretation of the clinical relevance of change may be difficult. This is the first study to illustrate the concept of minimally important difference to define clinically important changes rather than statistically significant changes in PAD patients.

Objective: Interpreting whether changes in quality of life (Qol) in patients with peripheral arterial disease (PAD) are not only statistically significant but also clinically relevant, may be difficult. This study introduces the concept of the minimally important difference (MID) to vascular surgeons using Qol outcomes of patients treated for chronic critical limb ischemia (CLI).

Methods: The Vascular Quality of Life (VascuQol) questionnaire was recorded at baseline before treatment and after 6 months follow-up in consecutive patients with CLI treated between May 2007 and May 2010. Statistical significance of change in VascuQol score was tested with the Wilcoxon Signed Rank test. The MID for the VascuQol score was determined using a clinical anchor-based method and a distribution-based method.

Results: A total of 127 patients with CLI completed the VascuQol after 6 months. The VascuQol sum scores improved from 3.0 (range 1.1–5.9) at baseline to 4.0 (range 1.2–6.7) at 6 months ($p < .001$). The MID on the VascuQol sumscore indicating a clinically important change determined with the anchor-based method was 0.36, and with the distribution-based method was 0.48. On an individual level, depending on the method of determining the MID, this resulted in 60% to 68% of the patients with an important benefit.

Conclusions: Expression of changes in Qol by means of the MID provides better insight into clinically important changes than statistical significance.

Article history: Received 7 June 2013, Accepted 8 October 2013, Available online 22 October 2013

Keywords: Quality of life, Critical limb ischemia

INTRODUCTION

Traditionally, the effectiveness of therapies in patients with peripheral arterial disease is expressed in easy to measure "hard endpoints" such as (bypass) patency or limb salvage. Yet, the level of functioning or quality of life may matter more to the patient than the patency of a bypass. This has been recognized by the vascular surgery community and has resulted in an increasing interest in patient-reported outcomes (PRO) in research.[1–3] The most commonly used instruments in patients with peripheral arterial disease (PAD) include generic quality of life (Qol) questionnaires, such as the Short Form-36 (SF-36) and disease specific Qol questionnaires, such as the Vascular Quality of Life questionnaire (VascuQol).[4–6] Both instruments rate the patient's quality of life on a numerical scale, and differences in scores can be used to evaluate the effectiveness of therapies. The interpretation of scores on these questionnaires is hampered by the lack of a definition as to what amount of change or difference in scores constitutes a clinically meaningful change or difference. For example, is a statistically significant mean change of 0.44 from the baseline score sufficient for an individual patient?

The concept of the minimally important difference (MID) was developed to better express clinically important benefit or deterioration rather than just statistically significant differences or changes in PRO scores.[7] The MID can be

CME To access continuing medical education questions on this paper, please go to www.vascularedu cation.com and click on 'CME'

* Corresponding author. F.A. Frans, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
E-mail address: francelinefrans@gmail.com (F.A. Frans).

1078-5884/$ – see front matter

http://dx.doi.org/10.1016/j.ejvs.2013.10.012

thought of as the smallest change in an outcome measure that is important to patients. Approaches to estimate the MID have been classified as either anchor-based or distribution-based.[8,9] Anchor-based methods compare Qol scores with another measurement, such as a patient rated global change question, and distribution-based methods build on the variability of the Qol scores.

In this paper we want to introduce the concept of the MID to vascular surgeons using Qol outcomes of patients treated for chronic critical limb ischemia (CLI) as an example by applying anchor-based and distribution-based approaches.

MATERIAL AND METHODS

Study population

Between May 2007 and May 2010 we conducted a prospective observational cohort study in which we included all consecutive patients with chronic CLI, who visited our vascular surgery department, and gave written informed consent to participate. Chronic CLI was defined as Fontaine stage III or IV with symptoms present for more than 2 weeks. Patients with insufficient knowledge of the Dutch language, an estimated life expectancy of less than 6 months or unable to give informed consent were excluded. The study was approved by the local medical ethical committee.

Treatment

Patients received treatment as agreed with their vascular surgeon independent of the study. Endovascular revascularization when possible is the first line treatment in our institution. Patients were treated with revascularization (endovascular or surgical), primary major amputation, or conservative treatment. Endovascular revascularization included both percutaneous transluminal angioplasty (PTA) and percutaneous subintimal angioplasty (SA), with or without stent placement. Surgical revascularization included both bypass surgery and endarterectomy. Assessment of patency, limb salvage, or comparison of outcomes between endovascular or surgical revascularization was not the aim of this study.

Assessments

History. At baseline before treatment we recorded patient demographics (sex, age, body mass index [BMI]), risk factors for atherosclerosis (diabetes mellitus, hypertension, smoking, renal failure, hypercholesterolemia, history of coronary heart disease, history of stroke, family history of cardiovascular disease, history of vascular interventions [endovascular and surgical]), and major contralateral amputation.

VascuQol. All patients completed the disease-specific VascuQol questionnaire at baseline before treatment and again at 6 months follow-up. The VascuQol is a sumscore-based instrument and consists of 25 items on five domains, that is Pain (4 items), Activity (8), Emotional (7), Symptoms (4), and Social (2). Each item is rated on a seven point response scale, with a score of one being the worst and a score of seven the best possible. The total average sumscore is the sum of all 25 item scores divided by 25. For each separate domain an average score can be calculated (sum of all items of one domain divided by the number of items of that domain). So, both the overall score and the scores per domain range from one to seven. The VascuQol has shown to be a reliable and valid instrument for assessment of Qol in patients with PAD.[4] The VascuQol was sent by postal mail and completed by the patients at home.

Analysis of treatment effect on quality of life

Traditional approach. Differences between VascuQol scores at baseline and at 6 months were assessed using a paired Student *t* test (normally distributed data) or the Wilcoxon Signed Ranks test (non-normally distributed data) where appropriate. A p value $<.05$ indicated statistical significance.

Minimally important difference. It is currently recommended that estimation of a MID for a specific PRO instrument should be based on multiple approaches.[10]

Anchor-based approach. The anchor-based approach requires the use of an independent, objective criterion to determine a threshold value for the MID, such as a clinical measure or a patient-rated global change question. This can be done, for example, by asking the patient whether the clinical status has deteriorated, is unchanged, or has improved. There are several approaches to using a clinical anchor to determine the MID. One method is to define the MID as the average change in score between patients rating themselves as improved minus the average change in patients rating their status as unchanged. In another approach the MID is defined as the average change in patients who improve. A third method to define the MID is to calculate the 95% confidence interval (CI) of the average change in PRO in patients who rate themselves as unchanged. The upper and lower limits of the 95% CI is the MID.[7,8]

In our study, we used the first approach by relating the average VascuQol score changes to the change in Fontaine classification as an anchor to estimate the MID.[11] The change in Fontaine classification was defined according to the change in patient reported symptoms of PAD at the 6-month follow-up visit. The change in Fontaine classification was rated by one of the investigators (FAF or RM) at the 6-month follow-up visit on a four point scale (much improved – improved – unchanged – worse) (Appendix I). According to Revicki and Cohen, the MID should be based on a patient-based or clinical anchor that has a correlation $\geq$0.30 with the PRO instrument.[11,12] Therefore correlation coefficients (Pearson or Spearman's Rank when appropriate) were calculated between the change in VascuQol sumscore and the change in Fontaine classification between baseline and 6 months follow-up.

First, for each category (much improved – improved – unchanged – worse) the mean change in VascuQol sumscore was calculated. Then the MID for improvement and the MID for deterioration was calculated as the difference between the mean change in VascuQol sumscore of the improved or