The Effect of Peripheral Percutaneous Transluminal Angioplasty on Quality of Life in Patients with Intermittent Claudication

K. Cassar¹, P. Bachoo² and J. Brittenden¹

¹Department of Vascular Surgery, University of Aberdeen and ²Vascular Unit, Aberdeen Royal Infirmary, Foresterhill, Aberdeen, U.K.

Background and Objective: intermittent claudication is associated with a significant reduction in quality of life. Treatment of claudicants aims to reduce mortality from cardio- and cerebro-vascular events and to improve quality of life. Quality of life assessment should be used to guide and evaluate treatment in this group of patients. Peripheral percutaneous transluminal angioplasty (PTA) is now widely used in the treatment of intermittent claudication. The aim of this review is to examine the effect of PTA on quality of life (QOL) in patients with intermittent claudication.

Methods: a review was conducted of prospective clinical trials assessing the effect of peripheral PTA on QOL. Publications were retrieved by searching Medline and PreMedline, EMBASE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of systematic reviews, AMED and CINAHL. The reference lists of the relevant publications were also searched.

Results: seven prospective studies (10 publications) on the effect of PTA on QOL in claudicants were identified. Several different questionnaires were used to measure quality of life (Nottingham Health Profile, SF-36, EuroQol) none of which were disease specific. All the studies showed some improvement in QOL after PTA at follow-up periods of between 6 weeks and 24 months, except for one which showed some improvement at 6 months but not at 24 months.

Conclusions: despite the fact that studies on the effect of PTA on QOL in claudicants have used generic QOL questionnaires which are relatively insensitive, the findings suggest that PTA may result in some improvement in QOL in these patients, although level I evidence to support this is lacking. The availability of disease-specific questionnaires should enable a more accurate assessment of PTA on QOL in these patients.

Key Words: Angioplasty; Intermittent claudication; Quality of life.
been shown to exist between these modalities.\textsuperscript{18} The Trans-Atlantic Inter-Society Consensus (TASC) stated that if QOL could be accurately assessed, then it should be the ideal primary endpoint.\textsuperscript{19} To aid the decision-making process, information should be available not only on the degree of impairment in quality of life but also on the expected improvement in quality of life obtained by different treatment options.

The aim of this review is to examine the effect of PTA on quality of life in patients with intermittent claudication.

Methods

The Medline and PreMedline database from 1966 to 2002 was searched using the keywords “intermittent claudication”, “angioplasty” and “quality of life”, with the Boolean operator “and”. The search was restricted to titles and abstracts. Criteria for inclusion of studies in this systematic review were prospective studies of the effect of PTA on quality of life (QOL) in patients with intermittent claudication. Further searches were performed using the same keywords in EMBASE (1980–2003), the Cochrane Central Register of Controlled Trials, the Cochrane Database of systematic reviews, AMED (Allied and Complementary Medicine: 1985–2003), and CINAHL (1982–2003). References from the relevant articles were also searched. When more than one article was available from a single study, an attempt was made to extract the information required from all relevant publications.

Studies investigating the effect of PTA on QOL

Seven prospective studies investigating the effect of PTA on QOL in patients with intermittent claudication were identified,\textsuperscript{20–29} three of which reported twice at different follow-up intervals\textsuperscript{21–26} giving a total of 10 publications (Table 1).

Randomised controlled trials

Of the seven studies, two were randomised controlled trials\textsuperscript{20–22} although only one has compared PTA to conservative treatment.\textsuperscript{21,22} Whyman and colleagues reported their results of a randomised controlled trial of PTA for intermittent claudication at 6 months\textsuperscript{21} and 2 years\textsuperscript{22} post-PTA. The patients in the PTA group received the same medical treatment (low dose aspirin plus advice on smoking and exercise) as the conservative treatment group besides their endovascular procedure. None of the patients took part in a supervised exercise programme. A modified Nottingham Health Profile (NHP)\textsuperscript{30} was administered to all patients at baseline, at 3, 6 and 24 months’ follow-up. The NHP enquires about six modalities of quality of life: pain, mobility, sleep, emotion, energy and isolation. Other outcome measures such as treadmill exercise test, ankle-brachial pressure index, and Duplex ultrasound were also measured in this study.

Only 62 patients out of 600 claudicants assessed were found to have lesions suitable for angioplasty. Thirty were randomised to PTA and 32 to the control group. This was a mixed group with either femoral stenoses, femoral occlusions or iliac stenoses. Hunt and colleagues,\textsuperscript{30} who developed the NHP, recommended that the weights for each item are transformed to yield scores from 0 to 100, but the investigators in this study used a simpler scoring system which only counts the number of affirmative responses in each section. There were no differences at baseline but at 6 months the PTA group had a lower pain score than the control group. There were no identifiable differences however between the two groups in the other five quality of life modalities. At 2 year follow up there was no difference between the two groups in any of the six quality of life modalities leading the investigators to conclude that PTA did not result in a significant improvement in QOL compared to controls. These findings imply that the initial improvement in QOL seen with PTA in the short-term is not maintained.

These findings however are in conflict with those of the Dutch Iliac Stent Trial Study Group.\textsuperscript{15} In a multicentre randomised controlled trial exploring the QOL in patients with iliac disease undergoing primary stent placement or primary angioplasty followed by selective stent placement, Bosch and colleagues showed that at 2 years both forms of treatment resulted in a significant improvement in QOL compared to baseline values. RAND 36-Item Health Survey, which is equivalent to the Medical Outcomes Study Short Form 36, was used in this study which included 254 patients with iliac stenoses or occlusions. The RAND 36 includes eight health dimensions: physical functioning, physical role functioning, emotional role functioning, social functioning, bodily pain, general health perception, mental health and vitality. For each dimension responses to items are summed and scores are converted to a 0 to 100 scale. Euro-Qol-5D, which is a generic utility measurement instrument, was also used. The EuroQol measures five dimensions of health: mobility, self care, usual activities, pain/discomfort and anxiety/depression.\textsuperscript{31} At 2 years the
<table>
<thead>
<tr>
<th>Author/Year</th>
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<tr>
<td>Whyman et al., 1996&lt;sup&gt;21&lt;/sup&gt;</td>
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<td>Femoral/iliac</td>
<td>30 (32 controls)</td>
<td>NHP</td>
<td>6</td>
<td>Improvement in QOL</td>
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<tr>
<td>Whyman et al., 1997&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Randomised controlled trial</td>
<td>Femoral/iliac</td>
<td>30 (32 controls)</td>
<td>NHP</td>
<td>24</td>
<td>No difference in QOL from baseline</td>
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<tr>
<td>Bosch et al., 1999&lt;sup&gt;23&lt;/sup&gt;</td>
<td>Randomised controlled trial</td>
<td>Iliac</td>
<td>254</td>
<td>RAND-36, EuroQol</td>
<td>24</td>
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<td>Currie et al., 1995&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Prospective observational</td>
<td>Iliac/common femoral/superficial femoral/popliteal/mixed</td>
<td>74</td>
<td>SF-36</td>
<td>3</td>
<td>Improvement in QOL</td>
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<td>Cook et al., 1996&lt;sup&gt;25&lt;/sup&gt;</td>
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<td>Cook et al., 1997&lt;sup&gt;26&lt;/sup&gt;</td>
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<td>12</td>
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<td>Pell et al., 1997&lt;sup&gt;27&lt;/sup&gt;</td>
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<td>Chetter et al., 1998&lt;sup&gt;28&lt;/sup&gt;</td>
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<td>117</td>
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<td>Chetter et al., 1999&lt;sup&gt;29&lt;/sup&gt;</td>
<td>Prospective observational</td>
<td>Superficial femoral/iliac/combined</td>
<td>108</td>
<td>SF-36, EuroQol</td>
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<td>Improvement in QOL</td>
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<td>Klevsgard et al., 2000&lt;sup&gt;30&lt;/sup&gt;</td>
<td>Prospective observational</td>
<td>?</td>
<td>42</td>
<td>NHP</td>
<td>6</td>
<td>Improvement in QOL</td>
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SF-36 = The Medical Outcomes Study Short Form-36; NHP = Nottingham Health Profile; RAND-36 = Research and Development Medical Outcomes Study Short Form-36; ? = Site of Disease not specified.
scores of all RAND-36 dimensions were significantly higher than before treatment. Unfortunately both groups randomised received some type of treatment and there was no control group that was treated conservatively.

Prospective observational studies

The other five studies, reported between 1995 and 2000, were all prospective observational studies with sample size varying from 19 to 117. Chetter and colleagues reported on a mixed group of 117 patients with either femoral, iliac or combined iliofemoral disease undergoing PTA. Short form 36 (SF36) and EuroQol were used to measure QOL at baseline, and at 1, 3, 6 and 12 months following intervention. SF-36, like RAND-36, is a generic questionnaire containing 36 questions covering the same eight health domains. For each dimension, question scores are coded, summed and transformed onto a scale from 0 (worst possible score) to 100 (best possible score). The U.K. version of the SF36 was used in this study. Chetter and colleagues found that PTA resulted in an immediate and lasting improvement in the QOL of claudicants. Unilateral claudicants undergoing PTA to a solitary iliac lesion demonstrated the most marked improvement in QOL, and at 12 months post PTA their QOL approached that of a healthy age-matched population. On the other hand iliac PTA above a significantly disease SFA did not result in any significant improvement in QOL.

Currie and colleagues also used the SF-36 to study the effect of PTA on QOL in 74 patients with femoral, iliac, popliteal or mixed disease. They found that physical function, pain scores, general health perception as well as mental health improved significantly in this group of patients group at 3 months after PTA. In another study, 28 patients with intermittent claudication treated with PTA were found to have a significant improvement in their quality of life 6 months after PTA. No information is available in the paper as to the site or severity of disease in the patients with intermittent claudication treated with angioplasty. The NHP was used to evaluate quality of life in this study. The QOL measure after PTA for particular domains such as sleep, social isolation, paid employment and family relationships approached that of 102 healthy controls from a local population study. Improvement was also seen in the QOL measure for pain, emotional reactions, physical mobility, energy, housework, hobbies, holidays, sex and social life but this did not reach the same level as in the healthy controls.

Cook and colleagues followed up 29 patients with intermittent claudication who underwent successful PTA of the femoropopliteal or iliac arteries for 6 weeks, and 24 of these for 1 year. EuroQol scores were used to assess quality of life at baseline and at 6 weeks and 1 year after PTA. Following successful PTA the EuroQol score, perceived health state, mobility, usual activities, pain and discomfort and mental state were all significantly improved. These improvements were maintained at 1 year although perceived health state deteriorated slightly.

Pell and colleagues used the SF-36 questionnaire to assess QOL in 201 claudicants. 19 underwent PTA, 19 underwent surgical reconstruction and the rest were managed conservatively. At 6 months patients who had undergone PTA or arterial reconstruction showed significant improvements in quality of life, while those treated conservatively showed deterioration in all aspects of quality of life.

Discussion

All the seven studies reporting on the effect of PTA on QOL in claudicants found an improvement in QOL that was observed soon after PTA and that was maintained for up to 2 years, except for the study by Whyman and colleagues who found that the initial improvement in QOL at six months was not maintained at 2 years. No randomised controlled trial has been conducted that follows patients' QOL for longer periods of time. This is unfortunate as it is essential to know the longterm outcome especially because of the natural history of intermittent claudication.

The low risk of amputation in patients with intermittent claudication combined with the significant incidence of coronary artery disease has led to recommendations to treat these patients conservatively with regards to their lower limb symptoms. However this ignores the considerable impairment in quality of life associated with the condition. Patients with intermittent claudication have a quality of life comparable to patients with osteoarthritis or rheumatoid arthritis affecting the hip or knee joint or patients with coronary heart disease. Clinicians are poor at assessing the impact of disease on patients' perception of quality of life particularly in patients with intermittent claudication and it is therefore important for QOL measures to be used not only in the research setting but also in the clinical setting to aid the decision-making process. In assessing outcome QOL should also be considered besides the traditional efficacy/safety model. Information on the improvement in QOL of different treatment options should be
available to clinicians in order to allow them to inform and advise patients effectively.

Medical outcomes measured from the patients’ perspective should have a more important role in determining who should receive therapy than more traditional outcome measures such as ankle-brachial pressure indices, treadmill walking distance, and patency rates. Brevetti and colleagues have argued that QOL evaluation appears to be the most appropriate tool to evaluate the net result of treatment in patients with intermittent claudication. This concurs with the recommendation of the Trans-Atlantic Inter-Society Consensus statement that QOL is the ideal primary endpoint in intermittent claudication especially as there is poor correlation between traditional outcome measures such as exercise capacity assessed by treadmill or improvement in ankle pressure with quality of life.

However, in order to assess QOL, a sensitive and reliable instrument is required. In the studies reported above various instruments have been used to assess QOL but all of these were generic questionnaires such as the SF-36, RAND-36, and the NHP. Three of the studies have used EuroQOL which is a utility measurement instrument. The major disadvantage of using generic health questionnaires is that these tend to be less sensitive and often require large sample sizes to demonstrate statistically significant differences due to the large standard deviations of health profiles. The NHP, used by Whyman et al. in the only RCT comparing PTA with conservative treatment, is particularly insensitive. The authors themselves conceded that in patients with intermittent claudication “patients’ quality of life has to be markedly impaired before a difference can be established”. A simplified method for scoring the questionnaire was used rather than the actual scoring recommended by the developers of the NHP. Besides, their sample size was small (30 PTA vs 32 controls). The combination of an inappropriate health profile questionnaire and a small sample size casts doubt on their conclusion that there is no improvement in QOL in patients with IC after PTA at 2 years. Indeed their findings are not supported by any of the other six studies on the effect of PTA on QOL. It might be argued that the lack of QOL improvement at 2 years reflects the durability of PTA. However, Bosch et al. did show improved QOL at 2 years after iliac PTA and/or stenting.

The SF-36, another generic questionnaire, was found to be more valid and reliable than the NHP for use in the vascular setting. Four of the seven studies, comprising a total of 464 patients, used SF-36 or a modification of it (RAND-36) to assess quality of life and all of these found an improvement in QOL after PTA.

Disease specific instruments would have the added advantage of demonstrating more responsiveness between patients depending on disease severity, or within patients before and after therapy than the generic questionnaires. For this reason various attempts have been made to develop a disease-specific questionnaire for use in intermittent claudication. The Walking Impairment Questionnaire (WIQ) was one of the first disease-specific health profile instruments to be developed for peripheral vascular disease. This 15-item questionnaire examines four dimensions of peripheral vascular disease: claudication-specific pain, walking speed, walking distance and stair climbing. The VascuQol is another questionnaire designed to measure quality of life in patients with lower limb ischaemia but its ability to detect small but important changes in QOL impairment in claudicants after treatment is questionable as it is not specific to claudication. Silvestro and colleagues have developed a disease-specific questionnaire for use in intermittent claudication in Italian and another questionnaire, the CLAU-S has undergone validation in English, French, German and Flemish. More recently Chong and colleagues have developed the Intermittent Claudication Questionnaire (ICQ) which has been shown to be a practical, reliable, valid and responsive measure of patient health-related quality of life in intermittent claudication. This questionnaire was initially piloted in 20 patients and then administered to 124 stable claudicants. The instrument is scored on a scale from 0 to 100, where 0 is the best possible and 100 the worst possible health state. Responsiveness of the questionnaire to changes in health was assessed in 60 patients treated conservatively and 40 treated with angioplasty. The patients undergoing PTA showed a significant improvement in their ICQ score at 3 months while those treated conservatively showed no improvement. The availability of sensitive disease-specific questionnaires should make the assessment of QOL in this group of patients more accurate.

Patency results after angioplasty are better for iliac lesions rather than femoropopliteal lesions. This suggests that improvement in QOL may also be different when different sites are treated. Unfortunately five of the seven studies had patients with different sites and or severity of disease treated and in one study no information is given as to the site or severity of the disease. In future, studies on the effect of angioplasty on QOL should analyse results from patients with different sites of disease separately.

Unfortunately, despite the fact that PTA has been used for almost 40 years and despite its widespread
use in the treatment of intermittent claudication,
there is still a lack of level I evidence to show that
PTA in IC results in significantly better QOL than
conservative or exercise treatment. This is particularly
important given the natural history of intermittent
cladication which may result in improvement in QOL
without endovascular intervention. Disease-specific
questionnaires are ideally suited to demonstrate the
value of different treatment options for patients with
intermittent claudication and should be used in ran-
domised controlled trials to establish the treatment of
choice in intermittent claudication, thus guiding
appropriated resource allocation. The weight of the
evidence available to date however suggests that
PTA in claudicsants is associated with a significant
improvement in quality of life which appears to be
maintained at least until 24 months after the procedure.

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Accepted 6 March 2003