Eur J Vasc Endovasc Surg (2018) ■, 1–8

Critical Appraisal of the Quality of Evidence Addressing the Diagnosis, Prognosis, and Management of Peripheral Artery Disease in Patients With Diabetic Foot Ulceration

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WHAT THIS PAPER ADDS

This study uses a newly devised disease specific research appraisal tool to critically appraise the quality of evidence addressing the diagnosis, prognosis, and management of peripheral artery disease in patients with diabetic foot ulceration. To date, no study has examined the utility or validity of this tool in assessing the current quality of published work on diabetic foot ulcers. Although this analysis reveals an improvement over time in the overall calibre of studies, the present quality remains poor. This study highlights areas the research community needs to adopt in future reports to improve reporting standards in the diabetic foot literature.

Aims: There is a paucity of robust evidence on prevention and management of diabetic foot ulcers (DFUs) to inform treatment. This study appraises the current quality of the evidence addressing diagnosis, prognosis, and management of peripheral artery disease (PAD) in patients with DFUs using a newly devised 21 point scoring (TOPS) disease specific research appraisal tool published by the International Working Group on the Diabetic Foot (IWGDF) and European Wound Management Association.

Methods: The 2015 IWGDF guidance on diagnosis, prognosis, and management of PAD in patients with DFUs was used to identify studies pertaining to prevention and management. Two reviewers assessed these articles against TOPS, which examines study design, conduct, and outcome reporting.

Results: The overall median score was 8 (3–12/21). The median design total score was 2 (0–4/11). The median conduct total score was 2 (1–4/6). The median outcomes total score was 3 (1–4/4). There was improvement with time in overall total (Spearman Rho 0.39, $p = .0005$), design total (0.35, $p = .0023$), and outcomes total (0.35, $p = .0002$), but not conduct total (−0.03, $p = .8132$) scores.

Conclusions: Although this analysis revealed an improvement over time in the overall calibre of studies, the present quality remains poor on which to inform the diagnosis, management, and prognosis of patients with PAD and diabetic foot ulceration.

Article history: Received 13 December 2017, Accepted 10 May 2018, Available online XXX

Keywords: Peripheral artery disease, Diabetes, Foot, Ulceration, Evidence, Reporting

INTRODUCTION

The global prevalence of diabetes mellitus is set to rise to approximately 600 million by 2035, with foot ulcers complicating the disease being burdensome for patients and costly for society.[1] Current European Society of Cardiology guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery provide a weighted and graded class of both recommendation and level of evidence for each management option according to predefined scales.[2] Despite best efforts to present and evaluate the available evidence, there is a paucity of robust evidence on prevention and management of diabetic foot ulcers (DFUs) to inform treatment, leading to calls for higher quality research from recently published systematic reviews.[3–8] Consequently, in 2016 a 21 point scoring checklist (TOPS) was published by the International Working Group on the Diabetic Foot (IWGDF) and the European Wound Management Association both highlighting and addressing shortcomings of existing appraisal methodologies. This integrates the exigencies of diabetic foot reporting standards into a single disease specific research appraisal tool.[9] TOPS summarises details for inclusion within study design, conduct, and reporting of publications addressing

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https://doi.org/10.1016/j.ejvs.2018.05.009

Please cite this article in press as: Ali SR, et al., Critical Appraisal of the Quality of Evidence Addressing the Diagnosis, Prognosis, and Management of Peripheral Artery Disease in Patients With Diabetic Foot Ulceration, European Journal of Vascular and Endovascular Surgery (2018), https://doi.org/10.1016/j.ejvs.2018.05.009

prevention and management of DFUs. The goal is, of course, that the research community adopts the specified criteria into future reports to improve reporting standards. No studies have examined the utility or validity of TOPS in assessing the current quality of published work on DFUs.

Diabetes is implicated in the development of both peripheral arterial disease (PAD) and foot ulceration. The aetiology of foot ulceration in patients with diabetes is multimodal with peripheral neuropathy, PAD, and immunosuppression all implicated. While the prevalence of PAD is 10—26% in the general population, with diabetes it can sometimes increase to over 50% in those with associated foot ulceration.[10—12] PAD in the latter is associated with both delayed healing and amputation.[13]

This study aims to appraise the current quality of the evidence addressing the diagnosis, prognosis, and management of PAD in patients with DFUs using TOPS.

METHODOLOGY

The 2016 IWGDF guidance on diagnosis, prognosis, and management of PAD was used to identify studies pertaining to prevention and management of DFUs.[14] This document cites three systematic reviews.[5,6,15] All conformed to PRISMA guidance. Inclusion and exclusion criteria applied within the methodology of these reviews are shown in (Table 1).

To assess the quality of published work within these systematic reviews, TOPS was used. Study design, conduct, and outcome reporting were assessed according to TOPS, with maximum scores of 11, 6, and 4, respectively, for each domain. For non-randomised studies, it was not possible to score in some domains of TOPS because of deficiencies in the study design.

The TOPS document provides clarity on what items are considered essential to facilitate interpretation and

Table 1. Inclusion and exclusion criteria of the systematic reviews used in the study design.

Systematic review	Inclusion criteria	Exclusion criteria
Diagnosis of PAD in patients with DFUs[4]	Studies reporting separately on $\geq$ 10 patients with diabetes Studies evaluating an index test for PAD against a reference test considered appropriate including DSA, CTA, MRA, and CDUS	Patients with PAD only Studies lacking a non-diseased control group, where calculation of sensitivity and/or specificity values was not possible Studies that reported data in a fashion that did not permit the calculation of sensitivity and/or specificity values, and therefore likelihood ratios Studies of mixed cohorts of patients with and without diabetes where the proportion of patients with diabetes <80% Studies comparing two reference tests
Prognosis of PAD in patients with DFUs[15]	Studies reporting separately on $\geq$ 30 patients with diabetic foot ulceration Studies evaluating ulcerated patients only Cohort studies involving patients undergoing revascularisation when a risk ratio was reported, adjusted for revascularisation Studies evaluating outcome and those based on an index measure of PAD Studies evaluating investigations of PAD/reduced perfusion and their level of abnormality that would predict healing or major amputation	Studies evaluating the prognosis of the asymptomatic (intact) foot were excluded Studies evaluating demographic factors and their association/predictive value for outcome Studies that excluded patients with PAD or those with insufficient information on the revascularisation status of the cohort during follow up Where studies reported on mixed cohorts of patients with and without diabetes; those with a proportion of patients with diabetes of <80% were excluded Studies that reported data in a fashion that did not permit the calculation of sensitivity and specificity values, and therefore likelihood ratios Studies with unspecified or < 6 month duration of follow up
Management of PAD in patients with DFUs[16]	Studies of more than 40 patients where > 80% of the population had diabetes or when the results of at least 30 patients with diabetes were reported separately Studies reporting ulcer healing, limb salvage, major amputation, or survival as the primary outcome measures Studies in which > 80% of patients had evidence of tissue loss (defined as any lesion of the skin breaching the epithelium or ulceration or gangrene)	Studies solely reporting interventions on aortic and iliac arterial disease Studies that only had data on quality of life, on costs, and on diagnosis and prognosis of PAD that were only concerned with medical or topical therapy or on improvement of oxygen delivery Studies comparing one form of revascularisation technology with another

DSA = digital subtraction angiography; CTA = computed tomography angiography; MRA = magnetic resonance angiography; CDUS = colour Doppler ultrasound.

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