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SUPPLEMENT ARTICLE

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Effectiveness of revascularisation of the ulcerated foot in patients with diabetes and peripheral artery disease: A systematic review

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Abstract

In patients with diabetes, foot ulceration and peripheral artery disease (PAD), it is often difficult to determine whether, when and how to revascularise the affected lower extremity. The presence of PAD is a major risk factor for non-healing and yet clinical outcomes of revascularisation are not necessarily related to technical success. The International Working Group of the Diabetic Foot updated systematic review on the effectiveness of revascularisation of the ulcerated foot in patients with diabetes and PAD is comprised of 64 studies describing >13 000 patients. Amongst 60 case series and 4 non-randomised controlled studies, we summarised clinically relevant outcomes and found them to be broadly similar between patients treated with open vs endovascular therapy. Following endovascular revascularisation, the 1 year and 2 year limb salvage rates were 80% (IQR 78-82%) and 78% (IQR 75-83%), whereas open therapy was associated with rates of 85% (IQR 80-90%) at 1 year and 87% (IQR 85-88%) at 2 years, however these results

were based on a varying combination of studies and cannot therefore be interpreted as cumulative. Overall, wound healing was achieved in a median of 60% of patients (IQR 50-69%) at 1 year in those treated by endovascular or surgical therapy, and the major amputation rate of endovascular vs open therapy was 2% vs 5% at 30 days, 10% vs 9% at 1 year and 13% vs 9% at 2 years. For both strategies, overall mortality was found to be high, with 2% (1-6%) perioperative (or 30 day) mortality, rising sharply to 13% (9-23%) at 1 year, 29% (19-48%) at 2 years and 47% (39-71%) at 5 years. Both the angiosome concept (revascularisation directly to the area of tissue loss via its main feeding artery) or indirect revascularisation through collaterals, appear to be equally effective strategies for restoring perfusion. Overall, the available data do not allow us to recommend one method of revascularisation over the other and more studies are required to determine the best revascularisation approach in diabetic foot ulceration.

KEYWORDS

amputation, diabetes, diabetic foot, endovascular treatment, foot ulcer, mortality, peripheral artery disease, revascularisation, vascular surgery

1 | INTRODUCTION

Peripheral artery disease (PAD) affects up to 50% of patients with a diabetic foot ulcer (DFU)[1-3] and its presence is associated with poor outcomes. The natural history of patients with PAD and DFU is difficult to predict and is affected by more than just the severity of arterial disease. Concurrent infection increases the risk of poor outcomes even more, and other factors such as medical co-morbidities, microvascular dysfunction, poor glycaemic control and abnormal mechanical load may also contribute. While it is important to recognise and address all of these clinical abnormalities, there is evidence that early revascularisation in patients with PAD is associated with improved outcomes.[4] However, the decision whether, when and how to revascularise is not straightforward. Up to 50% of patients for whom revascularisation is not thought technically possible or reasonable due to comorbidities may heal their ulcer within a year without revascularisation[5]; conversely, amongst those who had a successful and patent revascularisation, >20% of patients underwent a major limb amputation within 12 months in one large series.[6]

The anatomical distribution of PAD is more challenging in patients with, as opposed to without, diabetes. There is a predilection for multi-level distal disease often involving multiple crural arteries, with long occlusions, poor propensity to form collaterals and a high prevalence of medial arterial calcification. All of these factors pose additional technical challenges when attempting revascularisation, either by open surgical or endovascular means. In addition, there are no major randomised trials addressing the most appropriate methods of revascularisation specifically for patients with DFU and PAD, nor are there informative subgroup analyses in general PAD trials.

The International Working Group on the Diabetic Foot (IWGDF) is a multi-disciplinary group of experts in the management of patients with DFU. The present systematic review of the effectiveness of revascularisation is an updated iteration of our previous review, launched in 2015,[7] and informs the most recent IWGDF guidance addressing the diagnosis, prognosis and management of patients with PAD and DFU, which is published separately in this journal.[8]

2 | METHODS

2.1 | Search methods

We updated our previous systematic review,[7] guided by a recent consensus document on updating systematic reviews.[9] We searched the MEDLINE and EMBASE databases for studies relating to therapies to revascularise the ulcerated foot amongst patients with diabetes, updating the previous search and therefore capturing any new records published between June 2014 and September 2018. The search string is shown in Data S1. Two reviewers independently screened the abstracts of retrieved articles to determine if they might meet the preset inclusion criteria, and a third reviewer adjudicated any conflicts. We accessed full-text articles of screened articles and assessed them for inclusion; members of the IWGDF PAD working group then extracted and verified data.

2.2 | Inclusion / exclusion criteria

To be eligible for inclusion, a study was required to meet the following criteria: (a) it reported on the outcomes of revascularisation (open or endovascular) for patients with DFU and PAD; (b) patients included had objective evidence of PAD (such as angiography);

(c) >80% of patients included had tissue loss (defined as any lesion of the skin breaching the epithelium or ulceration or gangrene); (d) it included at least 40 patients with >80% of the population diagnosed with diabetes or where the results of at least 30 patients with diabetes were reported separately; and (e) it reported on primary outcomes including ulcer healing, limb salvage, major amputation or survival.

Studies reporting only on aortoiliac disease were excluded, as the treatment of supra-inguinal disease is similar in patients with or without diabetes. Studies were excluded if they reported only on medical, pharmacological or topical therapies or if they compared different revascularisation technologies.

We only included studies published in the English language.

2.3 | Primary outcome measures and definitions

The primary outcome measures of interest included wound healing, limb salvage, major amputation and survival.

For the purpose of this systematic review, *PAD* was defined as any flow limiting atherosclerotic lesion of the arteries below the inguinal ligament. We accepted the diagnosis of *diabetes mellitus* as it was made according to the individual publication. *Tissue loss* was defined as any lesions of the skin breaching the epithelium, or the presence of ulceration or gangrene. *Early* mortality was considered within 30 days or within the period of the first hospital admission. A *major complication* was defined as any that resulted in a systemic disturbance of the patient or prolonged hospitalisation (or as defined by the individual study).

2.4 | Data extraction and quality assessment

This systematic review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[10] Two reviewers assessed studies for inclusion based on titles, then a review of the abstract, and finally upon review of the full text. The data for the evidence table were then extracted by members of the IWGDF PAD working group, confirmed by other members. Studies were assessed for methodological rigour using the Scottish Intercollegiate Guidelines Network (SIGN) guidelines.[11] Pooling of data and weighting of studies was not possible because of study heterogeneity and the generally low quality of evidence. Data was summarised for individual items as interquartile range (IQR) and median (not weighted).

Patient demographics were summarised, along with specific details of the foot lesion where available, and any reported concurrent infection. Objective assessments of perfusion were reported where available. We made no distinction amongst various endovascular techniques (eg, angioplasty, stenting, subintimal angioplasty, atherectomy), which were all referred to as *endovascular therapy*. Neither did we distinguish among methods of open revascularisation (eg, *in situ* vs reversed vein bypass graft).

3 | RESULTS

3.1 | Search results

Our updated search included articles published between June 2014 and June 2018 (Figure 1). A total of 8877 articles were screened, of which 301 articles were assessed for inclusion based on the abstract and 92 assessed for inclusion based on the full text. Ultimately, seven new studies deemed eligible were identified and, when added to those from our previous review,[7] a total of 64 studies, comprising 13 434 patients, are included in this updated systematic review. There were no randomised controlled trials, all included studies were case series (SIGN 3) that reported on bypass surgery, endovascular intervention or both techniques used in combination. Few studies provided sufficient detail on severity of PAD or baseline foot lesion characteristics, however most studies provided adequate information on patient demographics and co-morbidities. In the event that more than one study reported on patients from the same institution, we highlighted this in the evidence table, but accepted that it is likely that some patients were reported more than once. A complete evidence table with all results from included studies can be found in Data S2.

3.1.1 | PICO (patient, intervention, comparison, outcome)

What are the aims and methods of revascularisation and onward management in a person with diabetes, foot ulceration and PAD?

3.1.2 | Summary of the literature

Patient demographics and comorbidities

Amongst the 13 434 patients were included, 69% (IQRs 68-71%) were men, with a median age of 71 (69–72). As expected, there was a high prevalence of cardiovascular comorbidities, including 47% (43-55%) with coronary artery disease, 21% (18-23%) with cerebrovascular disease and 21% (20-26%) with end-stage renal disease (variably defined).

3.1.3 | Clinical outcomes

It is important to note that the quantitative interpretation of outcomes cannot be considered cumulative, as there was a discrepancy of outcome reporting between studies and studies had different duration of follow-up. The results reported for each time point are based on a variable number of studies and should not be directly compared.

3.2 | Wound healing

Only 12 studies reported wound healing as an outcome measure, using variable follow-up periods. Wound healing was achieved in a

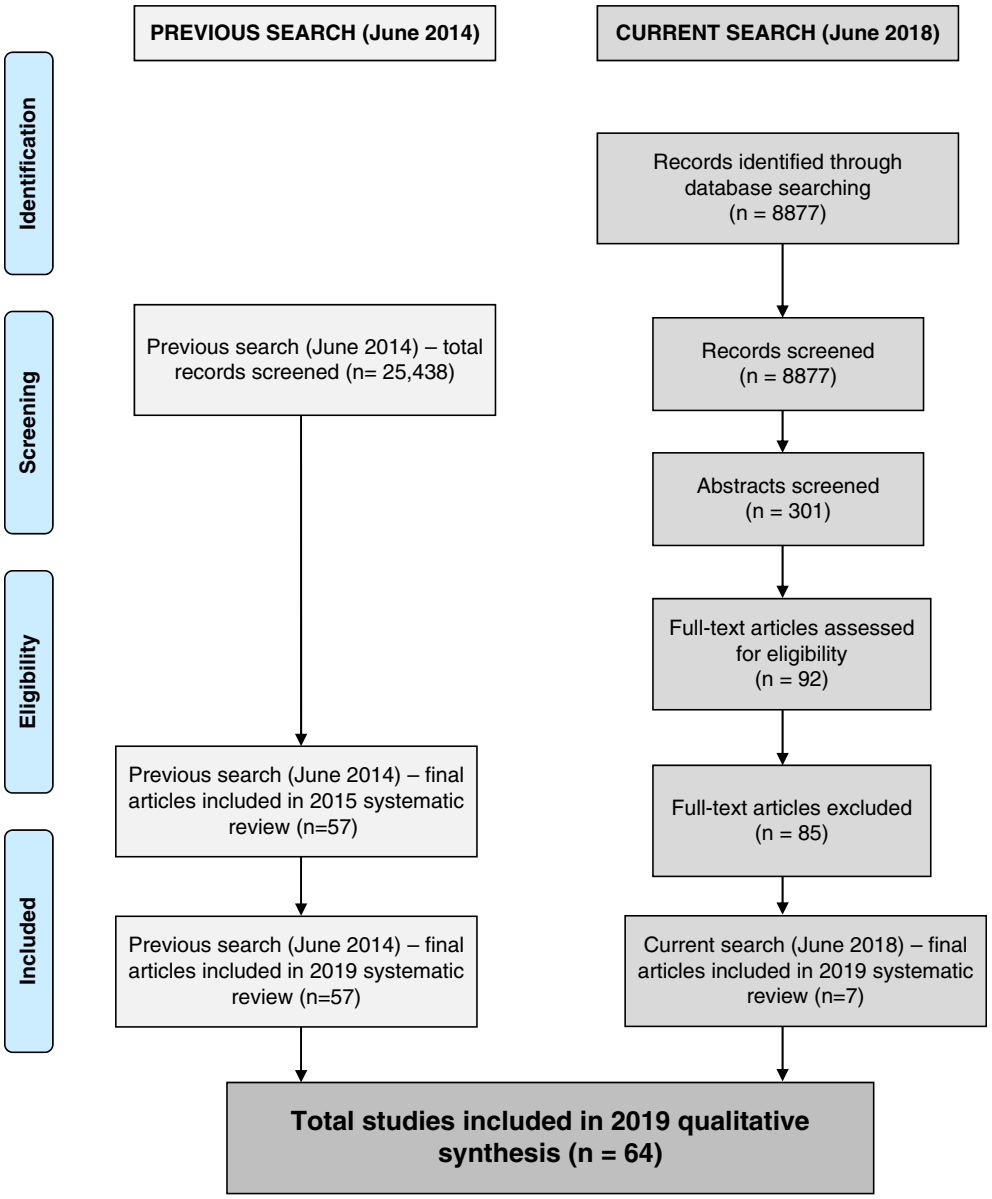

FIGURE 1 PRISMA Flow Diagram

median of 60% (50-69%) at 1 year. Of 3 studies reporting separately on endovascular outcomes, wound healing at 1 year was 75% (68-77%), while for two studies reporting on open therapy, the median wound healing at 1 year was lower (52%; 46-57%).

3.3 | Limb salvage and major amputation

Limb salvage was reported at a predefined time point by 39 studies. The overall limb salvage rates were 82% (IQR 79-89%) at 1 year (based on 28 studies), 86% (77-88%) at 2 years (based on 12 studies) and 76% (73-78%) at 5 years (based on 14 studies). Following endovascular treatment, 1 and 2 year limb salvages rates were 80% (78-82%; based on 9 studies) and 78% (75-83%; based on 5 studies), respectively. In those studies reporting limb salvage following open revascularisation (n = 25), the rates were 85% (80-90%) at 1 year (based on 19 studies) and 87% (86-89%) at 2 years (based on 7 studies).

The definition of major amputation was variable amongst the included studies but, where reported with a specified time point, the median rate of major amputations within 30 days was 4% (2-5%), which increased at 1 year to 9% (4-12%) and 11% (7-18%) at 2 years. The early (30 day) major amputation rate appeared somewhat lower for endovascular therapy when compared to open therapy (2% vs 5%) but higher at 1 year (10% vs 9%) and 2 years (13% vs 9%). However, this finding must be interpreted with great caution, due to the heterogeneity of studies and patients included and the inconsistency in reporting time points between studies.

The rates of minor amputation varied widely, with a median of 38% (IQR 23-59%). There were similar rates of minor amputation between patients undergoing open (36%, 23-57%) and endovascular (38%, 23-57%) therapies.

3.4 | Mortality and survival

Perioperative or 30 day mortality was reported in 30 studies, and was 2% (IQR 1-5%) overall. Perioperative mortality was the same following endovascular vs open revascularisation (2% vs 2%). Overall 1 year mortality was 13% (9-23%), rising to 29% (19-48%) at 2 years and 47% (39-71%) at 5 years. At 2 years, the highest mortality rates were amongst patients with ESRD (72% in one study[12]). At 5 years, amongst those in seven studies who underwent open therapy, the mortality rate was 43% (39-60%). In the single study that reported 5 year mortality following endovascular therapy it was 74%,[13] however very small numbers remained in follow up at 5 years and the validity of these findings is therefore questionable.

The five studies reporting survival as compared to mortality yielded poorer results, with a median survival of 83% (75-87%) at 1 year (four studies) and 39% (26-46%) at 5 years (four studies), which translates into mortalities of 17% and 62% at 1 and 5 years, respectively.

3.4.1 | Specific revascularisation strategies

Pedal bypass

Amongst the twelve studies that reported on pedal bypass surgery, the median 1, 2 and 5 year limb salvage rates were 86% (80-92%), 85% (68-86) and 87% (78-95%). Perioperative mortality was similar to that in the overall population at 2% (1-4%), with 1 year, 2 year and 5 year mortality rates of 14% (11-32%), 48% (32-60%) and 42% (39-45%), respectively. These outcomes are again based on a variable number of studies, with different duration of follow-up, reporting at each time point.

Infra-popliteal angioplasty

Eight studies reported exclusively on infra-popliteal angioplasty; at 1 year the median rate of wound healing was 71% (65-75%) and limb salvage was 77% (71-85%).

In a review of 448 patients (83% with diabetes) who underwent infrapopliteal angioplasty for tissue loss (86%) or rest pain (14%), there was no significant difference in major amputation rates at 1 year between single-vessel angioplasty and multiple-vessel intervention (16% vs 10%, $P = .24$).[14] Another smaller study (n = 92),[15] also comparing single vs multiple endovascular revascularisation attempts, found no difference in outcomes between the two groups. In a third study of 93 patients undergoing endovascular therapy, the presence of a complete pedal arch following the intervention was associated with increased rates of wound healing, limb salvage and survival at 1 year compared to absence of a complete pedal arch.[16]

Angiosome-directed revascularisation

Angiosome-directed revascularisation is a method of improving perfusion of an area of tissue loss directly, via its feeding artery (also called direct revascularisation, DR). This is based on the theory that the foot can be divided into three-dimensional units of tissue (angiosomes), each of which is supplied by a specific feeding artery. By targeting a feeding artery that directly supplies an area of tissue loss, the concept is that this is the best way to improve perfusion to that specific area. The more traditional "best vessel approach" can be considered non-angiosome directed or indirect revascularisation (IR), whereby the most suitable target vessel is chosen for revascularisation, regardless of its anatomical location.

The majority of literature relating to outcomes based on the angiosome concept in patients with diabetes and foot ulcers is retrospective. We identified eight such studies, all of which were retrospective case series or cohort studies and had a high risk of bias. Six studies concluded that direct revascularisation according to the angiosome concept was associated with higher rates of wound healing when compared with indirect revascularisation,[15,17-21] however only four of these studies reported higher rates of limb salvage.

In one study,[15] patients who underwent indirect revascularisation (ie, non-angiosome directed) were stratified further by the role of collaterals – those in whom pulsatile flow was restored to the affected area indirectly (ie, not targeted to the feeding artery) but by collaterals (indirect revascularisation, via collaterals; IRc) and those in whom there were no collaterals between the target artery and the affected angiosome (indirect revascularisation, no collaterals). In this series, 92 patients underwent endovascular infra-popliteal intervention (including those with concurrent supra-popliteal angioplasty), and the outcomes were similar for DR and IRc – limb salvage rates were 89% and 85% at 2 years and wound healing was 66% and 68% at 12 months. However, in those patients who underwent indirect revascularisation with no collaterals, limb salvage and wound healing rates were poor (59% and 7%, respectively).

A more recent study compared angiosome-based intervention during endovascular and open techniques in a series of 545 patients with diabetes and foot ulceration undergoing a first time infrapopliteal revascularisation.[20] The highest rates of wound healing were in patients who underwent open revascularisation classified as DR (77% healing at 1 year) and the worst rates were in those who underwent endovascular treatment classified as IR (52% healing at 1 year). Amputation rates were also highest in the IR endovascular group, but if IR was achieved via collaterals then this improved limb salvage.

3.4.2 | Significant clinical comorbidities

End-stage renal disease

In the nine studies that analysed patients with end-stage renal disease (ESRD, defined variably) separately, its presence increased perioperative mortality (4.6%, 2.6-8.8%) and high mortality over 5 years (48% and 72% at 2 years[12,22] 56% at 3 years[23] and 91% at 5 years[24]), albeit based on small study numbers. For those who did survive to 1 year, salvage rates were 70% (65-70%).

Infection

While it is a well-recognised risk factor for poor outcomes in patients with diabetes and foot ulceration, only two studies specifically

reported on outcomes in patients with diabetes, PAD and foot infection.[25,26] Both studies were retrospective case series of patients with an acutely infected ulcer. In a study of 53 patients who underwent pedal bypass,[25] 20% required minor amputation prior to bypass; however, the resulting limb salvage was excellent, at 98% at 1 year, 98% at 2 years and 95% at 3 years. In a study of 114 patients with foot infection, 38% underwent open revascularisation and the overall limb salvage for the case series was 87% at 2 years and 73% at 4 years.[26]

3.4.3 | Evidence statement

Evidence is inadequate to establish whether an endovascular, open or hybrid revascularisation technique is superior in restoring blood flow and improving prognosis in patients with diabetic foot ulceration and PAD.

3.4.4 | Quality of the evidence

Low, based on cohort studies and case series.

3.4.5 | Evidence statement

Restoration of direct blood flow to at least one of the foot arteries, preferably the artery that supplies the anatomical region of the ulcer is associated with the best outcome. Both revascularisation directly to the area of tissue loss via its main feeding artery or indirect revascularisation through collaterals, appear to be equally effective strategies for restoring perfusion.

3.4.6 | Quality of evidence

Low, based on cohort studies and case series.

4 | DISCUSSION

This systematic review is an update of the version launched in 2015[7] and, in addition to the 56 studies included previously, includes a further seven studies describing outcomes of revascularisation in patients with diabetes, PAD and foot ulceration. All of the new studies were retrospective reviews of medical care encounter databases in either single or multiple institutions across the world and had a high risk of bias, as well as significant heterogeneity in included participants as well as outcome reporting. Of particular note, none of these new studies included a control group. There was also inconsistency in reporting of some key variables such as the severity of arterial perfusion deficit, indication for revascularisation and ulcer characteristics. For these reasons, it was not possible to pool the data or conduct a meta-analysis.

One of the main obstacles in revascularisation of patients with diabetes is the often complex, distal pattern of disease, which poses a challenge for performing both endovascular and open therapy. Crural vessel angioplasty and distal bypasses are often more time-consuming and technically demanding than revascularisation with a more proximal outflow target vessel, and thus require additional expertise. The presence of multi-level disease, highly calcified lesions and paucity of collaterals each further contributes to this challenge. Overall, however, the current rates of reported limb salvage presented here (82% at 1 year and up to 78% at 5 years) are greatly improved on those reported by two studies documenting the natural history of patients with diabetes and foot ulcers for whom revascularisation was deemed unsuitable (50-54% at 1 year).[5,27] Even amongst patients included in this review who underwent pedal bypass or crural angioplasty, limb salvage rates were reported as 86% and 77% at 1 year.

Because there are no randomised trials comparing methods of revascularisation specific to patients with diabetic foot disease, it is not possible to determine which method of revascularisation is more effective. Results from the bypass vs angioplasty in severe ischaemia of the leg (BASIL) trial, the only completed RCT comparing open or endovascular treatment of severe limb ischaemia, published in 2005,[28] cannot be directly extrapolated to patients with diabetes and foot ulceration, as only around 40% of the patients in BASIL had diabetes and the main pattern of disease was femoropopliteal. Moreover, there has been substantial advancement of endovascular technologies that were not captured by the BASIL trial. A more recent sub-group analysis of the BASIL trial that included only those enrolled patients with infra-popliteal disease demonstrated no difference in outcomes in open vs endovascular intervention[29]; however since <50% of these patients had diabetes, this information is again not directly transferable to the problem of the best revascularisation method for the diabetic foot. At the time of writing, BASIL-2 is recruiting patients with severe limb ischaemia due to infra-popliteal disease (with or without the presence of femoropopliteal disease) and will compare vein bypass-first vs best endovascular-first revascularisation. Given that a higher proportion of patients in BASIL-2 are likely to have diabetes, this study may facilitate further sub-group analyses that may be more informative for patients with diabetic foot ulcers and PAD.

Nevertheless, the outcomes presented in this review are broadly similar for open and endovascular therapy, albeit in very heterogeneous populations. Wound healing was infrequently reported as an outcome (and variably defined) and while it appeared that endovascular compared to open revascularisation was associated with improved ulcer healing at 1 year (75% vs 52%), one of the two studies reporting open therapy included patients in whom almost 75% had ultra-distal bypass, which may skew the overall outcomes due to its technical complexity. Otherwise, the rates of limb salvage and major amputation were broadly similar between patients undergoing open vs endovascular treatment. The results of both of these methods, however, will of course depend on the expertise and resources at a given institution. Our review does not summarise the data pertaining to technical success or feasibility of revascularisation in patients with diabetes, as the most important outcomes to report, are in our opinion,

clinical. While the aim should be to use a durable revascularisation approach, the overall goal of healing the foot may be met even if a revascularisation site does not remain patent in the long term.

The angiosome concept is an area of much debate. Traditionally, the best vessel is chosen as the target for revascularisation, with a goal of restoring inline pulsatile blood flow to the foot through any means. More recently described, angiosome-directed revascularisation is based on the principle that the foot can be divided into six 3-dimensional blocks of tissue, each supplied by a feeding artery. The theory is that by identifying the specific feeding artery to an area of tissue loss and targeting that artery for revascularisation (ie, direct revascularisation; DR), restoration of pulsatile blood flow directly to an area of tissue ischaemia renders it more likely to heal. Alternatively, non-angiosome directed therapy (indirect revascularisation; IR) adopts the "best vessel" approach, whereby the most suitable target artery is chosen, regardless of whether it relates to the area of tissue loss and blood flow is therefore restored to the area by collaterals. Given that patients with diabetes typically have poor collaterals, it seems intuitively that angiosome-directed revascularisation might be more effective.

The results of six out of eight retrospective studies in this review suggest that direct revascularisation (ie, angiosome-based therapy) is associated with improved wound healing and in four studies, this translated to improved limb salvage. Those of one study[15] suggest that indirect endovascular revascularisation through collaterals has similar outcomes to direct revascularisation and that both offer significantly improved rates of limb salvage and wound healing when compared to indirect revascularisation without collaterals. These findings are reflected in two recent meta-analyses that combined include >4000 limbs with foot ulcers (>80% of which had diabetes), which both concluded that endovascular IR significantly improves wound healing and major amputation rates, but that, in the presence of collaterals, IR and DR have similar outcomes.[30,31] However, the populations included were highly variable, the definitions poorly defined and it is not possible to draw any firm conclusions from these data. Despite this, we think it would be sensible to pursue an angiosome-based revascularisation strategy if possible, particularly in patients with diabetes who have poor collaterals and may therefore benefit from the restoration of blood flow directly to the area of tissue loss.

That said, since several patients (>20% of patients in one study), who undergo a successful revascularisation procedure will still require a major amputation within 12 months,[6] there is clearly more to the story than optimising perfusion. While other clinical variables that affect outcomes (such as infection, wound characteristics, neuropathy, and comorbidities), it is difficult to know what proportion each of these factors contributes to an individual patient's chance of clinical success. The evidence indicates that patients with diabetes, ulceration and severe perfusion deficit should be considered for early revascularisation, however the role for intervention in those with mild to moderate ischaemia is less well defined. The studies included in our review provided few data about the perfusion deficit, the duration of attempted conservative management or the indication for vascular investigation and treatment. In addition, there is no known threshold value of perfusion towards which we should aim when attempting revascularisation. So as part of a goal to optimise all approaches to heal a diabetic foot ulcer, those patients with mild to moderate ischaemia should be investigated further for the presence of a perfusion defect amenable to revascularisation if there is no significant improvement in healing within 4-6 weeks of optimal care.

Unfortunately, there are some clinical characteristics that contribute significantly to poor outcomes but cannot be optimised. ESRD is a known risk factor for foot ulceration and major amputation in patients with diabetes[32] and outcomes of revascularisation in this group are typically poor. Our review found that patients with ESRD undergoing revascularisation had lower 1 year limb salvage rates (70% vs 82%). Moreover, there was increased perioperative mortality, and > 50% of patients were dead at 3 years and up to 90% at 5 years. This appears much higher than the overall median mortality rates of almost 30% at 2 years and 46% at 5 years.

The poor survival rates in patients with diabetes, PAD and foot ulceration is in a large part attributable to the systemic nature of arterial disease. Many patients with PAD will also have ischaemic heart disease and cerebrovascular disease on presentation. It is imperative, therefore, to ensure that all patients with PAD receive comprehensive medical management of concomitant cardiovascular disease and control of cardiovascular risk factors, including at a minimum, smoking cessation, anti-platelet and statin therapy.

This systematic review once again highlights the paucity of robust evidence to guide the treatment of patients with diabetes, PAD and foot ulcers. To date, there are no randomised trials of endovascular vs open revascularisation in these patients and the vast heterogeneity of the available data precludes meaningful data pooling or meta-analysis. There remains an urgent need for improved research in this field. Better study design, use of predefined and standardised outcomes reporting, including wound healing, will go some way towards producing better quality evidence. However, the fate of a patient with diabetes, foot ulceration and PAD remains difficult to predict, and is affected by a multitude of clinical characteristics that cannot always be identified and ameliorated. The high mortality rates observed amongst these patients should alert the clinician to the significant contribution of concomitant cardiovascular diseases to outcomes, and the overall frailty of the patient cohort. The goals of revascularisation should be reflected in the decision-making process between both the patient and the treating clinician, given the many areas of uncertainty that exist.

5 | CONCLUSIONS

This updated systematic review of studies including more than 13 000 patients with diabetes and PAD demonstrates adverse high event rates even when revascularisation is undertaken. This highlights the importance of optimising care of concomitant cardiovascular disease, including medical management and lifestyle modification, particularly in light of the mortality rates of almost 50% at 5 years, worse than many common cancers. There is no appreciable difference in

clinical outcomes when comparing endovascular and open therapy and both remain reasonable strategies, depending on the local expertise. Planning a revascularisation approach based on the angiosome concept appears to be a sensible approach in patients with diabetes (especially in those undergoing angioplasty), who typically have poor collateralisation and would likely benefit from revascularisation directly to the feeding artery at the area of tissue loss. However, the data to support this concept are almost entirely retrospective, lacking in standardisation of techniques, definitions and outcome measures. More robust evidence is therefore required in order to understand the best strategy for revascularisation in patients with diabetes, foot ulceration and PAD.

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CONFLICT OF INTEREST

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All individual conflict of interest statement of authors of this guideline can be found at: https://iwgdfguidelines.org/about-iwgdf-guidelines/biographies/

AUTHOR CONTRIBUTIONS

R.O.F performed the updated literature search, screened the titles, abstracts and full papers, assessed the literature, extracted data, drew conclusions for the PICOs, completed the evidence tables, and wrote the manuscript. J.A. checked the evidence table and reviewed the manuscript. E.B. assessed the literature, extracted data, checked and revised the evidence tables, reviewed and critically revised the manuscript. R.F. screened the abstracts, assessed the literature, extracted data, checked and revised the evidence tables, and reviewed the manuscript. J.P.H. checked the evidence tables and reviewed the manuscript. K.K. checked the evidence tables and reviewed the manuscript. J.L.M. extracted data, checked the evidence tables and reviewed the manuscript. S.N. checked the evidence tables and reviewed the manuscript. J.R. checked the evidence tables and reviewed the manuscript. M.V. checked the evidence tables and reviewed the manuscript. R.E.Z. extracted data, checked the evidence tables and reviewed the manuscript. N.C.S. assessed the literature, drew conclusions for the PICOs, checked and revised the evidence tables, reviewed and critically revised the manuscript. R.J.H. reviewed and provided final consensus for the data extraction, drew conclusions for the PICOs, reviewed and critically revised the manuscript. R.O.F acted as secretary of the working group, R.J.H. as chair of the working group. The authors take full responsibility for the content of the publication.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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