DIABETES/METABOLISM RESEARCH AND REVIEWS
Diabetes Metab Res Rev 2004; **20**(Suppl 1): S90–S95.
Published online in Wiley InterScience (www.interscience.wiley.com). **DOI:** 10.1002/dmrr.464

RESEARCH ARTICLE

Diabetic foot ulcer classification system for research purposes: a progress report on criteria for including patients in research studies

N. C. Schaper*

Department of Internal Medicine/Endocrinology, University Hospital Maastricht, Maastricht, The Netherlands

*Correspondence to: N. C. Schaper, Chairman, International Consensus group on research classification, Department of Internal Medicine/Endocrinology, University Hospital Maastricht, Maastricht, The Netherlands.
E-mail: nsc@sint.azm.nl

Received: 10 December 2003
Revised: 11 December 2003
Accepted: 28 January 2004

Abstract

Various different systems have been proposed to classify diabetic foot ulcers, but none has gained widespread acceptance. The International Working Group of the Diabetic Foot (IWGDF) developed a classification system for research purposes, which is described in this report. In this PEDIS system, all foot ulcers should be classified according to five categories: perfusion, extent/size, depth/tissue loss, infection and sensation. The methods to determine the presence and severity of these factors are described; each (sub)category is defined according to strict criteria, which are applicable worldwide. All experts involved and all members of the IWGDF reached consensus on this system, which will be validated first, before it can be formally introduced. Copyright © 2004 John Wiley & Sons, Ltd.

Introduction

Until now, more than 10 different systems have been developed to classify diabetic foot ulcers for daily clinical practice [1–8]. However, no system has found universal acceptance and different centres of excellence use different classification systems; reaching consensus on this topic was clearly a challenge for all experts involved. In the earlier projects of the International Working Group of Diabetic Foot (IWGDF), solid scientific data was the basis for consensus, but, in the present project, much more arbitrary choices had to be made, and this could contribute to differences in opinion between the experts involved. Moreover, the design and content of a classification strongly depends on its aims and it was decided that the current system was to be used in research. The characteristics of such a research system will clearly differ from a system for daily clinical practice, although efforts were to be made to ensure that the basis of both systems was identical.

Various classification systems can be used for diabetic patients who are at risk of (potential) foot ulcers. A system in which patients are categorized according to their risk for future ulceration has already been described by the IWGDF [8]. This risk classification system did, in one study, predict the development of a foot ulcer during follow-up [9]. The aims of a classification system for diabetic foot ulcers for clinical practice should, in the opinion of the IWGDF, facilitate communication between health-care providers, influence daily management and provide information about the healing potential of an ulcer. In addition, such a system should be very easy to use, applicable worldwide and should enable the classification of any patient with a diabetic foot ulcer. If used for audit and patients are followed over time, it should allow repeated classification.

Aims of the ulcer research classification system

The aims of the research classification are to enable the categorization of different populations of diabetic patients with a foot ulcer for the purposes of research, at a certain time point, according to strict criteria and using terms that are relevant, unambiguous and applicable worldwide. Such a classification system should facilitate communication and enable the comparison of the results of different research projects. It needs to be reproducible, reliable and robust.

The research system does not primarily aim to influence clinical management or to predict the outcome of individual foot ulcers, nor is it designed as a monitor of the healing process. These items can be covered by a clinical classification system or could be included as part of specific research projects. The research classification should be in line with the International Consensus on the Diabetic Foot with regard to intention and definitions, and it should follow the same structure as other consensus texts produced in related fields.

The present research classification system was particularly developed to facilitate communication in the field of research. The system should help in correctly interpreting data in research projects; it should include the major dimensions affecting pathogenesis, management and outcome of a diabetic foot ulcer. It was not the aim to develop a classification system that can be used to predict the outcome of an individual patient or that can act as a guide for daily management. The research system should categorize and define patients with the use of relevant clinical items in such a way that intra- and inter-observer variability is low (good reproducibility). Strict criteria defining categories of patients should be given to reduce the chance of a patient being misclassified.

The consequence of such a rather 'rigid' system is that some patients cannot be classified. To optimize comparison between clinical trials, it is preferable that some patients are not included when they do not fit into the pre-specified categories, rather than that patients are included when they should have been excluded. The latter situation would clearly hamper the generalization of the results obtained. The consequence is also that, as far as possible, objective, reproducible techniques should be used to reduce variability. A concern is that if objective, reproducible techniques are to be used, these techniques can become too complex or expensive. The consequence would be that only patients attending highly specialized foot clinics could be classified. Therefore, in several categories of the current system, a compromise was made between the ideal world and daily life, and a minimal set of criteria was given. Depending upon the aim of an individual research project, additional criteria can, and, in some cases, should be added to the current system to improve correct categorization (inclusion and exclusion criteria) of the different subcategories. The current system is primarily developed to characterize patients participating at a certain time point in a research project, usually during the inclusion phase of a project and it should be the basis for the inclusion and exclusion criteria. Therefore, temporal aspects are not included in the current system. However, wounds clearly change in time and complications can develop. When, for instance, the chronobiology of wounds is studied, an extra category on wound characteristics can be added.

Validation

The current system needs to be validated before it can be introduced as an international classification system. The term validation can be confusing in the present context. The categories and grades of the system were defined on the basis of their relevance for research by experts in the field and the comments of the members of the IWGDF were, in general, favourable. The face validity of the current system seems, therefore, high. This system will be tested for its ability to correctly categorize a population of diabetic patients with a foot ulcer. In addition, the reproducibility (intra- and inter-observer variability) will be defined. As the research system does not aim to predict outcome or influence management, these items will not be used as outcome parameters in this validation phase.

The definition of an ulcer

A diabetic foot ulcer is defined in the research system as a 'full-thickness' lesion of the skin, that is, a wound penetrating through the dermis; lesions such as blisters or skin mycosis are not included in this system. The term ulcer can be ambiguous in this context. In medicine, a skin ulcer is generally defined as a non-healing or poorly healing wound. Information on the duration of the ulcer is essential to define non-healing. Unfortunately, this temporal information is frequently missing in patients with a diabetic foot ulcer; due to loss of sensation and impaired vision, the duration is frequently not known. A foot ulcer is defined in the current system, according to the International Consensus on the Diabetic Foot, as a full-thickness wound below the ankle in a diabetic patient, irrespective of duration [8]. Skin necrosis and gangrene are also included in the current system as ulcers. Gangrene was defined in the International Consensus on the Diabetic Foot as a continuous necrosis of the skin and the underlying structures (muscle, tendon, joint or bone) [8].

The categories and grades

On the basis of the scientific literature and expert opinion, five categories were identified, which were considered the most relevant items for research projects in diabetic foot ulcers:

Perfusion
Extent/size
Depth/tissue loss
Infection
Sensation.

Loss of protective sensation and impaired tissue perfusion caused by atherosclerotic peripheral arterial disease (PAD) are two basic mechanisms in the pathway to ulceration. They both affect wound management, and, in addition, PAD can have a major impact on the outcome [5,6,8]. Also, infection and depth have a major effect on management and outcome, and the size is particularly relevant for the time to heal and wound management [5,6,8].

For each category, a grading system is provided, and this grading system should describe the severity within each category. As the system has been developed for primarily clinical research, the criteria for each category are based upon objective techniques that can be part of the up-to-date management of patients with a foot ulcer, as described in The International Consensus on the Diabetic Foot [8]. How each category is graded depends upon the characteristics of that category and the current evidence base. A system that for instance has three grades, such as none, a little, a lot, seems very attractive. Moreover, if all categories are graded identically, it could render the system more easy to use. However, at present the disadvantages of such a symmetrical system seem greater than the advantages. The evidence base (and consensus) to subdivide all categories in three strict grades is lacking. For instance, in the current system there is no grading for size, it is reported in square centimetres and sensation is defined as loss or no loss of protective sensation. The system does not include a grade 0 because, in many instances, it will be impossible to exclude subclinical abnormalities, for example, in neuropathy or PAD.

The backbone of the present system can be used in any country, but resources are clearly absent in some countries to classify patients according to the strict criteria of the current system. When resources are lacking, the system can easily be adapted for local use. However, lack of resources cannot be an excuse for inadequate research.

Perfusion

The classification system for the diabetic foot is designed to be in line with the system for classification of PAD as developed by the TransAtlantic interSociety Consensus group (TASC) [10]. More specific criteria are used in the present system, as the TASC system is an inclusive clinical system and not an exclusive research system. Moreover, the categories described below were also defined in the document of the International Consensus on the Diabetic Foot [8].

GRADE 1 No symptoms or signs of PAD in the affected foot, in combination with

- palpable dorsal pedal and posterior tibial artery

or

- ankle-brachial index 0.9 to 1.10 or
- toe-brachial index >0.6 or
- transcutaneous oxygen pressure ($tcpO_2$) >60 mm Hg.

GRADE 2 Symptoms or signs of PAD, but not of critical limb ischemia (CLI):

- Presence of intermittent claudication (in case of claudication, additional non-invasive assessment should be performed), as defined in the document of the International Consensus on the Diabetic Foot [8] or
- Ankle-brachial index < 0.9, but with ankle pressure >50 mm Hg or
- Toe-brachial index < 0.6, but systolic toe blood pressure >30 mm Hg or
- $TcpO_2$ 30− to 60 mm Hg or
- Other abnormalities on non-invasive testing, compatible with PAD (but not with CLI).

Note: if tests other than ankle or toe pressure or $tcpO_2$ are performed, they should be specified in each study.

GRADE 3 Critical limb ischemia, as defined by

- systolic ankle blood pressure <50 mm Hg or
- systolic toe blood pressure <30 mm Hg or
- $tcpO_2$ < 30 mm Hg.

Comments

Physical examination is one of the cornerstones in diagnosing PAD and needs to be performed by a health-care worker with adequate knowledge and skills. Pain at rest is a criterion for critical ischaemia in non-diabetic patients with PAD [10]. Pain at rest is not included in the current research system, as it is difficult to differentiate from other causes of pain in the lower extremity in diabetic patients.

In the UKPDS study, symptoms of claudication were reported in only 23% of the patients with an ankle arm index < 0.8, indicating that for each patient with claudication, there are three patients with silent PAD [11]. On the basis of the present literature, the presence of both pulses in the foot, in combination with the absence of intermittent claudication, renders significant PAD unlikely. However, palpation of pulses has only a moderate reproducibility, and severe ischaemia can be present in a minority of diabetic patients with palpable pulses [12,13]. On the other hand, if one or two pulses are absent, clinically relevant PAD is more likely, but pulses can be absent because of anatomical abnormalities or oedema [12,13]. Therefore, in the absence of one or two palpable pulses, additional objective vascular assessment is necessary to exclude PAD or to further grade PAD, if present.

In non-diabetic patients, measurement of the systolic ankle blood pressure with a hand-held Doppler device is the first step in the evaluation of patients with suspected PAD [10]. The ankle/brachial index (ABI) is calculated by dividing this ankle pressure by the Doppler pressure measured in the brachial artery. An ABI <0.9 confirms haemodynamically significant occlusive disease between the heart and the ankle, which, in most cases, lies distal

to the renal arteries [10]. Moreover, the ABI can give a rough estimate of the severity of the occlusive disease in non-diabetic subjects [10]. The index is decreased to values between 0.5 to 0.9 in asymptomatic patients or in patients with claudication, and most of these patients will have single-segment occlusions. Values below 0.5 indicate severe multi-segment disease, and, in (non-diabetic) patients with rest pain, the absolute ankle pressure is usually <40 mm Hg [10]. Unfortunately, the usefulness of this technique can be limited in the diabetic patient. Owing to arterial media calcification, the arteries of the lower leg may be less compressible, and incompressible arteries have been observed in up to 30% of diabetic patients [12]. An ABI >1.10 suggests that the ankle pressure is falsely elevated. Several studies have shown that the ABI or the absolute ankle pressure is a poor predictor of outcome (amputation) in diabetic patients with PAD and/or a foot ulcer [12,13]. In contrast, the more complex techniques such as systolic toe pressure measurement or measurement of the transcutaneous partial pressure of oxygen ($tcpO_2$) were better predictors of outcome in several studies [10,13].

Media arterial calcification seems to be less of a problem when measuring systolic toe pressures. For screening purposes, a toe systolic blood pressure index of >0.60 can be interpreted as normal [12,13]. Toe pressures can predict outcome in diabetic patients with foot ulcers, and primary healing of a foot ulcer occurred in most patients with a toe pressure >30 mm Hg [12,13]. Unfortunately, this measurement also has limitations. Toe arteries can be affected by media calcification, although to a lesser extent than the arteries in the lower leg, resulting in falsely elevated values [13]. In addition, falsely low values can be obtained if the skin temperature of the toe is too low, and, in these cases, the foot must be warmed prior to the investigation. The transcutaneous partial pressure of oxygen ($tcpO_2$) can be measured with a heated oxygen sensitive probe, which is placed on the dorsum of the foot. Subsequently, the skin oxygen tension can be determined, reflecting local microcirculatory blood flow. In healthy subjects, a wide range of values can be observed, but normal values are usually >60 mm Hg [10]. Several studies have shown that $tcpO_2$ values can predict healing or amputation in patients with a foot ulcer. An oxygen tension <30 mm Hg suggests critical limb ischaemia in a patient with a foot ulcer [8,12,14]. However, it should be noted that various systemic factors (such as hypoxia) or local factors (such as oedema and inflammation) can affect the measurement, resulting in falsely low values. Given the uncertainties related to the ABI, it is suggested that in studies aiming to exclude patients with clinical relevant vascular disease, toe pressures or $tcpO_2$ should be determined.

Extent/size

Wound size (measured in square centimetres) should be determined after debridement, if possible. The outer border of the ulcer should be measured from the intact skin surrounding the ulcer. If wound healing is one of the end-points in a study, tracing of the wound, planimetry or the grid technique should be used for sequential measurements of the wound area. If, on the other hand, wound size is measured only at the time of recruitment into a study and intact skin is the primary end-point, the surface area can also be estimated by multiplying the largest diameter by the second largest diameter measured perpendicular to the first diameter. However, this technique is clearly less precise. The frequency distribution of the size of the ulcers should be reported in each study as quartiles.

Depth/tissue loss

Depth is difficult to determine and is relative; an ulcer that is only a few millimeters deep on a toe can penetrate into a bone or a joint, but, in other regions, ulcers can be several centimeters deep without involvement of deeper structures. Therefore, ulcers are divided into lesions confined to the skin and those deeper than the skin. Even if an ulcer does not seem to penetrate below the skin, clinical infection in subcutaneous tissues (e.g. an abscess or osteomyelitis) means it is a 'deep' ulcer. The extent of tissue loss should be evaluated after initial debridement, but this should be performed judiciously when critical limb ischaemia (Grade 3) is suspected.

GRADE 1 Superficial full-thickness ulcer, not penetrating any structure deeper than the dermis.

GRADE 2 Deep ulcer, penetrating below the dermis to subcutaneous structures, involving fascia, muscle or tendon.

GRADE 3 All subsequent layers of the foot involved, including bone and/or joint (exposed bone, probing to bone).

Infection

Infection of a diabetic foot ulcer is defined as invasion and multiplication of micro-organisms in body tissues associated with tissue destruction or a host inflammatory response [8]. Infection is defined clinically, by the symptoms and signs of inflammation, as described below, regardless of the results of any wound culture. Studies on accuracy and validity of different tests for diagnosing infection in diabetic foot disease are scarce. Therefore, the scheme described below is based mainly on expert opinion. In grading infection, three parameters, in particular, are relevant to clinical management and possibly to the outcome: the involvement of skin only, the involvement of deeper structures and the systemic inflammatory response of the patient. In daily practise, the term a 'limb-threatening' infection is also frequently used. However, this category is very difficult to define and overlaps with the other categories.

GRADE 1 No symptoms or signs of infection.

GRADE 2 Infection involving the skin and the subcutaneous tissue only (without involvement of deeper tissues and without systemic signs, as described below). At least two of the following items are present:
- Local swelling or induration
- Erythema >0.5 to 2 cm around the ulcer
- Local tenderness or pain
- Local warmth
- Purulent discharge (thick, opaque to white or sanguineous secretion).

Other causes of an inflammatory response of the skin should be excluded (e.g. trauma, gout, acute Charcot neuro-arthropathy, fracture, thrombosis, venous stasis).

GRADE 3 Erythema >2 cm plus one of the items described above (swelling, tenderness, warmth, discharge) or infection involving structures deeper than skin and subcutaneous tissues such as abscess, osteomyelitis, septic arthritis, fasciitis. No systemic inflammatory response signs, as described below.

GRADE 4 Any foot infection with the following signs of a systemic inflammatory response syndrome [15]. This response is manifested by two or more of the following conditions:
- Temperature >38 or <36 °C
- Heart rate >90 beats/min
- Respiratory rate >20 breaths/min
- PaCO2 <32-mm Hg
- White blood cell count >12.000 or <4.000/cu mm
- 10% immature (band) forms.

Comments

The presence of ischaemia has a large effect on the signs and symptoms, the clinical course and the outcome of an infection. The combination of infection and ischemia had the poorest prognosis in prospective studies [5,6,8].

Unfortunately, there is as yet no consensus on criteria for diagnosing osteomyelitis as part of the International Ulcer Research Classification. The following procedures may be useful in evaluating the presence of an osteomyelitis [8]:

- *Plain X-ray* abnormalities are relatively insensitive and non-specific, but repeated X rays over several weeks can be highly suggestive of, or largely exclude, osteomyelitis.
- *Probing to bone* in the presence of an infected foot ulcer, based on limited data, appears to have intermediate sensitivity and specificity. The predictive value of the test varies directly with the prevalence of osteomyelitis in the population and no information has been published on intra- and inter-observer variability.
- *Nuclear medicine scanning* has good sensitivity, but has low to moderate specificity depending on the type of scan; leukocyte and immunoglobulin scans appear to be more specific than bone scans.
- *MRI* has shown good sensitivity and specificity in many studies, but false-positive findings can occur, and quality depends on the expertise of the technicians and radiologists.
- *Bone biopsy with histology and culture* is usually viewed as the gold standard, but published literature in diabetic foot disease is sparse. Moreover, inaccurate results occur when patients are receiving antibiotics, when incorrect techniques are used or because of sampling error.

Sensation

The system categorizes patients as having present or absent protective sensation in the affected foot. The system does not categorize patients as having (diabetic) polyneuropathy, and additional information is needed for this diagnosis. Moreover, it does not provide information on the cause of the loss of protective sensation, nor is the severity of the sensory loss graded. Both pressure and vibration sensation should be determined in each patient.

GRADE 1 No loss of protective sensation on the affected foot detected, defined as the presence of sensory modalities described below.

GRADE 2 Loss of protective sensation on the affected foot is defined as the absence of perception of the one of the following tests in the affected foot:
- Absent pressure sensation, determined with a 10-g monofilament, on two out of three sites on the plantar side of the foot, as described in the International Consensus on the Diabetic Foot.
- Absent vibration sensation, (determined with a 128-Hz tuning fork) or vibration threshold >25 V (using semi-quantitative techniques), both tested on the hallux.

Comments

Loss of protective sensation plays a crucial role in the pathogenesis of most diabetic foot ulcers treated in diabetic foot clinics [8]. However, in diabetic patients with a foot ulcer treated in these clinics, protective sensation can be present, albeit in a minority of patients. Moreover, it is likely that loss of protective sensation is less prevalent in diabetic patients with foot problems treated in departments of vascular surgery. Therefore, loss of protective sensation is included in the present classification scheme. The testing of light touch and testing of blunt/sharp sensation are not recommended because of lack of scientific evidence.

References

1. Megitt B. Surgical management of the diabetic foot. *Br J Hosp Med* 1976; **16**: 227–332.

2. Wagner FW. The dysvascular foot: a system for diagnosis and treatment. *Foot and Ankle* 1981; **2**: 64–122.
3. Knighton DR, Ciresi KF, Fiegel VD, Austin LL, Butler EL. Classification and treatment of chronic non-healing wounds: successful treatment with autologous platelet-derived wound healing factors (PDWHF). *Ann Surg* 1986; **204**: 322–330.
4. Pecoraro RE, Reiber GE. Classification of wounds in diabetic amputees. *Wounds* 1990; **2**: 65–73.
5. Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system: contribution of depth, infection, and vascular disease to the risk of amputation. *Diabetes Care* 1998; **21**: 855–859.
6. Oyibo SO, Jude EB, Tarawneh I, Nguyen HC, Harkless LB, Boulton AJ. A comparison of two diabetic foot ulcer classification systems: the Wagner and the University of Texas wound classification systems. *Diabetes Care* 2001; **24**: 84–88.
7. Macfarlane RM, Jeffcoate WJ. Classification of diabetic foot ulcers: the S(AD) SAD system. *The Diabetic Foot* 1999; **2**: 123–131.
8. Apelqvist J, Bakker K, van Houtum WH, Nabuurs-Franssen MH, Schaper NC. International Working Group on the Diabetic Foot. International Consensus on the Diabetic Foot. Maastricht, 1999.
9. Peters EJ, Lavery LA. Effectiveness of the diabetic foot risk classification of the International Working Group on the Diabetic Foot. *Diabetes Care* 2001; **24**: 1442–1447.
10. Management of peripheral arterial disease (PAD). TransAtlantic Inter- Society Consensus (TASC). *Eur J Vasc Endovasc Surg* 2000; **19**(Suppl. A): S1–S250.
11. Adler AI, Stevens RJ, Neil A, Stratton IM, Boulton AJ, Holman RR. UKPDS 59: hyperglycemia and other potentially modifiable risk factors for peripheral vascular disease in type 2 diabetes. *Diabetes Care* 2002; **25**: 894–899.
12. Takolander R, Rauwerda JA. The use of non-invasive vascular assessment in diabetic patients with foot lesions. *Diabet Med* 1996; **13**: S39–S42.
13. Schaper NC, Kitslaar PJEM. Peripheral vascular disease in diabetes. In *International Textbook of Diabetes Mellitus* (3rd edn), deFronzo R, Ferrannini E, Keen H, Zimmet P (eds). J Wiley and Sons: Chichester; 2004; (In press).
14. Kalani M, Brismar K, Fagrell B, Ostergren J, Jorneskog G. Transcutaneous oxygen tension and toe blood pressure as predictors for outcome of diabetic foot ulcers. *Diabetes Care* 1999; **22**: 147–151.
15. The ACCP/SCCM Consensus Conference Committee. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest* 1992; **101**: 1644–1655.

