REVIEW

Amputation-free limb survival in diabetic foot lesions: a review

Mohamed Sharkawy

Department of Vascular Surgery, Cairo University, Cairo, Egypt

Correspondence: Mohamed Sharkawy
E-mail: sharkawy@kasralainy.edu.eg
Received: November 08, 2016
Published online: December 27, 2016

In this review, we examine the current status of amputation-free survival among patients with diabetic foot lesions in terms of the prevalence of diabetic foot lesions and amputations among diabetics. Next, we examine the etiological factors that are responsible for the development of diabetic foot lesions and subsequent amputation. We have previously conducted a retrospective investigation from 2004 to 2007. From our analysis of the data collected over this period from patients with diabetic foot lesions, we were able to identify some of the main etiological categories related to the amputation risk. Based on these etiological categories, we were able to develop a color-coded etiological key that can be easily applied in clinical practice for the assessment of the amputation risk and thereby guide the referral and management of the disease in the future. Between 2007 and 2012, we conducted a prospective study to test the applicability of the etiological key. The amputation-free survival rates achieved with this key were found to be comparable to those reported with the use of the currently applied approach of using a multidisciplinary team. We found that changes in blood quality, mainly, anemia and hypoalbuminemia, and peripheral artery disease were the etiological factors that were associated with the least chances of requiring amputation. On the other hand, tissue loss and pervious surgical procedures were found to be indicators of the highest risk for amputation. We also examine the etiological factors conventionally considered to increase the risk of amputation and examine the current practices followed in the management of cases of diabetic foot. We also examine the traditional and advanced treatment options available for the various etiological factors with a view to reducing amputations. We believe that our etiological key has the potential for widespread applicability in developing countries where resources for a multidisciplinary approach may be scarce.

Keywords: Amputation-free limb; diabetic foot; lesions; risk of amputation

To cite this article: Mohamed Sharkawy. Amputation-free limb survival in diabetic foot lesions: areview. Evid Based Med Public Health2016; 2: e1477. doi: 10.14800/emph.1477.

Introduction

Diabetes has become increasingly prevalent all over the world. With it, there has been an increase in the long-term complications of the disease, including diabetic foot, cardiovascular events, loss of vision, and end-stage renal disease. The early detection of these complications and their timely management is of paramount importance to ensure a good quality of life for patients. One of the most important sequelae of long-standing diabetes is diabetic foot and possible lower limb amputation. Lower limb amputations in diabetic populations are a global concern, with the rates varying across different regions. In fact, the recent WHO report on the global burden of diabetes states that the lower

limb amputations among diabetics are generally 10 to 20 times that in non-diabetic individuals and over the past decade have ranged from 1.5 to 3.5 events per 1000 persons [1].

One of the main reasons that makes foot ulceration a prime concern is that apart from increasing the amputation risk, the condition also poses a high risk of mortality. A recent systematic review by Jupiter *et al.* [2] showed that in terms of demographics and comorbidities, the 5-year mortality rates after ulceration were around 40%. The main risk factors for mortality associated with diabetic foot lesions are age, male gender, peripheral vascular disease, and renal disease [2].

Over the course of 4 years, 2004 to 2007, we conducted a retrospective investigation of data collected from all the patients visiting our diabetes clinic to identify the risk factors associated with diabetic foot. From the analysis of the data thus collected, we were able to identify six key etiological factors responsible for diabetic foot. These include abnormal blood quantity, abnormal blood quality, associated comorbidities, bone lesions, previous foot surgery, and tissue loss.

With regard to the blood quality, it was considered as a significant etiological factor if the serum hemoglobin level was below 9 g/dL and/or serum albumin was below 3 g/dL[3-6]. The factors considered to influencing blood quantity were absence of pedal pulses and ankle brachial index of less than 0.9 or ankle peak systolic velocity of <75 cm/s [7-9]. Associated comorbidities taken into consideration included both systemic and regional conditions likely to impair wound healing or impede interventional measures, as follows: systemic diseases, such as heart failure (congestive or ischemic); chronic renal failure; and autoimmune collagen likely to cause vasculitis such as rheumatoid arthritis, systemic lupus, scleroderma, and non-specific arteritis [10-14]. The regional diseases that were considered in this category were conditions involving the limbs such as chronic lymphedema and chronic venous insufficiency. Bone lesions of the foot considered in this etiological key were foot bone deformities, Charcot's neuroarthropathy (CN), and radiological proven fracture, dislocations, and/or osteomyelitis. Surgical interventions considered were those that were aimed at the treatment of the foot lesion, as provided in the patient's medical history and invasive investigations and/or surgical procedures that were undertaken under wrongful impression of the patient's medical condition. The category of tissue loss included all conditions that resulted in loss of tissue such as gangrene or necrotizing infection of the foot resulting in the loss of the weight-bearing function of the foot.

Early investigation Procedure

Each of these six etiological categories defined in our etiological key was assigned a distinctive color. The color corresponding to the category applicable in any given case was then posted on the first page of the patient's medical record. This allowed easy identification of the etiological factors that need to be addressed in each case. The categories were defined in such a manner that referral to the concerned specialties would help address all the conditions that fall under that particular category. This would enable efficient management of the patient's condition and promote wound healing and reduce the work pressure on the medical and paramedical personnel. Further, we used color codes in order to assist easy identification. In keeping with our view of developing a tool for simple application in a busy clinical practice, we used colors to identify the various categories. This would help further reduce the work pressure on the medical and paramedical staff and smoothen the entire process.

Our early investigations revealed that the most common etiological factors responsible were blood quality, mainly, the presence of hypoalbuminemia and anemia. Blood quality was followed by blood quantity, i.e., occlusive diseases, and comorbidities, of which the most common were hypertension, chronic renal impairment, and ischemic heart diseases. Bony deformities and Charcot foot were next in the order of frequency. Previous procedures conducted mostly included incision, drainage, and debridement and the most frequent causes of tissue loss were gangrene and neuropathic ulceration.

These findings are in agreement with the other factors reported in other studies. For instance, Riaz*et al.* [15] reported that the severity of the foot ulceration at presentation showed a significant correlation to the amputation rate. Similarly, Chen *et al.* [16] showed that patients with diabetic foot ulcers that are accompanied by necrotizing fasciitis are at high amputation risk and similar to patients with high-grade fasciitis as well low serum albumin level.

Several studies have shown that diabetic neuropathy is a significant risk factor for the development of foot ulceration [15, 17]. A study by Fei*et al.* [18] showed that longer duration of hospitalization, higher white blood cell count, elevated HbA1c levels, and low serum levels of hemoglobin and albumin were significantly associated with the occurrence of amputation. These factors are similar to the factors included in our etiological key. Sun *et al.* [19] also reported that the generally implicated risk factors of amputation, including low serum albumin and hemoglobin, low ankle brachial index, elevated white blood cell count, as well as low

estimated glomerular filtration were all associated with more severe foot ulceration (Wagner grade 3) and increased risk of amputation.

Diabetic foot ulcers are generally evaluated using the following tools of clinical assessment: (i) the diabetic ulcer severity score (DUSS); (ii) University of Texas (UT) diabetic wound classification; (iii) Meggitt-Wagner classification; (iv) depth of the ulcer, extent of bacterial colonization, phase of ulcer and association etiology (DEPA) scoring system; and (v) site, ischemia, neuropathy, bacterial infection and depth (SINBAD) score. Retrospective investigations have shown that these classification systems show good accuracy in predicting lower extremity amputation [20].

Management of diabetic foot ulcers

The predominant approach adopted currently for the management of diabetic foot ulcers is the multidisciplinary approach. Based on evidences, the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine developed guidelines for the clinical management of diabetic foot. The proposed guidelines focus on addressing the following areas: (1) prevention of ulceration in diabetic foot, (2) off-loading, (3) detection of osteomyelitis, (4) adequate wound care, and (5) peripheral arterial disease. However, these points do not account for all aspects of diabetic foot. There is therefore a need for the development of more universal and easily accessible approaches [21]. Further, most of these approaches would require specialized personnel for their application in practice.

Current trends of management of diabetic foot emphasize the use a multidisciplinary approach involving medical personnel of various specialties co-operatively addressing the patient's issues to provide optimal care and prevent amputation.

The involvement of multiple organ systems such as the vascular system, bone tissue, nervous system make it necessary that patients be managed by personnel from multiple of departments. Therefore, current practices involve the use of multidisciplinary teams that most often include a diabetologist, a specialist podiatrist, a vascular surgeon, a diabetes specialist nurse, and an orthoptist and may sometimes also include orthopedic surgeon, tissue viability nurse, microbiologist, and interventional radiologist [22].

On one hand, studies have shown that the prevalence of lower limb amputations has decreased in some developed countries, including United Kingdom, Sweden, Denmark, Spain, the United States of America and Australia, following the adoption of various policies and practices that enable effective management of diabetic foot [23]. Similarly, the implementation of specialized pedagogical foot care practices and the widespread use of below-knee percutaneous endoluminal angioplasties have been shown to have led to a reduction in the major amputation rates among patients with diabetic foot in Germany [24-25].

However, the same trends have not been observed in other parts of the world, particularly, low- and middle-income countries where the resources necessary for a multidisciplinary team may not be readily available. The economic and manpower concerns that arise with the multidisciplinary approach that is largely applied in developed countries makes the widespread implementation of this strategy difficult, despite the fact that it has been proven to be beneficial in reducing the rates of amputation. In developing countries, diabetic foot and associated lower limb amputation still remain major burdens to patients and economy. For example, a recent report from China showed that the incidence of foot ulcers and amputations in the country is much higher than that in Western countries [17].

Due to the absence of dedicated teams in most clinics of developing countries, patient care is administered by referral to any given specialty, the selection of which is made on the basis of the history taking and initial assessment. Thus, this approach is inadequate in adequately addressing all the issues that may be present in any given case.

Reasons for no or lack of improvement

Several reasons may be provided to explain the lack of improvement in the amputation-free survival of patients in developing countries. These include lack of awareness regarding self-care for the prevention of diabetic foot among both patients and attending health care personnel; lack of adequate number of personnel equipped to provide specialized care for the diabetic foot or trained to provide specialist treatment; inaccessible or non-existent podiatry services; difficulty in accessing health care centers; patient-based delay in seeking medical attention due to several issues such as work pressure or economic constraints, lack of training among health care providers to identify and refer patients to appropriate specialists for treatment of complications; bare-foot walking; and lack of surveillance facilities [26, 27].

In such countries, referral of patients would be department-based, focusing on accessible specialties, rather than adopting a problem-targeted approach. Therefore, there is clearly a need for developing strategies that make the process of diabetic foot assessment and subsequent

prevention of amputations a feasible one in terms of both economy and manpower. This would allow for the large-scale implementation of the assessment tools in diabetic populations and subsequent reduction in the rate of amputation.

This is where tools such as the one we have developed come into play. Our color-coded etiological key helps clearly highlight all the etiological factors that are relevant in any given case. Even in the absence of a multidisciplinary team, this tool can be used by a registered nurse and medical secretary to fix up appointments with the required specialists and carry on the referral and treatment under the usual clinical settings, thereby precluding the need for the viability of several specialists as well as avoiding additional strain on manpower and therefore cost of consultation.

Color-coded Etiological Keys

During the course of the years 2007 to 2012, we conducted a prospective study wherein we applied our color-coded etiological key for the assessment of patients with diabetic foot lesions and planned further treatment accordingly. In our model, at an initial consultation with the chief resident at our clinic, the patients were provided a list of investigations that needed to be completed for further assessment. With these results, the patients then visited the attending physician on the second visit, who examined them and the investigative reports. Depending on the number of etiological applicable in each case the appropriate color was posted in the patient's medical records, using which the registered nurse fixed up appointments with the respective specialists under consultation with the medical secretary. This method allowed seamless referral to all required specialists and thereby allowed the management of all etiological factors involved in each case.

With the application of this method, the overall amputation-free survival achieved in our study was 72.5%, which is similar to the percentage (77%) reported previously by Prompers*et al*. [28].

We found that patients with the chances of amputation-free survival were the lowest among patients with tissue loss or previous foot surgery. On the other hand, it was the highest among those with poor blood quality, which is correctable, and among those with peripheral arterial diseases.

Treatment options that have been traditionally available for peripheral arterial disease and critical limb ischemia include the following: 1), skin replacement (2), hyperbaric oxygen (2), ketanserin (3), prostaglandins (3), growth factors (5), dressings and topical applications (9), debridement (2) and antibiotics (2). A systematic review of all the treatment options available for diabetic foot ulcers revealed the following: total contact casting afforded better healing than standard treatment; topical growth factors, particularly platelet-derived growth factor, enhanced the healing of diabetic foot ulcers; topical ketanserin improved the ulcer healing rate; and systemic hyperbaric oxygen therapy decreased the frequency of major amputations. Further, the review also indicated that iloprost and prostaglandin E1 also have beneficial effects on diabetic foot ulcer healing [29].

Management of critical limb ischemia

Considerable advances have been made in the management of diabetic foot ulcers. Most recent research promotes the use of topical oxygen, which has shown some potential in promoting wound healing [30]. The use of bioengineered skin substitutes, namely, Apligraf, Dermagraft, OASIS, and MatriStem has also been shown to yield factorable results in terms of shortening the time required for wound healing [31]. Furthermore, dehydrated human amnion/chorion membrane (dHACM) preparations including EpiFix, MiMedx Group Inc., Marietta, GA have also been shown to be beneficial in the treatment of non-healing diabetic foot ulcers [32]. These newer technologies have been shown to reduce the overall costs for the treatment of diabetic foot ulcers [33].

Considerable in-roads have been made in the management of critical limb ischemia (CLI). It is considered as the end stage of peripheral arterial disease. Both percutaneous transluminal angioplasty and open arterial reconstruction have been found to be feasible for revascularization. While conservative treatment involves wound care and also consists of antiplatelet therapy and anti-inflammatory therapy with statin or ACE inhibitors, surgical therapies include distal bypass surgery and thromboendartectomy. Endovascular techniques include percutaneous transluminal angioplasty, bare metal stent placement, atherectomy, and drug-coated balloon and drug-eluting stent implantation [34]. Despite these therapeutic measures, sometimes amputations may be required in cases of CLI due to other complicating factors such as infection.

Aggressive endovascular techniques for the management of peripheral artery disease include subintimal angioplasty, retrograde approach with transpedal access, subintimal arterial flossing [35] with antegrade-retrograde intervention [36, 37], trans-collateral angioplasty [38], and pedal-plantar loop [39, 40]. These techniques have brought about an improvement in the management of peripheral artery disease in diabetics. The availability of effective revascularization techniques may

explain why we observed that the chances of amputation are low in patients with peripheral artery disease (PAD).

Risk assessment tools similar to ours have been proposed by other investigators as well. For example, Monteiro-Soares and Dinis-Ribeiro [41] proposed DIAFORA, a tool for the assessment of diabetic foot risk. The etiological factors included in their tool include presence of neuropathy, foot deformity, peripheral arterial disease and previous foot problems, multiple diabetic foot ulcer, infection, gangrene, and bone involvement. They found that their model tool showed equal or better accuracy in the prediction of the amputation rates as compared to currently applied ones. The rate of amputation in their study (23.2%) was close to that obtained in our study (27.5%). However, their study included fewer patients than ours and was conducted over a shorter duration than ours.

Conclusion

From the standpoint of economic feasibility and manpower utilization, we believe that our etiological key would be a very effective tool in the assessment of the risk for amputation in cases of diabetic foot. We believe that the implementation of this tool for the routine assessment of all diabetic foot patients would eventually bring about a reduction in the amputation rates among diabetic populations. In particular, we believe that in countries that fall under the low- or middle-income categories, the inclusion of our etiological key in the examination sheet for diabetic foot patients would greatly simplify the assessment and further referral process. Further, we encourage the use of this sheet by all medical departments that encounter cases of patients with increased diabetic foot problems in, to ensure efficient detection of all pertinent risk factors in each case and subsequent prompt correction of the issues identified in the best possible manner. This in turn would allow for the proper and timely administration of adequate and appropriate treatment, thereby reducing the risk for amputation in diabetic populations. Steps in these directions would eventually pave the way for the reduction in the amputation rates among developing countries to match those in the developed world.

Conflicting interests

The authors have declared that no conflict of interests exist.

Acknowledgements

The author would like to thank Diabetic Foot Salvage-Egyptian Foundation and Egyptian Vascular Academy (EVA) for extending help and support for this research work. The authors are also thankful to www.manuscriptedit.com for providing English language editing and proofreading services for this manuscript.

Author Contributions

Mohamed Sharkawy participated in the Study conception and design, Acquisition of data, Analysis and interpretation of data, Drafting of manuscript and all other critical revisions.

Abbreviations

DUSS: Diabetic Ulcer Severity Score; DEPA: Depth of the ulcer, Extent of bacterial colonization, Phase of ulcer, and Association etiology; SINBAD: Site, Ischemia, Neuropathy, Bacterial Infection, and Depth; dHACM: Dehydrated Human Amnion/Chorion Membrane; CLI: Critical Limb Ischemia.

References

1. World Health Organization. Burden: mortality, morbidity and risk factors. In Global status report on noncommunicable diseases 2010. [http://www.who.int/nmh/publications/ncd_report_chapter1.pdf?ua=1].
2. Jupiter DC, Thorud JC, Buckley CJ, Shibuya N. The impact of foot ulceration and amputation on mortality in diabetic patients. I: From ulceration to death, a systematic review. Int Wound J 2016; 13:892-903.
3. Boulton AJ, Meneses P, Ennis WJ. Diabetic foot ulcers: a framework for prevention and care. Wound Repair Regen 1999; 7: 7-16.
4. Scholl D, Langkamp-Henken B. Nutrition recommendations for wound healing. J Intraven Nurs 2001; 24:124-132.
5. Thompson C, Fuhrman MP. Nutrients and wound healing: still searching for the magic bullet. NutrClinPract 2005; 20:331-347.
6. Crowe T, Brockbank C. Nutrition therapy in the prevention and treatment of pressure ulcers. Wound Pract Res 2009; 17:90-99.
7. Schaper NC, Andros G, Apelqvist J, Bakker K, Lammer J, Lepantalo M, *et al*. Specific guidelines for the diagnosis and treatment of peripheral arterial disease in a patient with diabetes and ulceration of the foot 2011. Diabetes Metab Res Rev 2012; 28:236-237.
8. Hirsch AT, Allison MA, Gomes AS, Corriere MA, Duval S, Ershow AG, *et al*. A call to action: women and peripheral artery disease: a scientific statement from the American Heart Association. Circulation 2012; 125:1449-1472.
9. Lipsky BA, Sheehan P, Armstrong DG, Tice AD, Polis AB, Abramson MA. Clinical predictors of treatment failure for diabetic foot infections: data from a prospective trial. Int Wound J 2007; 4:30-38.
10. Waked IS, Nagib SH. Efficacy of hyperbaric oxygen therapy in the treatment of vasculitic skin ulcers in systemic lupus patients.

Bull Fac Ph Th Cairo Univ 2010; 15:77-85.

11. Reddy V, Dziadzio M, Hamdulay S, Boyce S, Prasad N, Keat A. Lupus and leg ulcers–a diagnostic quandary. Clin Rheumatol 2007; 26:1173-1175.
12. Grossberg EB, Scherschun L, Fivenson DP. Ulcerating plantar keratoderma in association with systemic lupus erythematosus. Lupus 2001; 10:650-652.
13. Labropoulos N, Manalo D, Patel NP, Tiongson J, Pryor L, Giannoukas AD. Uncommon leg ulcers in the lower extremity. J Vasc Surg 2007; 45:568-573.
14. Spentzouris G, Labropoulos N. The evaluation of lower-extremity ulcers. Semin Intervent Radiol 2009; 26:286-295.
15. Riaz M, Miyan Z, Zaidi SI, Alvi SF, Fawwad A, Ahmadani MY, *et al*. Characteristics of a large cohort of patients with diabetes having at-risk feet and outcomes in patients with foot ulceration referred to a tertiary care diabetes unit. Int Wound J 2016; 13:594-599.
16. Chen IW, Yang HM, Chiu CH, Yeh JT, Huang CH, Huang YY. Clinical Characteristics and Risk Factor Analysis for Lower-Extremity Amputations in Diabetic Patients with Foot Ulcer Complicated by Necrotizing Fasciitis. Medicine (Baltimore) 2015; 94:e1957.
17. Jiang Y, Wang X, Xia L, Fu X, Xu Z, Ran X, *et al*. A cohort study of diabetic patients and diabetic foot ulceration patients in China. Wound Repair Regen 2015; 23:222-230.
18. Fei YF, Wang C, Chen DW, Li YH, Lin S, Liu GJ, *et al*. Incidence and risk factors of amputation among inpatients with diabetic foot. [Article in Chinese] Zhonghua Yi Xue Za Zhi. 2012; 92:1686-1689.
19. Sun JH, Tsai JS, Huang CH, Lin CH, Yang HM, Chan YS, *et al*. Risk factors for lower extremity amputation in diabetic foot disease categorized by Wagner classification. Diabetes Res Clin Pract 2012; 95: 358-363.
20. Jeon BJ, Choi HJ, Kang JS, Tak MS, Park ES. Comparison of five systems of classification of diabetic foot ulcers and predictive factors for amputation. Int Wound J 2016; doi: 10.1111/iwj.12642.
21. Hingorani A, La Muraglia GM, Henke P, Meissner MH, Loretz L, Zinszer KM, *et al*. The management of diabetic foot: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J VascSurg 2016; 63(Suppl 2):3-21.
22. Kerr M. Foot care for people with diabetes: the economic case for change. Newcastle-upon-Tyne: NHS Diabetes. [http://bit.ly/xjY7FS].
23. Moxey PW, Gogalniceanu P, Hinchliffe RJ, Loftus IM, Jones KJ, Thompson MM, *et al*. Lower extremity amputations – a review of global variability in incidence. Diabet Med 2011; 28:1144-1153.
24. Kröger K, Moysidis T, Feghaly M, Schäfer E, Bufe A. Association of diabetic foot care and amputation rates in Germany. Int Wound J 2016; 13:686-691.
25. Pütter C, Stausberg J, von Beckerath O, Reinecke H, Schäfer E, Kröger K. Determinants of decreasing major amputation rates in Germany. Vasa 2016; 45:311-315.
26. Abbas ZG, Archibald LK. Challenges for management of the diabetic foot in Africa: doing more with less. Int Wound J 2007; 4:305-313.
27. Viswanathan V, Rao VN. Managing diabetic foot infection in India. Int J Low Extrem Wounds 2013; 12:158-166.
28. Prompers L, Schaper N, Apelqvist J, Edmonds M, Jude E, Mauricio D, *et al*. Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease. The EURODIALE Study. Diabetologia 2008; 51:747-755.
29. O'Meara S, Cullum N, Majid M, Sheldon T. Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration. Health Technol Assess 2000; 4:1-237.
30. Yu J, Lu S, McLaren AM, Perry JA, Cross KM. Topical Oxygen Therapy Results in Complete Wound Healing in Diabetic Foot Ulcers. Wound Repair Regen 2016; doi: 10.1111/wrr.12490.
31. Martinson M, Martinson N. A comparative analysis of skin substitutes used in the management of diabetic foot ulcers. J Wound Care. 2016; 25 (Suppl 10):8-17.
32. Zelen CM, Serena TE, Gould L, Le L, Carter MJ, Keller J, *et al*. Treatment of chronic diabetic lower extremity ulcers with advanced therapies: a prospective, randomized, controlled, multi-centre comparative study examining clinical efficacy and cost. Int Wound J 2016; 13:272-282.
33. Rice JB, Desai U, Ristovska L, Cummings AK, Birnbaum HG, Skornicki M, *et al*. Economic outcomes among Medicare patients receiving bioengineered cellular technologies for treatment of diabetic foot ulcers. J Med Econ 2015; 18:586-595.
34. Gulati A, Botnaru I, Garcia LA. Critical limb ischemia and its treatments: a review. J Cardiovasc Surg (Torino). 2015; 56:775-785.
35. Bolia A. Subintimal angioplasty in lower limb ischaemia. J Cardiovasc Surg 2005; 46: 385-394.
36. Gandini R, Pipitone V, Stefanini M, Maresca L, Spinelli A, Colangelo V, *et al*. The "Safari" technique to perform difficult subintimalinfragenicular vessels. Cardiovasc Intervent Radiol 2007; 30:469-473.
37. Spinosa DJ, Harthun NL, Bissonette EA, Cage D, Leung DA, Angle JF, *et al*. Subintimal arterial flossing with antegrade-retrograde intervention (SAFARI) for subintimal recanalization to treat chronic critical limb ischemia. J VascInterv Radiol 2005; 16:37-44.
38. Graziani L, Silvestro A, Monge L, Boffano GM, Kokaly F, Casadidio I, *et al*. Transluminal angioplasty of peroneal artery branches in diabetics: initial technical experience. Cardiovasc Intervent Radiol 2008; 31:49-55.
39. Manzi M, Fusaro M, Ceccacci T, Erente G, Dalla Paola L, Brocco E. Clinical results of below-the knee intervention using pedal-plantar loop technique for the revascularization of foot arteries. J Cardiovasc Surg (Torino) 2009; 50:331-337.
40. Fusaro M, Dalla Paola L, Brigato C, Marangotto M, Nicolini S, Rripay R, *et al*. Plantar to dorsalispedis artery subintimal angioplasty in a patient with critical foot ischemia: a novel technique in the armamentarium of the peripheral interventionist. J Cardiovasc Med 2007; 8:977-980.
41. Monteiro-Soares M, Dinis-Ribeiro M. A new diabetic foot risk assessment tool: DIAFORA. Diabetes Metab Res Rev 2016, 32:429-435.