Diabetic Foot Disease and its Management

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Introduction

Diabetic foot ulcer (DFU) without treatment and regular review will progress from an ulcer to an infection (1). An estimated 10-15% of people with diabetes will have a DFU at some point in their lives. More than 80% of the amputations in patients with diabetes are due to DFU. This makes diabetes the most common cause of non-traumatic limb loss greatly impacting the quality of life of patients and their families. It is associated with major morbidity and mortality (2).

National Institute for Clinical Excellence (NICE) recognized the need for detailed and structured guidelines to be applied across all the National Health Service (NHS) areas that care for patients with DFD (2). The main aim of this guideline was to avoid variation in clinical practice both in primary and secondary care and to ensure adequate training and expertise is available when managing these patients.

The guidelines may also help standardize the non-surgical care of DFU in a multi-disciplinary (MDT) diabetes foot clinic setting. It also looks at different aspects of the care from conservative management using dressings to assessing the risk and management of infections (2). When there has been a delay in seeking medical review of affected foot lesion, it has resulted in a 25-50% risk of immediate amputation by the first clinical encounter with the health professionals (3).

Background

Diabetes is a serious chronic metabolic disease. The prevalence has increased from 108 million in 1980 to 422 million in 2014. The World Health Organization (WHO) estimates a 114% increase during the next 20 years leading to the emergence of 330 million new cases. The International Diabetes Federation (IDF) estimated that the total global health-care spending on diabetes has more than tripled over the period from 2003 to 2013. This was due to the increase in those affected and, as a result, an increase in spending per capita on diabetes. Beyond the financial costs, diabetes was the direct cause of 1.6 million deaths globally in 2015 (5,6).

Poor diabetes management was associated with micro and macro-vascular complications such as nephropathy, neuropathy, and retinopathy that damage vital organs and the development of foot ulcers that could result in lower extremity amputations (7). DFU has received more attention because of the high rates of amputation and mortality (8).

In addition to the physical and psychological costs to the individual, the societal costs of diabetes care are staggering. In 2011, the cost to the NHS (UK) was almost £10 billion. This formed 10% of the total NHS budget and most of this cost (80%) was spent on managing avoidable complications. When indirect costs, which included potential loss of productivity due to sickness for example, were added, the cost increased to £23.4 billion (9).

Foot disease in Diabetes

This disease is defined as a “foot affected by ulceration that is associated with neuropathy and/or peripheral arterial disease (PAD) of the lower limb in a patient with diabetes” (10). If the ulcerated lesion affects the toes and if it is not treated adequately, it may lead to toe necrosis and gangrene (11) and eventual amputation. Overall, it is estimated that approximately 50-70% of all lower limb amputations are due to diabetes (12). In England, approximately 60,000 people with diabetes present with DFU annually and the rates of recurrence of foot ulcers are greater than 50% after three years (13). The five-year mortality rate for these patients is around 50% (12).

DFD poses a significant economic problem, particularly if amputation results in prolonged hospitalization, rehabilitation, and an increased need for home care and social services input (14). In 2014-15, the annual cost to the NHS was estimated at £1 billion; this is in addition to the high personal and social costs (£972m–£1.130bn) of reduced mobility and sickness absence which is equivalent to 0.7–0.8 percent of the entire NHS budget (12). As primary care clinicians, we need to make our patients aware of these risks to prevent ulcer formation in the first place, and once affected by ulcers, to prevent their recurrence.

An infected foot is the outcome of progressive vascular and neurological damage caused by persistent chronic hyperglycaemia. Additionally, peripheral diabetic neuropathy is present in almost 100% of these patients (12).

Due to acute hypoxia and infection, the tissues develop an ulcer which may lead to extensive necrosis and gangrene often requiring amputation if left untreated (15). With dry gangrene, blood supply is impaired to the affected area due to peripheral vascular disease (PVD); consequently, the tissue dries up and a well-demarcated area is noted often leading the affected area of the digit to auto-amputate eventually (16). Infection is usually not present with dry gangrene; but when present, the lesion progresses to wet gangrene which, if it is not treated rapidly, can spread and lead to sepsis. This makes wet gangrene a very serious and potentially life-threatening condition (17).

There are two main types of conditions leading to ulceration: neuropathic and neuro-ischaemic foot (18). This classification by Pecoraro et al. (1990) was published in 1990 but it is still relevant to current day practice as explored by both papers of Dalla Paola et al. (2006,2015) (19, 20):

1. Neuropathic foot develops ulceration at the sites of high mechanical pressure usually on the plantar surface. It is usually difficult to treat these ulcers due to the loss of protective sensitivity to pain and the weakening of the intrinsic foot muscles giving rise to foot deformity. Therefore, insults and infection proceed rapidly.

2. Neuro-ischaemic foot has both neuropathy and ischaemia. It develops ulcers on the margins of the foot and toes often at sites of pressure from poorly fitted shoes. This pressure is unperceived by patients because of a coexisting neuropathy.

In a systematic review of available literature published between 1980 and 2003, Jupiter et al. (2016) examined the role of foot ulceration on mortality. They identified common risk factors for death in patients presenting with foot ulceration and amputation which were: increased age, male gender, peripheral vascular disease and renal disease (21, 22). Shahbazian et al. (2013) identified statistically significant risks for DFU (22) with similarities to Jupiter et al.'s paper (2016) (21). Patients in the higher-risk groups in Shahbazian et al.'s paper (2013), had higher age, longer diabetes duration, retinopathy, and higher HbA1C (p=0.0001, 0.001, 0.005, 0.0001 respectively) (22). However, patients' gender and nephropathy risks were different between the two papers (21, 22). Yazdanpanah et al. (2015) described localized contributors for ulcer formation including peripheral neuropathy which can cause local trauma leading to the formation of the ulcer. General reasons included uncontrolled hyperglycaemia, as an example (23).

Management of established DFD

NICE in its latest guidance focused on the importance of managing the causes which lead to amputation such as uncontrolled infection. It highlighted the important role the multi-disciplinary diabetic foot clinic plays in the prevention and the management of DFD and DFU (2).

To examine clinical outcome of the care provided by the MDT foot clinic, the relevant literature that explored different treatment options available for the management of a DFU as well as the necrotic toe were reviewed. A structured search was carried out using OVID/MEDLINE, Google scholar, and the Web of Science databases looking for cohort studies, conference abstracts, systematic reviews or case reports, and clinical trials on the management of infected and/or necrotic toe in a diabetic foot. The searches were limited to studies published in English between 2000 and 2016, on adult humans over 18 years old, diagnosed with T1DM or T2DM.

The key words used included: necrotic toe, auto-amputation, T1DM, T2DM, gangrene, dry gangrene, diabetic foot, and amputation. In total, 192 papers were identified in OVID and an additional 170 papers from Google scholar and PubMed combined. Web of Science search yielded no results. Out of the 192 papers from Ovid, only 30 were suitable for this project; another 35 from Google scholar/PubMed included the key words. Treatment options for this patient population were divided into conservative management, antibiotics therapy, surgical management, and auto-amputation. Below is a brief description of each option.

Conservative management:
Appropriate ulcer dressing is an essential part of foot care once ulcers are established. The choice of the dressings depends on the characteristics of the ulcer but the main aim is to alleviate symptoms such as pain, provide wound protection, and to encourage healing. Non-adhesive dressings are simple, inexpensive, and well tolerated. Foam and alginate adhesive dressings are highly absorbent and are effective in heavily exuding ulcers. For DFU treatment, non-adhesive dressings usually fulfil all the requirements (24, 25).

Snyder et al. (2014) sought to develop a consensus statement for the use of offloading in the management of DFU. They found that off-loading was important but they recognised the difficulty in applying this in clinical practice usually due to the lack in patient adherence to the use of the offloading devices (26). This is a common problem encountered by those who treat DFU in primary as well as in secondary care. The use of a non-removable cast has recently been shown to be a more effective treatment choice than a half-shoe for the management of plantar neuropathic ulcers.

This is important when making recommendation to patients who may develop plantar ulcer to prevent the progression to infection or necrosis (20). Simple offloading techniques may include casts and boots, sandals, half shoes, or felted foam dressings. In a systematic review and meta-analysis of offloading methods for the treatment of DFU, Elraiyah et al. (2016) found that benefits were demonstrated when total contact casting and irremovable cast walkers were used. The results of this review were based on low quality evidence and they found that the risk of bias in the included studies was moderate; so results should be interpreted cautiously (27).

A substantial number of patients with diabetes are often elderly who may suffer from peripheral neuropathy and/or PVD and who may have difficulty accessing medical care. These patients are at a higher risk of foot ulceration and would benefit from preventive foot care such as appropriate footwear, especially as some are frail with multi co-morbidities. When ulcers occur, early and effective conservative management is critical because surgical intervention in these patients, if required, may not be possible due to this complex profile (28).

Management with antibiotics therapy:
Infections in the feet of patients with diabetes are common, complex and costly (29). Infections may spread rapidly leading to an overwhelming tissue destruction and amputation which is why 85% of amputations are usually preceded by an ulcer (20). The International Working Group on the Diabetic Foot (IWGDF) recognised the lack of published guidelines and recommendations for the treatment of DFU despite the large number of infections and complications. Therefore, they published their guidelines at the last International Symposium in 2004 (20).

Infections of DFU can be classified into mild, moderate, or severe. This classification, along with a vascular assessment, helps determine which patient should be hospitalized, which may require special imaging or surgical interventions, and which will require amputation (30). Most diabetic foot infections (DFIs) are poly-microbial with aerobic gram-positive cocci (GPC), especially staphylococci, being the most common causative organism. Aerobic gram-negative bacilli are frequently co-pathogens in infections that are chronic. This can also occur following repeated antibiotic treatment. Obligate anaerobes may be co-pathogens in ischaemic or necrotic wounds (30).

Fungal communities found in chronic wounds can form mixed bacterial-fungal biofilms. This can be associated with poorer outcomes and longer healing times and may lead to complications such as bone infection and amputation. Up to 80% of the infected DFI harboured the fungi with no single species being responsible (31).

Post-debridement specimen should be collected for aerobic and anaerobic culture from infected wounds. Empiric antibiotic therapy can be narrowly targeted at GPC in acutely infected patients, but those at risk of infection with antibiotic-resistant organisms or with chronic, previously treated, or severe infections usually require broader spectrum regimens (30, 32). NICE guidance supports this approach (2). The primary goal remains to expedite complete healing; secondary goals include the avoidance of superimposed infection, repeated hospitalisations, and subsequent amputations (33).

Due to the overuse of antibiotics, the fact that poor infection control procedures enable resistant organisms to spread, and the ability of the bacteria to mutate, antibiotics resistance has reached a critical point, especially since no new types of antibiotics are being developed (34). Antimicrobial stewardship defined as “an organisational or healthcare system wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness” is critical and the responsibility of each provider. This emphasis on stewardship was introduced due to the emergence of antimicrobial resistance and the loss of effectiveness of the current available therapies (35).

Surgical Management

Most DFIs require some surgical intervention ranging from debridement to amputation (30). Following the first amputation, patients are twice as likely to have a subsequent amputation (19, 36). The rate of complications and of mortality appeared to be greater the more proximal a surgeon needs to go to amputate. As such, when a minor amputation of a toe and part of the corresponding metatarsal bone (ray amputation) was removed, it seemed to carry a lower mortality rate when compared to below knee amputation (BKA) (37, 38).

In a retrospective study by Evans et al. (2011), eighty percent of the minor amputees were still alive after two years, and sixty four percent were fully mobile compared to the BKA group. Fifty two percent of BKA died within two years and only sixty four percent of patients were mobile with a prosthetic limb (38).

In a population-based survey carried out between 1982 and 2006, Svensson et al. (2011) reported that they were able to avoid major amputation in almost two-thirds of the patients who already underwent minor amputations. However, these patients had prolonged healing process. Despite this, sixty-four percent of all amputations and seventy-eight percent of amputations in surviving patients healed at a level below the ankle (39).

The Eurodiale study (2011) was a large prospective cohort multi-center study carried out in different European centers. It involved a total of 1,232 patients with new DFU who were followed regularly until healing, death, or major amputation occurred up to a maximum of one year. A small number of patients (18%) underwent minor amputation, which was a procedure frequently carried out in these centers. However, a variation was noted in terms of the triage system and when the amputation was performed which depended on the center’s assessment of the depth

of the ulcer, PAD, and infection (40). This may suggest that early referral to the foot clinic can prevent minor amputations and emphasized the need for an organized approach to the management of a DFU, which is an issue that NICE has highlighted in their current guidelines (2, 40).

Auto-amputation

Patients with diabetes undergoing surgery have greater complication rates, higher mortality rates, and prolonged length of hospital stay (41) with peri-operative mortality rates of up to 50% greater than those without diabetes (42). A few studies found that smokers, older patients with longer history of uncontrolled diabetes, and those with gangrenous infections and large ulcers have poorer outcome with amputations in general (43-45). Due to all these factors, an alternative to surgical amputation with less impact on the patient and less associated complications may be advantageous. Auto-amputation may possibly be this alternative.

Auto-amputation is the "spontaneous separation of non-viable tissue from viable tissue, and is usually associated with dry gangrene, occurring in the distal portions of the lower extremities" (46). Fikri et al. (2011) showed positive outcome when auto-amputation was offered in the management of a dry well-demarcated gangrenous toe (5). This was the first paper to describe this practice. The authors cited two papers (Levy et al.(1962) and Bronzini et al. (1962)) discussing case reports of patients with evidence of successful auto-amputation of the 5th necrotic toe (47). The literature search was unable to find RCT or systematic review to support this choice of treatment. However, weaker evidence from case reports were identified.

In a case managed by Boffeli et al. (2015), a neuropathic DFU affecting plantar hallux interphalangeal joint area was successfully managed by resecting the ulcer and aggressively treating the infection before it spread, followed by offloading. This resulted in complete healing of the ulcer with the avoidance of hallux amputation and the patient was ulcer free for six years (48).

Looking specifically at available literature on the use of auto-amputation for the management of a necrotic toe, there was a case report from India. An elderly patient with poorly controlled diabetes, presented with dry gangrene affecting both feet. Over the subsequent 18 months, she was managed conservatively as she was unwilling to consent for surgical intervention, resulting in the loss of the right foot and digits on the left foot. In this case, the gangrene was limited to below the knee area and did not result in her death (46).

MDT Clinical Management

"Tell Me and I Will Forget; Show Me and I May Remember; Involve Me and I Will Understand." Confucius (14)

The importance of educating patients, especially through involving them in their care, is paramount in achieving a successful outcome. Historically, Laffon in 1885 and Pryce in 1887 were the first to describe cases of DFU due to neuropathy (49). Until the 1980s, uncontrolled infections, "salami" procedures, major amputations and deaths were alarmingly common (50).

A retrospective study carried out between1981 and 1995 in Copenhagen, found a 75% reduction in the incidence of major amputations. This coincided with a sevenfold increase in revascularization procedures, such as infra-popliteal arterial bypass, being introduced for the treatment of critical lower limb ischaemia and the establishment of a MDT foot clinic. This has suggested that these measures were important in the prevention of leg amputations due to diabetes (51).

Rönnemaa et al. (1997) found that patients who were seen by a podiatrist had a statistically significant improvement in knowledge of diabetic foot care ($P = 0.004$), self-care ($P < 0.001$), and improvements in the prevalence of some minor foot problems such as callus formation when compared with the control group (52).

In the 1980's, great developments in foot care were taking place, including establishing MDT diabetic foot clinics and the publishing of the international consensus on the care of the diabetic foot by IWGDF(36). On the World Diabetes Day in 2005, IDF launched a year-long campaign with the slogan "Put Feet First: Prevent Amputations" (14).

There has been a long-standing interest in the role of MDT in achieving optimal outcomes for patients with DFU. Employing multidisciplinary foot teams' expertise in wound management in terms of appropriate dressings, the provision of the necessary footwear to allow adequate off-loading of pressure to the affected wound, and patients regular follow-up in the clinic have improved outcome for these patients (30). NICE supports this approach and incorporated this into their guideline (2).

In May 2017, the podiatry Clinic relocated from Hamad General Hospital (HGH) to its new facility at the Ambulatory Care Centre (ACC) in Doha, Qatar. A specialist Diabetic Foot and Wound Care Clinic was also set up within this clinic. This provided outstanding care for all patients with lower extremity and diabetic wound needs, using the most advanced techniques. Between May and September 2017, around 6,400 patients were seen, at a rate of 80 to 100 patients each day. The main goal of all the services provided by this clinic was to enable patients to live a healthy life and prevent wherever possible any re-occurrence of the condition being treated (53).

Conclusions

DFD with its disabling effects and the high mortality rate is an important disease to be aware of, treat, and try to prevent. The number of patients with diabetes are increasing and presenting with more and more complications of the disease with some being unsuitable to undergo surgical procedure due to their multiple co-morbidities. To ensure continuity of care and regular follow up, especially in these high-risk patients, utilization of the outpatient appointments is deemed necessary as part of the patient's commitment.

References

1. Ibrahim A. IDF Clinical Practice Recommendation on the Diabetic Foot: A guide for healthcare professionals. Diabetes Res Clin Pract. 2017;127:285-7.
2. National Institute for Health and Care Excellence, (NICE). NG19: Diabetic foot problems: prevention and management. . 2015.
3. Leone S, Pascale R, Vitale M, Esposito S. Epidemiology of diabetic foot. Infez Med. 2012;20(Suppl 1):8-13.
4. Chuah LL, Papamargaritis D, Pillai D, Krishnamoorthy A, le Roux CW. Morbidity and mortality of diabetes with surgery. Nutricion hospitalaria. 2013;28(2):6713.
5. Diabetes [Internet].; 2017 [updated 15 November; cited 28/02/2018]. Available from: http://www.who.int/en/news-room/fact-sheets/detail/diabetes.
6.World Health Organization. GLOBAL REPORT ON DIABETES. . 2016.
7. Mantovani AM, Fregonesi CE, Palma MR, Ribeiro FE, Fernandes RA, Christofaro DG. Relationship between amputation and risk factors in individuals with diabetes mellitus: a study with Brazilian patients. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2017;11(1):47-50.
8. Wang C, Mai L, Yang C, Liu D, Sun K, Song W, et al. Reducing major lower extremity amputations after the introduction of a multidisciplinary team in patient with diabetes foot ulcer. BMC endocrine disorders. 2016;16(1):38.
9. Hex N, Bartlett C, Wright D, Taylor M, Varley D. Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. Diabetic Med. 2012;29(7):855-62.
10. Alexiadou K, Doupis J. Management of diabetic foot ulcers. Diabetes Therapy. 2012;3(1):4.
11. Issa AA, Newman M, Simman R. Toe necrosis, etiologies and management, a case series. Journal of the American College of Clinical Wound Specialists. 2013;5(2):26-35.
12. Diabetic Foot Care should be a priority for every CCG in the country. [Internet].; 2017 [].
13. Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. The Lancet. 2005;366(9498):1719-24.
14. Das AK, Joshi SR. Put Feet First: Prevent Amputations-Diabetes and Feet. JOURNAL-ASSOCIATION OF PHYSICIANS OF INDIA. 2005;53(V):929.
15. Uysal S, Arda B, Taşbakan MI, Çetinkalp Ş, Şimşir IY, Öztürk AM, et al. Risk factors for amputation in patients with diabetic foot infection: a prospective study. International wound journal. 2017;14(6):1219-24.
16. Gangrene: Causes, Symptoms, and Treatments [Internet]. [cited Mar 11, 2018]. Available from: https://www.webmd.com/skin-problems-and-treatments/guide/gangrene-causes-symptoms-treatments.
17. Gangrene [Internet].; 2016 [cited 01/03/2018]. Available from: https://www.webmd.com/skin-problems-and-treatments/guide/gangrene-causes-symptoms-treatments#1.
18. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation: basis for prevention. Diabetes Care. 1990;13(5):513-21.
19. Dalla Paola L, Faglia E. Treatment of diabetic foot ulcer: an overview strategies for clinical approach. Current diabetes reviews. 2006;2(4):431-47.
20. Dalla Paola L, Carone A, Vasilache L, Pattavina M. Overview on diabetic foot: a dangerous, but still orphan, disease. European Heart Journal Supplements. 2015;17(suppl_A):A68.
21. 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. International wound journal. 2016;13(5):892-903.
22. Shahbazian H, Yazdanpanah L, Latifi SM. Risk assessment of patients with diabetes for foot ulcers according to risk classification consensus of International Working Group on Diabetic Foot (IWGDF). Pakistan journal of medical sciences. 2013;29(3):730.
23. Yazdanpanah L, Nasiri M, Adarvishi S. Literature review on the management of diabetic foot ulcer. World journal of diabetes. 2015;6(1):37.
24. Hilton JR, Williams DT, Beuker B, Miller DR, Harding KG. Wound dressings in diabetic foot disease. Clinical Infectious Diseases. 2004;39(Supplement_2):S103.
25. Moura LI, Dias AM, Carvalho E, de Sousa HC. Recent advances on the development of wound dressings for diabetic foot ulcer treatment—a review. Acta biomaterialia. 2013;9(7):7093-114.
26. Snyder RJ, Frykberg RG, Rogers LC, Applewhite AJ, Bell D, Bohn G, et al. The management of diabetic foot ulcers through optimal off-loading: building consensus guidelines and practical recommendations to improve outcomes. J Am Podiatr Med Assoc. 2014;104(6):555-67.
27. Elraiyah T, Prutsky G, Domecq JP, Tsapas A, Nabhan M, Frykberg RG, et al. A systematic review and meta-analysis of off-loading methods for diabetic foot ulcers. Journal of vascular surgery. 2016;63(2):68S. e2.
28. Kumar S, Ashe HA, Parnell LN, Fernando D, Tsigos C, Young RJ, et al. The prevalence of foot ulceration and its correlates in type 2 diabetic patients: a population-based study. Diabetic Med. 1994;11(5):480-4.
29. Hinojosa CA, Boyer-Duck E, Anaya-Ayala JE, Nunez-Salgado A, Laparra-Escareno H, Torres-Machorro A, et al. Impact of the bacteriology of diabetic foot ulcers in limb loss. Wound Repair and Regeneration. 2016;24(5):923-7.
30. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clinical infectious diseases. 2012;54(12):e173.
31. Fungi contribute to delayed healing of chronic wounds [Internet]. [cited Feb 27, 2018]. Available from: https://www.sciencedaily.com/releases/2016/09/160906103144.htm.
32. Lipsky BA, Berendt AR. Principles and practice of antibiotic therapy of diabetic foot infections. Diabetes Metab Res. 2000;16(S1).

33. Frykberg R, Martin E, Tallis A, Tierney E. A case history of multimodal therapy in healing a complicated diabetic foot wound: negative pressure, dermal replacement and pulsed radio frequency energy therapies. International wound journal. 2011;8(2):132-9.
34. Infectious Diseases Society of America, (IDSA). Combating antimicrobial resistance: policy recommendations to save lives. Clinical Infectious Diseases. 2011;52(suppl_5):S428.
35. Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use | Guidance and guidelines | NICE [Internet].: NICE [cited Apr 10, 2018]. Available from: https://www.nice.org.uk/guidance/ng15/chapter/1-Recommendations.
36. Apelqvist J, Bakker K, Van Houtum WH, Nabuurs-Franssen MH, Schaper NC. International consensus and practical guidelines on the management and the prevention of the diabetic foot. Diabetes Metab Res. 2000;16(S1).
37. Izumi Y, Satterfield K, Lee S, Harkless LB, Lavery LA. Mortality of first-time amputees in diabetics: a 10-year observation. Diabetes Res Clin Pract. 2009;83(1):126-31.
38. Evans KK, Attinger CE, Al-Attar A, Salgado C, Chu CK, Mardini S, et al. The importance of limb preservation in the diabetic population. J Diabetes Complications. 2011;25(4):227-31.
39. Svensson H, Apelqvist J, Larsson J, Lindholm E, Eneroth M. Minor amputation in patients with diabetes mellitus and severe foot ulcers achieves good outcomes. J Wound Care. 2011;20(6):261-74.
40. Van Battum P, Schaper N, Prompers L, Apelqvist J, Jude E, Piaggesi A, et al. Differences in minor amputation rate in diabetic foot disease throughout Europe are in part explained by differences in disease severity at presentation. Diabetic Med. 2011;28(2):199-205.
41. Barker P, Creasey PE, Dhatariya K, Levy N, Lipp A, Nathanson MH, et al. Peri-operative management of the surgical patient with diabetes 2015. Anaesthesia. 2015;70(12):1427-40.
42. Frisch A, Chandra P, Smiley D, Peng L, Rizzo M, Gatcliffe C, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. Diabetes Care. 2010;33(8):1783-8.
43. Lipsky BA, Berendt AR, Deery HG, Embil JM, Joseph WS, Karchmer AW, et al. Diagnosis and treatment of diabetic foot infections. . 2014.
44. Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggesi A, Bakker K, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. Diabetologia. 2007;50(1):18-25.
45. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic). Circulation. 2006;113(11):e654.
46. Fikri R, Bicknell CD, Bloomfield LM, Lyons SP, Samarasinghe DG, Gibbs RG, et al. Awaiting autoamputation: a primary management strategy for toe gangrene in diabetic foot disease. Diabetes Care. 2011;34(8):e134.
47. Kaushik R, Sree SB, Attri AK. Spontaneous auto-amputation of the foot in a case of diabetes, atherosclerosis and gangrene. J Indian Med Assoc. 2002;100(9):573-4.
48. Boffeli TJ, Hyllengren SB. Unilobed Rotational Flap for Plantar Hallux Interphalangeal Joint Ulceration Complicated by Osteomyelitis. The Journal of Foot and Ankle Surgery. 2015;54(6):1166-71.
49. Pendsey S. Diabetic Foot Infections. Contemporary Management of the Diabetic Foot. 2013:87.
50. Foster A. Changes in the care of the diabetic foot: part two. Practical Diabetes. 2001;18(5):165-9.
51. Holstein P, Ellitsgaard N, Olsen BB, Ellitsgaard V. Decreasing incidence of major amputations in people with diabetes. Diabetologia. 2000;43(7):844-7.
52. Rönnemaa T, Hämäläinen H, Toikka T, Liukkonen I. Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. Diabetes care. 1997 Dec 1;20(12):1833-7.
53. https://www.marhaba.qa/around-80-patients-podiatry-clinic-treated-diabetic-ailments/