"The foot in perspective"

Jan Apelqvist MD, PHD Diabetic Foot Centre , University hospital of Malmö , University of Lund, S-205 02 Malmö Sweden ; Jan.Apelqvist@skane.se

Abstract

The diabetic foot constitutes a tremendous challenge for patients, care givers and health care system and the International consensus document of 1999 was a milestone in the recognition of the importance and consequences of the diabetic foot. Since then there have an impressive number of original papers published. There is now a time to consider the present situation and future development after the presentation of the second International Consensus Document of the Diabetic Foot and the 5th European conference of the Diabetic foot
Large cohort studies have given us a deeper understanding regarding factors related to outcome in case of a diabetic foot ulcer. According to those studies the severity of diabetic foot ulcers is greater than previously reported more than 50% of individuals with foot ulcer having signs of infection at admission and one-third with both peripheral artery disease and infection. Co morbidity increasing significantly with increasing severity of foot disease. The trend in all these studies is a successive improvement in healing rate (50-60% at 20 wks, >75% at one yr). It is important to differentiate between neuropathic and neuroischemic ulcers with regard to factors related to outcome and co morbidity
Recent research has emphasized the importance of psychological factors in the development and outcome of diabetic foot ulcers. Studies have shown that perceptions of their own risks based on symptoms, and their own beliefs in the efficacy of self-care can affect foot-care practice.
The importance of health care organization and reimbursement should not be underestimated in the prevention and management of diabetic foot disease.
The Diabetic foot should be considered a life long condition since when developing an ulcer the patient is always in high risk of developing a new ulcer and the condition is related to substantial co morbidity with high mortality and future risk of amputation. In an individual with diabetes and foot ulcer the ulcer should be considered as a sign of multi organ disease and a holistic approach in management and prevention is recommended

Introduction

: Large clinical studies of diabetic foot ulcers describing the typical clinical presentation and factors related to outcome were limited before 2000 (1-15). Today the EURODIALE study (4-5) and other large cohort studies have given us a deeper understanding regarding factors related to outcome (6-15). According to those results in mostly European cohorts, the severity of diabetic foot ulcers at presentation is greater than previously reported. More than 50% of diabetic patients with foot ulcer had signs of infection at admission/arrival to a hospital based multidisciplinary foot team, 50% of ulcers being of neuroischemic origin and one-third of the patients with foot ulcer had signs of both PAD and

infection(3-4). Presence of diabetic foot ulcer is associated with an. extensive co morbidity that increased significantly with severity of foot disease.(3-15))

The trend in all these recent studies is a successive improvement in healing rate (50-60% at 20 wks, >75% at one yr) compared to older studies. In mixed cohort studies primary healing rates of 65-85 %, amputation rates of 10-20% (irrespective of level) and mortality rates of 10-20% respectively have been described (3-15). However when interpreting these studies and their result it is of utmost importance to recognize differences in design , patient selection , definitions and follow up time and other confounding factors:

Factors of importance when evaluating outcome of diabetic foot ulcer

•Foot ulcer-definition, type, site
•Population-hospital, clinic, area based
•Prevalence of diabetes
•Method-Clinical investigation-Screening-Medical Records-Survey
•Drop out rate-clinical investigation-self reported-survey
•Definition of healing
•Mortality
•Observation time
-Co morbidity
-Treatment strategies and resources

Non-plantar foot ulcers being more common than plantar ulcers, especially in patients with severe disease. Plantar for foot ulcer being the most commonly studied ulcer in clinical trials but constitutes only 20-25% of foot ulcers in large cohort studies (4-8,).Factors related to outcome of these neuropathic ulcers have been related to initial size of ulcer, duration of ulcer (9-11, 16-17) at admission/start of treatment and probing/exposure of bone with a high probability for infection (Osteitis, deep abscess). Most previous studies being single center hospital based retrospective cohort studies based on medical records with a limited observation period compared to more recent studies with consecutively recruited patients followed and defined according to preset criteria/protocol with a follow up time for 6 months or longer (4-17). Drop out rate in trials between 15-25% and in cohort studies often not known or presented (4-17). Definition of healing (usually intact skin with or without follow up) varies between studies according to design or definition. Definition of outcome (healing, amputation, death) can be very complex as shown in a model modified from Jeffcoate (6):

Various outcomes of diabetic foot ulcer in cohort studies

•Alive, healed without amputation
•Alive, persisting ulcer without amputation
•Alive, healed with amputation (minor/major)

•Alive, persisting ulcer following amputation
•Alive, Drop out with/without amputation
•Alive healed index ulcer with/without amputation-new ulcer
•Died unhealed with or without amputation
•Died, healed without amputation
•Died, healed after amputation (minor/major)

One key factor in many studies is if patients deceased unhealed are included or not and if a distinction between minor or major amputation is described. It has to be recognized that in many health care systems there are limited possibilities to follow patients until healing is achieved.. When amputation is used as marker for quality (usually major amputation) of care or outcome in studies it is important to know which indications have been used since amputation as a procedure can be used for various reasons. (18) It has to be recognized according to consensus (1-3)) that a non healing ulcer per se is not considered a primary indication for amputation.

Factors related to outcome

Most interventional studies are performed in neuropathic foot ulcer were improvement at 4 wks strongly correlates to outcome at 12 and 20 wks of observation (11, 16, 17). Today the expected healing rates in trials of neuropathic foot ulcers up to 20 wks should be 55-60 % according to recent data especially when strict off loading strategies are maintained indicating substantial improvement in basic care/control arms in recent studies. (3, 7-8, 12–15)
The recent large cohort studies indicate the importance to recognize the presence of co morbidity since they are strongly related to outcome. This was illustrated by findings from two large (1,200-2,500 patients) recently presented cohort studies (4-5, 7)

Factors related to outcome of foot ulcer-healing

- **Duration of diabetes**
- **No Heart Disease**
- **No end stage renal disease**
- No severe Eye Disease
- **No Claudication**
- **Toe Pressure >45 mmHg**
- **Wagner gr 1-2 vs 3**
- **Wagner gr 1-3 vs 4-5**
- Single vs multiple
- **Oedema**

- Annersten M et al 2007

- **Duration of Diabetes**
- Female- Sex
- **No severe Congestive heart failure**
- **No end stage renal disease**
- **No Peripheral Artery Disease**
- **Superficial vs deep ulcer**
- Plantar vs dorsal ulcer
- Size , Depth of ulcer
- **Oedema**
- **Neurological Disorder (CVI)**
- **Limited Walking capacity**

- Pompers L et al 2007 (Eurodiale)

These studies show the importance of co morbidity like cardiovascular disease, end stage renal disease, severity of PAD, extent of tissue involvement and oedema related to outcome (primary healing and healing with or without minor amputation respectively) The findings from these studies support observations that co morbidity is strongly related to outcome with regard to healing but that condition of the wound and local characteristics are more related to wound healing time. It is further of importance to recognize the difference between neuropathic and neuroischemic or ischemic foot ulcer.

Peripheral Artery Disease

Signs of peripheral arterial disease can be found in more than half of the patients with a foot ulcer (European cohort 3-5, 7). Studies performed in neuroischemic/ischemic show an improved/increased intervention rate as well healing rate ,an increased awareness of angioplasty to achieve healing in a diabetic foot ulcer and that co morbidity as well as tissue loss/involvement at intervention is strongly related to outcome i.e. probability of healing (19-23) It is essential to identify patients with foot ulcer and PAD with non invasive vascular techniques to avoid delay in possibility for angioplasty since majority of diabetic patients with foot ulcer and severe Pad do not have rest pain or claudication (3,5,6,8,23)But still we have a limited number of interventional studies in neuroischemic /ischemic ulcers compared to studies of wound treatment in neuropathic ulcer.

Infection

Infection is seldom the direct cause of an ulcer. However, once an ulcer is complicated by an infection, the risk for subsequent amputation is greatly increased. In a study by Lavery et al (24) factors related to development of a wound infection were duration of ulcer >30 days, recurrent ulcer, trauma, probing to bone and co existent PAD, In presented studies the outcome of deep foot infection has been related to extent of tissue involved, co morbidity and co existing peripheral vascular disease (3,25). In the EURODIALE study more than 50% of patients with a foot ulcer received antibiotics prior to admission to a diabetic foot center/clinic and 25-75% of patients at various centers were considered to have a wound infection at time of admission.(4-5) These finding is especially disturbing in a time of MRSA , multiresistent microbes and debate of “bioburden” and “biofilms” . Still the choice of antimicrobial treatment is empiric and most studies of antibiotics in diabetic foot infection include skin infection only and not ulcers with superficial/deep infection (3) these studies are further designed only to prove that the test drug is comparable to the control drug and not necessary more effective. The lethal combination of infection and

severe peripheral vascular disease in case of diabetic foot ulcers has to be recognized (4-5, 13)

Quality of life, attitudes and beliefs of health and illness

Recent research has emphasized the importance of psychological factors and quality of life in the development and outcome of diabetic foot ulcers.
•Decreased physical ,emotional and social function in patients with diabetic foot disease is well known (26-36).People with foot ulcer and amputations often suffer from depression and have reduced quality of life (27,30,36). Social isolation, poor education and low socio-economic status place people with diabetes at higher risk of foot problems due to limited access to care.(26-28) Studies have shown that perceptions of their own risks based on symptoms, and their own beliefs in the efficacy of self-care can affect foot-care practice and concordance by the patient (26-34). Risk of amputation increases when people with diabetes are socially isolated
Beliefs and expectations about health and illness relating to diabetes and the diabetic foot have to be taken into account when preventing and managing foot problems (31, 32, 33.34, and 37) as illustrated below:

Emotions as barriers to care –beliefs about heath and illness

- Frustration and anger
- Depression
- Fear of amputation
- Do not experience symptoms
- Reduction in physical activity
- Devices make the existence of medical problem obvious to other people
- Embarassment
- Males vs females
- Ethnicity

These factors are of utmost importance since only 56% of ulcers are detected by the patient him/herself and in 25% the patient denies the existence of the ulcer (31-33, 37-38) Patients with foot ulcer are often considered as non compliant not recognizing that, people with foot ulcers have a more”negative attitude” towards their feet, have limitations in daily living, leisure activities and employment, have attitudinal differences towards his/her disease. This attitude towards health and illness varies between men vs. woman, according to ethnic background, and economical circumstances (26-36). People with

diabetes who believe that pain is a reliable symptom of foot ulceration are less likely to seek foot care or follow advice

As a consequence a holistic approach has been recommended that allows the practitioner to look beyond the physical presentation of a wound to assess the patient as a whole when formulating management plans with the patient and to consider the importance of balance both within the person and between the person and his/her environment (39-41)
Multidisciplinary management has been associated with improved healing rate and reduction of amputation rate in comparative studies.(42-43) But there are studies that show no or unchanged incidence of diabetes related amputations (44-48)

Who is to blame?

- Day 0 foot ulcer recognized by home care
- Day 3 dressings-primary care nurse
- Day 8 Antibiotics prescribed by GP
- Day 23 Pain killers prescribed by GP
- Day 34 Gallbladder dysfunction - Department of Surgery
- Day 43 Change of antibiotics,pain killers prescribed,distal blood pressure performed
- Day 52 acute foot infection-Dep of infectious disease
- Day 58 returned home , Letter to vascular Surgeon
- Day 73 gangrene-Dep orthopedic surgery
- Day 74 Aortofemoral angiography performed
- Day 75 Femoro-distal by pass (pedal arch)
- Day 86 Amputation-partial foot

Management of the diabetic according to guideline-based care is cost-effective and even cost saving compared with standard care (51-54)Optimal foot care alone is cost-effective at levels of preventive foot care if a reduction of incidence of ulcer or amputation >25-40% is achieved (51-53)
The conclusions from these studies were that the management of the diabetic foot according to present guidelines would result in improved survival and a reduced number of diabetic foot complications. In addition, it would be cost-effective or even cost saving compared to standard care. However in many health care systems today management of ulcers are reimbursed but preventive strategies to avoid foot lesions or ulcers are not reimbursed (Podiatric care ,Shoes, Patient Education , Screening for high risk feet;54-55)Reimbursement are more favorable to perform an amputation than strategies to save a limb (54,56-57).
. In recent years, a number of reports have indicated the cost-effectiveness of different new technologies and dressings used for the treatment of diabetic foot

ulcers. Although many of these products are more expensive than the compared standard treatment, the use of them may be cost- effective if they result in less frequent dressing changes and/or if they result in more effective and faster healing (54). It is important to be aware that a treatment could be cost-effective in one group of patients or for one type of ulcers but not in another type. An intervention could also be cost-effective when used in one setting or country but not in another (54)

Long term outcome

The Diabetic foot should be considered a life long condition since when developing an ulcer the patient are always in high risk of developing an new ulcer (58) . There are limited data regarding long term outcome and development of new ulcers. But in some small studies of patients with previous neuropathic ulcers comparing patients with recurrent ulcers factors similar to those when developing a new foot ulcers (59) ie metabolic control , severity of neuropathy , previous ulcer , previous amputation were related to a high probability for recurrence.(60,61)
In a recent large mixed (neuropathic and neuroischemic ulcers)cohort study of more than 1,200 individuals with a healed index ulcer 32% with a previous foot ulcer developed an new a ulcer within one year of observation and 45% developed an new a ulcer within two year of observation (62%)
Patients with a new ulcer had shorter wound duration compared to their original index ulcer indicating increased awareness to seek care more early with their new ulcer. The cumulative mortality and amputation rate during 5 years was substantial indicating the importance of recognizing the diabetic foot ulcer as a sign of multiple cardiovascular diseases and the need for life long surveillance of the diabetic foot at risk

Conclusion

It can be concluded that there is a complexity of factors related to outcome of foot ulcers in patients with diabetes mellitus, and evaluating and recognizing these factors as well as a holistic approach is of utmost importance both for successful management and prevention.
With the present knowledge of factors related to short and long term outcome and development of more advanced technologies in wound healing we should be able to have more selective intervention strategies.
Future studies based on the type. Site, cause and condition of the wound as well as co morbidity have to recognize the different factors related to outcome and wound healing time between neuropathic and neuroischemic ulcers
It is important to recognize the importance and influence that local/regional health care organizations and reimbursement systems influences both management and prevention.

1. Schaper NC, Apelqvist J, Bakker K. The international consensus and practical guidelines on the management and prevention of the diabetic foot. Curr Diab Rep 2003;3(6):475-9
2. International Working Group on the Diabetic Foot. International consensus on the diabetic foot and Practical guidelines on the management and prevention of the diabetic foot. Amsterdam: IWGDF, 1999.
3. International Consensus on the Diabetic Foot and Practical Guidelines on the Management and the Prevention of the Diabetic Foot. International Working Group on the Diabetic Foot, 2007, Amsterdam, the Netherlands, on CD-ROM (www.idf.org/bookshop).
4. Prompers L, Huijberts M, Apelqvist J, Jude E, Piagessi A, Bakker K, Edmonds M, Holstein P, Jirkovska A, Mauricio D, Ragnarson Tennvall G, Reike H, Spraul M, Uccioli L, Urbancic V, van Acker K, van Baal J, van Merode F, Schaper N) High prevalence of ischemia, infection and serious co morbidity in patients with diabetic foot disease in Europe. Baseline results from the EURODIALE study. Diabetologia 2007.50:18-25
5. Prompers L, Huijberts M, Apelqvist J, Jude E, Piagessi A, Bakker K, Edmonds M, Holstein P, Jirkovska A, Mauricio D, Ragnarson Tennvall G, Reike H, Spraul M, Uccioli L, Urbancic V, Van Acker K, Van Baal J, Van Merode F, Schaper N () Optimal organization of health care in diabetic foot disease: introduction to the Eurodiale study. Int J Low Extreme Wounds 2007: 6:11-17