

Predictors of Outcome in Diabetic Foot: A Narrative Review

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ABSTRACT

Background: Diabetes is a life-changing disease associated with the severe morbidity and also mortality. Among the diabetic patients, the prevalence of foot ulcers will usually be as high as 20%. These ulcers usually become infected, cause very high morbidity, and are the usual first step for lower extremity amputation. The holistic care of diabetic foot ulcers requires a multidisciplinary approach. Apart from blood sugar control, treatment of ulcer involves wound debridement, appropriate dressings, vascular maintenance, and control of infections. The most important factor in preventing amputation is a repeated education of the patient in foot care and to really look into factors associated with amputation. This review article is an attempt to identify the statistically significant risk factors leading to lower extremity amputation.

Materials and methods: The research literature was searched for various studies reporting the risk factors for lower extremity amputation in patients with DFI. A systematic search of literature was conducted first in MEDLINE/PubMed and then in Cochrane Central Register of Controlled Trials till July 2019. This search retrieved 11 most relevant articles. The risk factors that led to LEA were studied and data were analyzed.

Results: Based on the comparison, we have concluded that male preponderance, duration of diabetes, and vasculopathy were found to be statistically significant in majority of the studies.

Keywords: Diabetic foot infection, Diabetic foot ulcer, Lower extremity amputation, Peripheral arterial disease.

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INTRODUCTION

The prevalence of diabetes mellitus (DM) is rising dramatically at present.¹ The World Health Organization has proclaimed an estimated number of patients with diabetes was nearly 425 million in 2017 and consequently, increasing the number of diabetes-related complications.² These complications have led to a decrease in quality of life and increase in financial costs, morbidity, and even mortality. The development of foot ulcers, one of the dominant complications of diabetes mellitus, is 15–25%.³ Diabetic foot ulceration is a major cause of nontraumatic lower extremity amputations.⁴ Exceeding number of diabetic foot ulcers undergoes infection, which paves way for higher amputation rates in the diabetes population.⁵ Hence, diabetic foot infections (DFIs) account for greater hospitalization and limb loss and thus have a compelling effect on quality of life.⁶ Diagnosis and management of infection in the foot are crucial because of expanded prevalence and the concern toward health in diabetic patients. Consequently, familiarity toward factors that cause exposure is essential to establish diagnosis along with management and protocols for treating and prevention of the lower extremity amputation for patients with DFIs.⁷ Multiple risk factors for lower extremity amputation in patients with diabetes have been explored, like peripheral arterial disease (PAD), peripheral neuropathy and osteomyelitis, and the correlated morbidities. Despite certain factors remain unclear those which are vital and to a limit for which they escalate the risk of amputation.⁸ In spite of the published research on multiple risk factors for the lower extremity amputations associated to DFI, none has been analyzed methodically in a meta-analysis. So this study reassesses multiple causes, which advance to lower extremity amputation in patients with diabetic foot.

MATERIALS AND METHODS

The research literature was searched for studies reporting risk factors for lower extremity amputation in patients with DFI. The literature was searched in a systematic order conducted first

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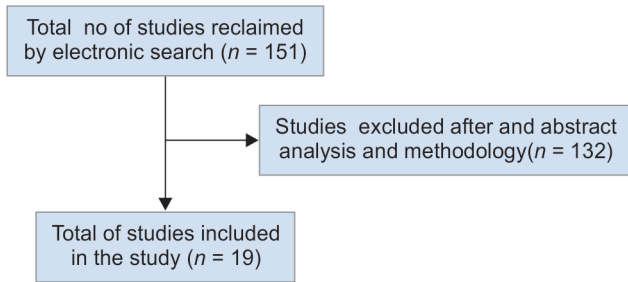
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in the MEDLINE/PubMed and later in Cochrane Central Register of Controlled Trials till December 2019. Strategies of the search included related keywords for the three concepts: “diabetic foot,” “infection,” and “lower extremity amputation.” This search retrieved 20 most relevant articles. They were taken into account in the review if it satisfied the forthcoming selection criteria: (i) theme: studies that estimated the relation between the variables (clinical data or diagnostic tests results) and DFU; (ii) type of study: cross-sectional studies; (iii) results: studies must end if no statistically relevant relationship between independent variables and DFU.

Study Selection

Appropriate articles for the narrative review were the studies over the risk factors for amputation in patients with DFI. Principle result variables comprised of minor and major amputations. Cross-sectional studies were only included. We also screened the reference lists of selected studies manually for the applicable articles. Articles were excluded if include studies without complete text, studies without assessment of risk factors for amputations, or with evaluations of diabetic foot ulcers. Every risk factors that were mentioned in the included study were analyzed in present study.



The various risk factors which were studied included age, duration of diabetes, ABPI, neuropathy, nephropathy, vasculopathy, hyperlipidemia, HbA1c, smoking, and bone involvement.

In our study, among 100 diabetic foot ulcer patients, 40 were managed conservatively and 60 underwent amputation (both minor and major). The various risk factors which led to lower extremity amputation were studied.

DISCUSSION

Age Distribution

Association of age with diabetic foot ulcer has been evaluated ($n = 11$), despite results are somewhat conflicting. Armstrong et al.⁹ in an RCT, established that younger patients being at higher risk, while four other studies^{3,10-12} with consecutive patient selection achieved the opposite (older patients presented with higher risk). Two other studies^{3,12} found a relation between age and active or recently healed DFU, with a lower age representing higher risk. In opposition, two studies^{10,11} concluded that for an active DFU history, a higher age represented a higher risk. Of the four studies^{3,11,12} that reported an association between age and DFU history, one concluded with greater than 75 years had greater risk.¹⁰

In our study, the mean age was in the fifth decade.

Diabetes Duration

All the studies reported a relation between diabetes of duration more than 10 years and the risk of LEA.

In our study also, among the amputated group, 70% had diabetes more than 5 years and p value was found to be statistically significant.

Ankle-brachial Index

In five studies, ankle-brachial pressure index less than 0.3 was associated with lower extremity amputation.^{2,6,7,9,11,13} Among three studies, ankle-brachial pressure index of 0 was associated with lower extremity amputation.^{4,5,8} In our study, however, in the amputated group, 44% had ABPI more than 0.8.

Neuropathy

This risk factor was found to be statistically significant in 4 out of 11 studies and was significantly associated with lower extremity amputation.^{3,4,6,7} Armstrong et al.⁹ declared by reporting the presence of single or multiple symptoms (numbness, burning, or tingling) had a sensitivity of an average of 100% to detect active or recently healed DFU. In our study, in the amputated group, 48% had neuropathy.

Vasculopathy

All reports proved a statistically important relation with lower extremity amputation. Peripheral pulses were examined clinically and then using a hand-held doppler. In our study, among the

amputated group, 60% did not have peripheral pulses and p value was found to be statistically significant.

Nephropathy

Half of the studies^{4,6,7,10,11,13} established a correlation of nephropathy with diabetic foot amputation. In our study, there was no statistical significance between nephropathy and lower limb amputation.

Hyperlipidemia

Only one study¹³ evaluated its association with LEA as the association was not statistically important. In our study also, there was no statistical significance between hyperlipidemia and lower extremity amputation.

HbA1c

Mostly studies assessing its association with DFU development showed that higher values marked a higher risk.^{3-6,8,9,11,13} In our study, among the amputated group, 60% had HbA1c of more than 10.5 and it was not statistically significant.

Smoking

We chose eight studies assessing its relation with DFU; still, only two studies proved statistically significant results showing a higher prevalence of amputation in current smokers.^{8,9} In our study among the amputated group, 64% were smokers and it was not statistically significant.

Mehmood et al. of Pakistan in his paper about clinical profile and management results of diabetic foot ulcer in a tertiary care hospital determined that out of 120 patients, majority of patients who underwent lower limb amputation ended up to be type II diabetic patients (95.7%), males (66%) with a duration of diabetes of more than 10 years ($p < 0.05$). The mean age was 54.29 ± 7.71 years.¹²

Al-Maskari et al. studied the prevalence of factors which accounts for diabetic foot complications. Out of the 513 diabetic patients (a mean age of 53 years), 12% had peripheral vascular disease. Significant risk factors were male gender, increased duration of diabetes, and presence of hypertension.¹⁴

Diabetic foot ulcers revascularize when possible and improve the flow of blood and aid wound healing. Amputation is also prevented by proper education of the diabetic patients, foot care, and appropriate footwear. This was proved by Casselini et al. in his paper on "Approach to the diabetic foot."¹⁵

Van Damme et al. studied proved that PVD is a major factor for amputation. PVD is not only involves the distal pulses but also fully involves femoral, popliteal, and tibial pulses. It can be treated by open or endovascular surgical procedures. Also Charcot's neuroarthropathy is specific for complication of neuropathy, which leads to fragmentation and destruction of the bones and joints.¹⁶

The article of infection and diabetic foot by Alwakeel et al. found that the end result of preexisting foot wound whose chronic nature is aggravated by the factor, such as, neuropathy and PVD, which is factor of bad outcome, regarding the risk for leg amputation.¹⁷

A case-control study over risk factors for toe amputation in a diabetic population by Deshpande et al. shows that obvious risk factors for toe amputation were male sex, osteomyelitis, digital deformity, diabetic nephropathy, diabetic neuropathy, and ischemia.¹⁸

Formosa et al. had elaborated that prevalence of infection was 6-11% in amputation and 3% in study group of 1,319. Neuropathy was significant factor leading to amputation (15%).¹⁹

Dalla Paola et al. discovered the separate effects of PVD, sensory neuropathy, and foot ulcer in the diabetic patients with lower extremity amputation. His study revealed that peripheral sensory neuropathy, PVD foot ulcers, and former amputation were the independent risk factors for LEA.²⁰

CONCLUSION

Based on the results, we have concluded that the maximum incidence of diabetic foot ulcers in the fifth decade of life and men are most commonly affected. Age of the patients (most common in 5th decade), duration of diabetes more than 5 years, and vasculopathy are statistically significant risk factors for LEA in most of the studies. Statistically important of associated complications like neuropathy, smoking, and osteomyelitis could not be determined. The study gives details for primary care and expert practitioners to seek for diabetic patients at increased risk for lower extremity amputation. Among the risk factors for LEA mentioned in our study, smoking, alcohol, and PVD are preventable factors.

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