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# An Analysis Of The Characteristics Of People With Type 2 Diabetes At Risk For Developing Diabetic Foot Problems

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***Abstract:***

*The diabetic foot problems, which are a significant consequence of having diabetes mellitus, are connected with a great load on individual patients as well as on the health care systems itself. It is vital to identify risk variables via large longitudinal studies in order to enhance early diagnosis and individualised screening of individuals who are at elevated risk. This is because preventative efforts have the potential to lower the occurrence of this problem. We carried out a retrospective cohort research utilising data from 10,688 individuals with type 2 diabetes mellitus who were less than 18 years old. The study was based on a registry. Cox regression models were used in order to identify risk variables for foot problems while also accounting for any confounding factors. In our patient group, we found a total of 140 cases of diabetic foot problems. According to the findings of a multivariate Cox regression model, neuropathy, peripheral vascular disease, and the presence of male gender are all positively related with foot issues. The similar impact was seen for nephropathy in the time period of more than ten years following a diagnosis of type 2 diabetes. On the other hand, a negative correlation was shown when accounting for a greater age at diagnosis and the usage of insulin. Patients with type 2 diabetes mellitus were shown to have an increased likelihood of developing future first foot issues, and male gender and various diabetes-related comorbidities were found to be risk factors for these complications. Based on these data, it seems that it may be possible to do individualised early identification of people who are at elevated risk by using information on demographics, medical history, and comorbidities.*

***Keywords: Diabetic Foot, Real-World Data, Risk Factors, Type 2 Diabetes Mellitus***

## Introduction:

The condition known as diabetes mellitus (DM) is one of the most significant issues facing public health all over the globe. It has been estimated that there are presently 463 million individuals aged 18–99 years old who are afflicted with diabetes mellitus, and it is anticipated that this figure will climb to almost 700 million people by the year 2045. The increasing incidence of diabetes may be attributed to factors such as an ageing population, expanding populations, and changes in lifestyles. [1–3] Patients with

diabetes are at a greater risk for developing future bad health disorders, which may be linked with severe morbidity, reduced life expectancy, and increased costs connected with medical treatment. [2,4] The occurrences of such late problems are growing at the same rate as the number of diabetic patients, which means that the two trends are related. Up to 25 percent of individuals who have diabetes may, at some point in their lives, experience the diabetic foot syndrome (also known as DF), which is considered to be one of the most serious late consequences. [5] out of these patients will need to have their lower extremities amputated, which means that someone loses a lower limb as a result of a DF every 20 seconds around the world. [7] According to the International Working Group on the Diabetic Foot (IWGDF), the DF syndrome, which encompasses several diagnoses such as foot ulcers, Charcot foot and lower extremity amputations, is defined as "Infection, ulceration, or destruction of tissues of the foot of a person with currently or previously diagnosed diabetes mellitus, usually accompanied by neuropathy and/or peripheral arterial disease in the lower extremity." This definition of the DF syndrome encompasses several different diagnoses, including According to the findings of several comprehensive research conducted all over the world, problems associated with 8 DF are linked to an increased risk of death. [9–11] The problems are also linked to a worse quality of life, which is connected with enormous increases in medical care expenses. [2,4] That will become larger with time. 13 Patients who have diabetes foot ulcers have healthcare expenses that are five times greater than diabetic patients who do not have foot complications. As a result, diabetic foot ulcers and amputations are the most costly diabetic late complication in terms of hospital costs.

On the other hand, there is evidence that foot ulcers may be avoided to a large extent. In the context of public health, the identification of the function of risk factors as a means of facilitating the early diagnosis of individuals at high risk for later foot difficulties is an essential component in the prevention of diabetic foot (DF) issues. [17] In a recent and extensive systematic analysis, the following findings about risk factors for diabetic foot complications in individuals with type 2 diabetes were compiled: An insulin use history, being male, having diabetes for a longer period of time, having poorer glycemic control, being taller, smoking, having neuropathy, retinopathy, or nephropathy, as well as using insulin, was found to have a relatively consistent positive association with subsequent DF development. On the

other hand, outcomes such as age, hypertension, dyslipidemia, and body mass index were obtained with varying degrees of consistency. In spite of the fact that this systematic review adhered to predetermined and severe inclusion and exclusion criteria, there was still a significant amount of variation across the included studies with respect to the research designs and the patient groups. [18] This heterogeneity and the inconsistencies in the results of the included studies highlight the need for further research on risk factor profiles for DF in different regions of the world. This will assist in the improvement of prevention and early detection strategies, which will increase the quality of life for patients while simultaneously reducing the financial burden on the public health system. [19] The need of using cutting-edge preventive and treatment methods for diabetic foot ulcers in order to lower the high amputation incidence was stressed by the International Working Group on Diabetic Foot Ulcers (IWGDF).

Using data collected from a large number of patients who were diagnosed with type 2 diabetes mellitus (T2DM), the authors of this study sought to determine which factors are associated with an increased risk for subsequent diabetic foot complications in order to help clinicians better treat their patients. Data from the Diabetes Registry of Tyrol (DRT) were used in order to accomplish this goal.

**Literature Review:**

Patients who have diabetes are at a significantly increased risk of acquiring major adverse health issues, which may result in a shortened life expectancy, a decrease in the quality of life, and an increase in the expenditures associated with medical treatment. The diabetic foot syndrome (also known as diabetic neuropathy and peripheral artery disease) is a significant late consequence of diabetes that is closely linked to both conditions. Necrosis of the tissues may lead to the necessity for amputation of the lower extremities (LEA). 1 Diabetes foot (DF) is defined as "infection, ulceration, or destruction of tissues of the foot of a person with currently or previously diagnosed diabetes mellitus, usually accompanied by neuropathy and/or peripheral arterial disease in the lower extremity" by the International Working Group on the Diabetic Foot (IWGDF). Foot complications are experienced by about one quarter of all diabetic patients at some point over the course of their condition. People who have diabetes are more likely to be hospitalised due to this illness, which was responsible for over 70 percent of all amputations performed in the United States in 1997. In addition,

diabetic foot ulcers (FU) and ampu-tations are the most costly kind of diabetes late complication when it comes to the expenditures incurred by hospitals. Patients with diabetes who have FUs have healthcare costs that are five times greater in the year after their first FU compared to patients with diabetes who do not have FUs, and these costs are roughly three times higher in the years that follow. In 2007, issues related to the feet accounted for one-third of the total expenditures associated with diabetes. Patients with diabetes who suffer from foot ulcers have a 10-20 times greater risk for amputation compared to those who do not have diabetes. Additionally, foot ulcers are related with a higher mortality risk compared to patients who do not have foot complications. The number of diabetic patients who need a lower leg amputation in high-income nations is around one percent, but the ratio is greater in low- and middle-income countries. Patients who have a previous history of problems related to DF are at an increased risk of developing re-ulcerations in the future.

DF problems are one of the most significant and avoidable diabetes late consequences. This is particularly true when they are accompanied by severe complications and the need for amputations. In addition to the efforts that have been made to perform routine foot exams and the development that has been made on risk categorization systems, there is a need to improve both preventive and early detection approaches. An additional required component of the prevention would be the creation of risk factor profiles that would enable the patients who were at an increased risk for foot disease to be identified.

**Material S and Methods:**

Since its founding in 2006, the Diabetes Research Team (DRT) has had the overarching mission of assessing and enhancing the level of medical care provided to diabetic patients in the state of Tyrol. Data are gathered in ten collaborating hospital locations, which comprise all of Tyrol's hospitals, as well as eight outpatient offices of internal medicine experts. Patients with newly diagnosed T1DM, T2DM, and gestational diabetic mellitus, as well as patients with prevalent diabetes who visit an outpatient department, are gathered in the DRT. Also included are patients with prevalent diabetes who have previously attended. Following the completion of a thorough clinical evaluation during the first visit at one of the participating facilities, patients are extended an invitation to return for further sessions on a quarterly basis. This registry gathered information on almost 24,000 diabetes patients up to the year

2019, when it was closed. [22,23] The registration is carried out inside the hospital's information systems, which include demographic data, clinical and biochemical indicators connected to diabetes, and data on late complications associated to diabetes. [23] After going through the pseudonymization process, the data are sent to the DRT. This enables the linking of data for a certain patient who has been enrolled in many departments and ensures that data confidentiality is maintained.

The retrospective cohort research followed the principles outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) document while developing its methodology and writing up its findings. [27] For the patient group that was going to be considered for inclusion in the analysis, the following inclusion criteria were defined: (1) an established diagnosis of type 2 diabetes; (2) a known year of diabetes diagnosis; (3) a patient's age at the time of diagnosis that was at least 18 years old; (4) no present or prior foot ulcer at the first visit of a patient in the registry; (5) patients with complete data sets concerning relevant demographic and clinical data that were considered potential risk factors for diabetic foot; Patients suffering from other forms of diabetes, such as type 1 diabetes or diabetes related to pregnancy, as well as patients who were younger than 18 years old at the time of diagnosis, were not included in this study. The study included the years 2006 through 2019, and it contained data from those years.

**Data Analysis:**

While the proportions of the categorical variables were given, the means and standard deviations of the continuous variables were used to characterise the data. The Chi square (2) test and the Mann–Whitney U test were used to compare the variables of the cohort of patients with DF to the variables of the cohort of patients without DF. These tests were used for categorical variables using the Chi square (2) test, and they were used for continuous variables using the Mann–Whitney U test. p-Values.

In order to investigate the relationship that may exist between probable risk variables and later DF problems, a Cox regression analysis was carried out. In order to do this, the amount of time that passed between the first diagnosis of diabetes and the occurrence of DF was calculated, and the conclusion of the follow-up period was regarded as the censoring event. At this point in time, the data were shortened since there were only 170 patients who had a follow-up length of more than 35 years. This represents 1.6

percent of all patients. The proportional hazard assumption, also known as PHA, was analysed via the use of two graphical methods (visual examination of log-log curves and fit of a univariate Cox regression model to the empirical survival curves) in addition to a test that was based on Schoenfeld residuals. In the case of nephropathy, stroke, and HbA1c, PHA guidelines were found to have been violated. In order to address these inconsistencies, a Heaviside function was implemented. This function split the follow-up period into two categories: before and after 10 years after a diagnosis of type 2 diabetes for nephropathy, and before and after 15 years for smoking and stroke.

After determining the association between each potential risk factor and the development of a foot complication in a univariate model, a time-dependent multivariate Cox model was established by employing a backward elimination method. This model was used to determine the likelihood of developing a foot complication. In line with the Akaike information criterion, the crucial alpha values for the removal of variables were selected (AIC). 30 An alternative Cox model was constructed using a forward selection method by therefore incorporating all risk variables with pvalues. This was done so that the robustness of the Cox model could be evaluated.

**Results:**

Out of a total of 23,593 patients, 10,688 were considered eligible for participation in the study because they met the criteria that had been established in advance. Figure 1 depicts a flow diagram of the patient selection process for your reference. The total mean age at diagnosis was 63.21 years old (SD), and 44.3% of those diagnosed were female. In all, there were 140 DF occurrences that took place over the course of a mean follow-up duration of 9.75 years. The characteristics of the study population at the beginning of the research are shown below. Patients who experienced a DF complication were found to be less likely to be female than male (30.0 percent vs. 44.5 percent), and they had a higher level of HbA1c (8.3 percent [SD 1.7] vs. 7.7 percent [1.5]) compared to patients who did not experience a DF event. Patients who did not experience a DF event also had a lower level of HbA1c. In addition, people with DF examined their feet more often than those without the condition. When compared to individuals who did not have any DF events, people who did have DF were more likely to have recorded instances of using insulin or insulin analogues. Concerning additional late

sequelae connected to diabetes, previous diagnoses of nephropathy, retinopathy, neuropathy, myocardial infarction, stroke, and peripheral arterial disease or coronary bypass/PTCA were more commonly present in the group of individuals with diabetic foot ulcers (DF). On the other hand, there was not a statistically significant difference between the two groups in terms of age at diagnosis, smoking status, level of physical activity, body mass index (BMI), hypertension, or involvement in education programmes.

**Figures and Tables:**

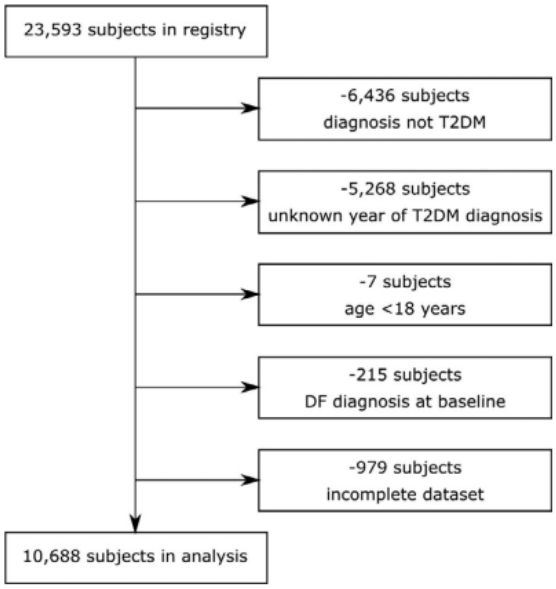


*Figure 1: Consort diagram showing patient selection. Abbreviations: DF, diabetic foot; T2DM, type 2 diabetes mellitus*

**Discussion:**

The need for a better knowledge of this late consequence is vital for the prevention of it. Considering the enormous personal and financial hardship associated with foot issues in patients with type 2 diabetes, this requirement is especially important. In a community of people with type 2 diabetes who had no history of foot problems, we carried out a large retrospective cohort study that was based on a registry. According to the findings of this research, the prevalence of DF was found to be 1.31 percent, which is a result that falls within the ranges that have been previously recorded for European nations (1.7–4.8 percent). In spite of this, it is possible that this is the result of the fact that all patients who had foot issues present at the initial visit recorded in the registry were omitted from the study in order to ensure that information gathered before to DF diagnosis was the only data included.

In the multivariate Cox model, the presence of male gender was shown to be a significant predictor for DF. If we compare male patients to female patients, we find that the recognised risk of developing DF is practically twice in male patients. Numerous more investigations also came to the same conclusion about the impact they saw. This impact may be explained, at least in part, by the greater foot pressure reported in male patients.

This finding is most likely attributable to the higher mean height of males in comparison to women. 40 In addition, it is common knowledge that women are more proactive when it comes to self-care and preventative care for diabetic foot lesions, whilst males tend to take a more passive approach to these issues. A protective effect against the development of DF has been observed to exist when there is a higher age (i.e. with increasing age at diagnosis, the hazard of foot ulcer was found to decrease). This impact was not only detected when comparing an age at diagnosis of more than 70 years to an age at diagnosis of less than 50 years, but it was also seen when comparing an age at diagnosis of between 51 and 70 years to an age at diagnosis of less than 50 years. Abbott et al. and Dekker et al. reported a negative association between age and foot ulcer development (hazard ratio 0.957 and odds ratio 0.991 for every year increase, respectively), and Yang et al. identified the same relationship when analysing lower extremity amputation as the endpoint of interest (odds ratio 0.8 for age 65 years compared to younger age groups). Additionally, other groups reported a negative association between higher age and various endpoints related 43 The data on the possible relationship between age and DF are very conflicting, which was brought to light in two recent systematic studies on risk factors for the development of DF. Several sets of researchers found a positive correlation between older age and a variety of outcomes, such as foot ulcers and lower limb amputations. Other groups of researchers did not detect any association between the two factors. There are many ideas that attempt to explain the protective impact of an older age at the time of diagnosis, including the following: It's likely that elderly individuals whose illness has progressed to a point where it has rendered them immobile are underrepresented in the register. This would be one potential reason. Because of the bias introduced by this selection process, it is possible that the older patient groups who are represented in the register are those that are in better health. In addition, Dekker and colleagues postulated that younger patients, who tend to engage in more strenuous physical activity than older patients, are more likely to experience stressful circumstances, which in turn raises the likelihood of developing foot ulcers. However, further research is required in order to get a more in-depth understanding of the association between age and the development of DF.

**Conclusion:**

In order to evaluate the connection between the numerous possible risk factors and the following first development of DF

problems in patients with T2DM, we carried out a large retrospective cohort research using data from previous examinations. The results of our research demonstrated that there is a statistically significant link between DF and neuropathy, peripheral vascular disease, nephropathy, and the usage of insulin or insulin analogues. In addition, demographic factors such as age at the time of diagnosis and gender have been shown to have a significant impact in the development of DF risk. Accordingly, we propose that making information publicly accessible on the demographic data, medical history, and comorbidities of patients may allow tailored screening. In order to evaluate whether or whether a reduction in the number of preexisting risk factors results in a reduction in the number of eventual foot issues in patients with type 2 diabetes, large longitudinal studies are required.

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