



STUDY OF SURGICAL MANIFESTATIONS OF DIABETIC FOOT PATIENTS AND VARIOUS FACTORS INFLUENCING IT

*Dr. Mikail Merchant, Dr. Dnyanesh Belekar and Dr. Hansel Misquitta

Dept of General Surgery, Terna Medical College & Hospital, Nerul, Navi Mumbai

ARTICLE INFO

Article History:

Received 13th January, 2020

Received in revised form 11th

February, 2020

Accepted 8th March, 2020

Published online 28th April, 2020

Key words:

Diabetic, Foot, Neuropathy, Ulcer, Edema, Debridement

ABSTRACT

Background: Diabetics have foot pathologies that are secondary to neuropathy and microvascular changes. They are at increased risk of Surgical manifestations such as infection, ulceration, trauma (sometimes trivial), etc. that can lead to a collapse of the foot, also called Charcot neuroarthropathy. To improve future prognosis of these manifestations, one has to understand the sequel/pattern of their occurrence and the factors influencing them so as to provide a targeted therapeutic approach to them accordingly, which will also prevent future complications.

Material & Method: A Retrospective study on a cohort of 30 patients was carried out post approval of the institutional scientific and research committee, between 1st January – 31st December 2019 in which data collection was done regarding Surgical foot manifestations and their influential factors in Diabetic patients attending the Surgical Out patient Dept. as well as In patient Dept. admitted patients within the specified time frame at Terna Hospital and Research Centre, Navi Mumbai and was documented with statistical evidence.

Results & Conclusion: Based on the result of our study and interpreting it in the context of available literature on the subject, we reached the following conclusions: Edema was the most common surgical manifestation of diabetic foot followed by infections & ulcers. These were most commonly seen in patients of low socioeconomic status. Hypertension was the most common co-morbidity along with Diabetes Mellitus nephropathy and Neuropathy following it and risk factors being duration of uncontrolled Diabetes Mellitus being greater than three years, peripheral neuropathy & pre-existing wounds/abscess.

Copyright © 2020 Dr. Mikail Merchant, Dr. Dnyanesh Belekar and Dr. Hansel Misquitta. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

A Diabetic Foot is a foot that exhibits any pathology that results directly from Diabetes Mellitus or any long term (or “chronic”) complications of Diabetes Mellitus. In today’s patient set up, a practicing General Physician or Surgeon witnesses various surgical manifestations in a patients diabetic foot, such as Edema, Numbness, Wounds, Ulcers, Gangrene, and infections, both superficial and some even deep involving bone (Osteomyelitis). These surgical manifestations may end up leading to further complications such as Neuropathic Arthropathy, Sepsis, or even surgical amputation secondary to Gangrene, etc.

Diabetic foot complications and associated co-morbidities in diabetic patients affect them physically, mentally, and physiologically as it contributes to both mortality and morbidity. It also seems to influence the community at large by creating a financial burden for the patients, relatives and health care facilities with estimations showing that 24.4% of total health care expenditure in the diabetic patient population is related to diabetic foot complications¹³; with the United States of America spending nearly 11 billion USD¹⁴ for their treatment and the United Kingdom spending up to 456 Million USD¹⁵. Foot ulceration is one of the preventable conditions seen, with patients being at risk of about 25%¹⁶ at developing it, ultimately accounting for 2/3rd for all non-traumatic amputations. Simple measures and interventions can reduce

risk of amputations by up to 70% through programs that could possibly reduce various risk factors¹⁷. Therefore, understanding the sequence of occurrence of these surgical manifestations and their complications along with bringing about appropriate therapy to control risk factors and other treatment modalities significant to the stage of the following diseases’ progression would help in better disease prognosis and overall improvement of the patients’ health.

Aims and Objectives

1. To study the incidence of surgical manifestations in the foot of diabetic patients.
2. To study patterns of complication occurrence in Diabetic Foot.
3. To study various Therapeutic modalities offered to the patients

MATERIALS AND METHODS

The following study was conducted after obtaining due permission from the Institutional Scientific and Ethics Committee.

Study Site: Patients attended Surgical Out-patients department and who were admitted in Surgical Wards for management of Diabetic Foot at a Tertiary Care Medical Institute in Navi Mumbai, Maharashtra.

*Corresponding author: Dr. Mikail Merchant

Dept of General Surgery, Terna Medical College & Hospital, Nerul, Navi Mumbai

Study Population: Both Males and Females between the age 18 to 80 years.

Study Design: The following was a retrospective study on patients admitted and post discharge with the follow up of at least 2 weeks.

Sample Size: 30 patients – 24 Males, 06 Females.

Time Frame to address the study: The Study was conducted tentatively from January 1st, 2019 to December 31st, 2019.

Inclusion Criteria

- a. Male and Female patients.
- b. Age between 18 to 80 years.
- c. Patients with diabetes and associated morbidities but not in sepsis.

Exclusion Criteria

- a. Patients below 18 years and above 80 years
- b. Patients in Sepsis.
- c. Pregnant patients.

Protocol

The following is a retrospective study carried out in the Department of Surgery at Terna Hospital & Research Centre, Nerul, Navi Mumbai, Maharashtra, from January 1st, 2019 to December 31st, 2019. All 30 patients, both male and female from Age 18 to 80 years having Diabetic Foot and its various surgical manifestations and complications.

A detailed history of symptoms and their duration, physical examination details, Hematological, Histopathological, and Radiological reports were documented weekly or as frequently done as earliest.

Complications arising on admission and/or during the hospital stay and/or post-surgical intervention/post-discharge were documented. Recurrence of disease post-discharge, if mentioned, was included as well.

Statistical compilations of disease occurrence, different diagnostic modalities, and different therapeutic modalities used along with post-operation/post-discharge disease regression for comparison of the effectiveness of therapeutic options, if any.

Study Plan

CASE RECORD SHEET

- (a) Age: _____
- (b) Sex: _____
- (c) Occupation: _____
- (d) Weight: _____
- (e) Drug history:
- (f) Socio- economic status (as per history/ address/ Kuppuswamy):
- (g) Diabetes status:
 - 1. Blood Sugar
 - 2. HbA1C
 - 3. RBS
 - 4. FBS
 - 5. PLBS
- (h) Co-morbid conditions (Hypertension/ Neuropathies/ Burns):

Surgical Manifestations

- 1. Edema
- 2. Gangrene
- 3. Wounds
- 4. Ulcers
- 5. Infections (excluding sepsis)
- 6. Osteomyelitis

(i) Dietary history (Veg/ Mixed):

(j) Risk Factors:

- ✓ Personal history:
- ✓ Footwear use:
- ✓ Trauma:
- ✓ Gender:
- ✓ Alcohol:
- ✓ Hyperlipidemia:
- ✓ Smoking:
- ✓ Occupation:
- ✓ Pre-existing abscess:
- ✓ Deformity:
- ✓ Pre-ulcer present:
- ✓ Nail pathology:
- ✓ Duration of DM >3yrs:
- ✓ Peripheral neuropathy:
- ✓ Hypertension:

(l) Treatment:

- ✓ Anti-hypertensives:
- ✓ Insulin:
- ✓ Anti-diabetics:
- ✓ Surgical procedure done previously at site of the foot:

Statistical Analysis

Data Collection

Data Entry: All Patient data was entered as per study proforma using Microsoft Excel, which is mentioned under a separate heading below. This data included all the details obtained from the clinical, laboratory, radiological, treatment modalities mentioned in the patient's case record sheets.

Data Tabulation: The data was tabulated and summarized using tables on MS Word.

Data Analysis: Data analysis was done by institutional statistician using MS Word.(Ver 16.1.6746.2048)

RESULT AND ANALYSIS

Table 1 Age and Sex wise distribution of Diabetes Patients

Age Group	Sex		Total
	Female	Male	
30 – 39	2	1	3
40 – 49	0	4	4
50 – 59	4	7	11
60+	0	12	12
Total (%)	6(20.0%)	24(80.0%)	30(100.0%)

Table 2 Drug History of Diabetes Patients

Drug History	No. of Patients	Percentage
Anti-Psychotics, THYROXINE	1	3.3
BIPOLAR Drugs, ANTI-HTN	1	3.3
Insulin, Anti-HTN	1	3.3
OHA	1	3.3
OHA, Anti-HTN	1	3.3
OHA, STATINS, THYROXINE, BIPOLAR DRUGS	1	3.3
Others (Not Mentioned)	24	80.0
Total	30	100.0

Table 3 Socio-Economic Status of Diabetes Patients

Socio-Economic Status	No. of Patients	Percentage
Upper	2	6.7
Upper Middle	7	23.3
Lower Middle	8	26.7
Upper lower	10	33.3
Lower	3	10
Total	30	100.0

Table 4 Co-morbidity condition of Diabetes Patients

Co-morbidity	No. of Patients	Percentage
HTN	19	63.3
Neuropathy	9	30.0
DM Nephropathy	11	36.7
Retinopathy	4	13.3
IHD	4	13.3
PVD	1	3.3
DVT	1	3.3
DKA	1	3.3
Obesity	1	3.3
Cellulitis	1	3.3

Table 5 Manifestation of Diabetes Patients

Manifestation	Yes (%)	No (%)	Total
Edema	20 (66.7%)	10 (33.3%)	30
Gangrene	7 (23.3%)	23 (76.7%)	30
Wounds	14 (46.7%)	16 (53.3%)	30
Ulcer	9 (30.0%)	21 (70.0%)	30
Infections (Exc. Sepsis)	19 (63.3%)	11 (36.7%)	30
Osteomyelitis	2 (6.7%)	28 (93.3%)	30

Table 6 Diet History of Diabetes Patients

Diet History	No. of Patients	Percentage
Vegetarian	7	23.3
Non- Vegetarian	23	76.7
Total	30	100.0

Table 7 Past History of Diabetes Patients

Past History	No. of Patients	Percentage
IHD	4	13.3
Bipolar	3	10.0
Hypothyroidism	2	6.7
Cystitis	1	3.3
Schizophrenia	1	3.3
Hydrocele	1	3.3
SIADH	1	3.3
Nil	17	56.7
Total	30	100.0

Table 8 Treatment of Diabetes Patients

Treatment	Yes (%)	No (%)	Total
Anti - HTN drugs	21 (70.0%)	9 (30.0%)	30
Insulin	19 (63.3%)	11 (36.3%)	30
OHA	27 (90.0%)	3 (10.0%)	30

Table 9 Risk Factors of Diabetes Foot Patients

Risk Factors	Yes (%)	No (%)	Total
Foot wear Use	0 (0.0%)	30 (100.0%)	30
Trauma	3 (10.0%)	27 (90.0%)	30
Alcohol	1 (3.3%)	29 (96.7%)	30
Hyperlipidemia	2 (6.7%)	28 (93.3%)	30
Smoking	6 (20.0%)	24 (80.0%)	30
Preexisting abscess	10 (33.3%)	20 (66.7%)	30
Deformity	4 (13.3%)	26 (86.7%)	30
Pre-ulcer present	10 (33.3%)	20 (66.7%)	30
Nail Pathology	0 (0.0%)	30 (100.0%)	30
Duration of dm > 3yrs	21 (70.0%)	9 (30.0%)	30
Peripheral neuropathy	11 (36.3%)	19 (63.3%)	30

Table 10 Treatment (Surgical Procedure) of Diabetes Patients

Treatment (Surgical Procedure)	No. of Patients	Percentage
Only debridement	9	30.0
Debridement & Abscess Drainage	6	20.0
Amputation	2	6.7
Debridement & Vacuum appl.	1	3.3
Debridement & Amputation	3	10.0
Abscess Drainage	1	3.3
None	9	30.0
Total	30	100.0

DISCUSSION

The Age of the patient plays a significant role in the progress of diabetes & the development of diabetic foot. As we can see from our study, around 36% of the patients fall in the highest age group that is 60 years+ whereas only 10% of all patients fall under the lowest age group, i.e., 30-39 years. The percentage of patients significantly increases as the age group progresses with 12% patients falling under 40-49 years of age group & 33% patients falling in 50-59 years of age group. Our findings match with the study of Khalid Al-Rubeaan¹. In our study, patients of extreme age groups, in exclusion criteria were not considered. Hence we could not comment on that aspect. Diabetic foot showed more prevalence in the male gender group (80%) v/s female gender group i.e. 20% again is consistent with the study of Khalid Al-Rubeaan¹.

From the drug history of diabetic patients, it was deduced that data was insufficient to conclude the influence of any past drug intake on the development of diabetic foot, as 80% of patients in the study did not have any drug history mentioned. The prevalence of diabetic foot was highest in the upper-lower class patients 33.3%, whereas it was lowest in upper-class patients, showing a prevalence of 6.7%. Upper-middle & lower-middle-class stood at 23.3% & 26.7% respectively. The study was consistent with the findings of M.R. Mudhaliar².

The presence of various co-morbidities has highly influenced the incidence of diabetic foot with hypertension being most significant at 63.3% and diabetic nephropathy being the second highest at 36.7% while neuropathy (30%) being the third highest. Other co-morbidities were retinopathy (13.3%), IHD (13.3%), PVD (3.3%), DVT (3.3%), DKA (3.3%), Obesity (3.3%), cellulitis (3.3%). There is a direct co-relation between hypertension and the incidence of diabetic foot in patients, which has also been proved in the study by H.M. Abdulghani³. Hypertension is known to worsen the prognosis of patients with Diabetes Mellitus by increasing the risk of both microvascular and macrovascular complications leading to surgical manifestations of diabetic foot disease⁹. Patients having nephropathy and neuropathy are also significant co-morbidities, which may possibly lead to the development of diabetic foot.

The surgical manifestations that most commonly occur in patients having diabetic foot are edema (highest at 66.7%), followed by infections at 66.3% (excluding sepsis), followed by wounds and ulcers at 46.7% & 30%, respectively, and lastly, gangrene which is 27.3%. Osteomyelitis was the least seen surgical manifestation at the incidence of 6.7%. Diabetic foot diseases are usually associated with infection and inflammation, which lead to edema of the foot as mentioned in the study by Teik K Ho⁴ which proves edema being a consistent finding in patients with diabetic foot along with infections, wounds and ulcers. Long-standing diabetes can

cause microvascular changes leading to endothelial damage causing microvascular leakage resulting in edema. Edema is also caused by inflammatory changes due to subsequent infections as a result of hyperglycemia and also injuries caused due to the presence of peripheral neuropathy.

Patients having a non-vegetarian diet (76.7%) showed higher chances of developing diabetes with secondary diabetic foot than those patients that consumed a vegetarian diet (23.3%). Hence, patients consuming vegetarian diets were shown to be at a lower risk of developing diabetes associated comorbidities compared to patients consuming non-vegetarian diets, confirmed by the study done by Tina H. T. Chiu⁵. However, the present study is limited to broad classification, and no account of specific types of meat intake (red meat, poultry, seafood, egg, etc.) data was available.

Past history of patients having Ischemic heart disease showed to have higher chances of developing diabetic foot (13.3%) within the data available. Notably, in our study, 10% of the patients suffered from bipolar disorder as well as 6.7% of patients had hypothyroidism. Other past histories noted at 3.3% each were cystitis, schizophrenia, hydrocele, SIADH. However, these seem insignificant due to insufficient data and possibly are co-incidental findings. 56.7% of patients had no significant past history mentioned in their data records. Patients having DM are at a higher chance of getting an MI and the common factor between both is increased coagulability with DM patients being in a prothrombotic and pro-coagulant state¹². Oxidative stress may represent a dangerous condition for organ and system function, and it is associated with several conditions such as diabetes mellitus, cardiovascular diseases, cancer, and neurological disorders as mentioned in the study by Paolo Severino⁶. Oxidative stress is likely the key etiology that links patients having IHD & neurological conditions like Bipolar Disorder/Schizophrenia to develop diabetic foot & associated complications.

Patients having diabetic foot were given medical management for their Diabetes Mellitus in two forms, i.e., Insulin & OHA's. From the study population, 63.3% of patients required insulin whereas 90% patients required OHA's to aggressively control their diabetes so as to improve the diabetic foot disease prognosis. Patients who received both insulin & OHA's were first given insulin to aggressively control their blood sugar and eventually discharged on OHA's. However, data is insufficient to state superiority of individual medical treatment over the other. Apart from these, 70% patients were treated for the most commonly appearing co-morbidity i.e. Hypertension.

Certain risk factors were important to consider when leading to the development of diabetic foot. 70% of patients showed a duration of uncontrolled diabetes mellitus being greater than three years before the incidence of diabetic foot to be the most common risk factor. Peripheral neuropathy was the 2nd most common risk factor with 36.3% patients having it whereas pre-existing ulcers and pre-existing abscess were the 3rd most common risk factors, with 33.3% patients having it each. The other risk factors were smoking at 20%, limb deformity at 13.3%, trauma at 10%, hyperlipidemia at 6.7% and alcohol intake at 3.3%. The Data was insufficient for footwear use and existing nail pathology. The two most common risk factors for diabetic foot, as mentioned above were confirmed in a study done by Marília Klein Reis⁷.

Wound debridement was the most common surgical management given to 30% diabetic foot patients by itself and along with other surgical treatments that are debridement with abscess drainage (20%), amputation (10%), and vacuum application (3.3%). Other sole surgical treatments given were amputation (6.7%) and abscess drainage (3.3%). 30% of the patients did not receive any surgical treatment for diabetic foot and were controlled medically only along with wound dressing as required. Although medical management of diabetes in a patient having diabetic foot is important for etiological control, surgical management is more effective for the acute treatment of the surgical manifestations of diabetic foot, as also mentioned in the study by Piaggese A⁸.

CONCLUSION

- ✓ The incidence of diabetic foot disease increases as age progresses, with the maximum number of patients being greater than 60 years of age. Diabetic foot shows greater preponderance to males than to females up to the age of 60.
- ✓ Diabetic foot occurrence varies across the socioeconomic strata, possibly due to lack of knowledge, late diagnosis, variation in diet consumption, lack of wound care. From the study, it is deduced that the prevalence of diabetic foot is highest in the upper-lower class due to the aforementioned factors.
- ✓ Hypertension was the leading co-morbid condition in patients with diabetic foot followed by diabetic nephropathy and neuropathy, showing a strong correlation between the former conditions to the development of diabetic foot disease.
- ✓ The most common manifestation of diabetic foot disease patients was edema, followed by infections and wounds.
- ✓ A non-vegetarian diet has an increased role over vegetarian diets for existing diabetic patients to develop diabetic foot complications; however, the data obtained is insufficient to draw a conclusion.
- ✓ Psychiatric disorders like Bipolar and schizophrenia are known to be associated with the development of diabetic foot directly due to its relation to impaired glucose tolerance and insulin resistance and indirectly due to the association between Bipolar Disorder and Diabetes Mellitus that focuses on the diabetogenic side effects of psychotropic medications¹⁰⁻¹¹.
- ✓ Our study also shows that there is a close relation between DM and IHD.
- ✓ Medical control of diabetes mellitus is an important adjuvant to surgical management of diabetic foot, however, surgical management is more effective for the acute treatment of the surgical manifestations of diabetic foot.
- ✓ Uncontrolled DM > 3years, peripheral neuropathy, and pre-existing abscess/ulcers are the three most important risk factors for developing diabetic foot.

Recommendations

1. Screening of population who are at a high risk of developing Diabetic foot disease and its surgical manifestations, i.e., age group > 50 years with the presence of IHD/HTN/ Psychiatric illnesses.
2. HGT measurements at home for pre-existing diabetic patients who are on OHA/Insulin as well as HbA1c

quarterly and regular clinic follow-ups to assess for peripheral neuropathy.

3. Education on personal hygiene, wound care, and diabetic diet for patients, especially belonging to Upper lower/lower socioeconomic class with the help of social workers and RHC/UHC workers.
4. Usage of special diabetic footwear for those diabetic patients having pre-existing abscess/wound/ulcer.
5. Quarterly screening for the development of new diabetic cases especially those who are undergoing antipsychotic drug therapy or having a past history of psychiatric illnesses/IHD/PVD/history of smoking.

References

1. Khalid Al-Rubeaan, Mohammad Al Derwish, Samir Ouizi, Amira M. Youssef, Shazia N. Subhani, Heba M. Ibrahim, and Bader N. Alamri. Diabetic Foot Complications and Their Risk Factors from a Large Retrospective Cohort Study. *PLoS One*. 2015; 10(5): e0124446. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4422657/>
2. Mohanraj Rathinavelu Mudhaliar, Ishrar Shaik Mohammad Ghouse, Veerendra Uppara, Malyadri Yesupogu, Divya Asavadi, Vidyasagar Chinnakotla, C. H. V. Suneel Babu. Association between socioeconomic status and diabetes in rural settings of India, *International Journal of Green Pharmacy*, Jan-Mar 2017 (Suppl 11) https://www.researchgate.net/publication/316542966_Association_between_socioeconomic_status_and_diabetes_in_rural_settings_of_India
3. Hamza Mohammad Abdulghani, Areej Salman AlRajeh, Budoor Hussain AlSalman, Lulwah Sami AlTurki, Norah Sulaiman AlNajashi, Mohammad Irshad, Khalid Hamad Alharbi, Yazeed Eid AlBalawi, Yazeed A AlSuliman, and Tauseef Ahmad. Prevalence of diabetic comorbidities and knowledge and practices of foot care among diabetic patients: a cross-sectional study. *Diabetes Metab Syndr Obes*. 2018; 11: 417–425. Published online 2018 Aug 16. DOI: 10.2147/DMSO.S171526 <https://www.dovepress.com/prev-alence-of-diabetic-comorbidities-and-knowledge-and-practices-of-foot-care-reviewed-fulltext-article-DMSO>
4. Teik K Ho, Richard D Leigh, and Janice Tsui. Diabetic foot disease and oedema. *The British Journal of Diabetes & Vascular Disease* 13(1) 45–50. DOI: 10.1177/1474651412472213 <https://journals.sagepub.com/doi/full/10.1177/1474651412472213>
5. Tina H. T. Chiu, Wen-Harn Pan, Ming-Nan Lin, corresponding author, and Chin-Lon Lin. Vegetarian diet, change in dietary patterns, and diabetes risk: a prospective study. *Nutr Diabetes*. 2018; 8: 12. Published online 2018 Mar 9. DOI: 10.1038/s41387-018-0022-4. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5856738/>
6. Paolo Severino, Andrea D'Amato, Lucrezia Netti, Mariateresa Pucci, Fabio Infusino, Viviana Maestrini, Massimo Mancone, and Francesco Fedele. Myocardial Ischemia and Diabetes Mellitus: Role of Oxidative Stress in the Connection between Cardiac Metabolism and Coronary Blood Flow. *J Diabetes Res*. 2019; 2019: 9489826. Published online 2019 Apr 4. DOI: 10.1155/2019/9489826 <https://www.hindawi.com/journals/jdr/2019/9489826/>
7. Marília Klein Reis, Júlia Scaravelli Mario, and Mari Cassol Ferreira. Main risk factors for diabetic foot. *Diabetol Metab Syndr*. 2015; 7(Suppl 1): A26. Published online 2015 Nov 11. DOI: 10.1186/1758-5996-7-S1-A26 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4653478/>
8. Piaggese A1, Schipani E, Campi F, Romanelli M, Baccetti F, Arvia C, Navalesi R. Conservative surgical approach versus non-surgical management for diabetic neuropathic foot ulcers: a randomized trial. *Diabet Med*. 1998 May; 15(5): 412–417. <https://www.ncbi.nlm.nih.gov/pubmed/9609364>
9. Antonino Tuttolomondo, Carlo Maida, and Antonio Pinto. Diabetic Foot Syndrome as a Possible Cardiovascular Marker in Diabetic Patients. *J Diabetes Res*. 2015; 2015: 268390. Published online 2015 Mar 26. DOI: 10.1155/2015/268390 <https://www.hindawi.com/journals/jdr/2015/268390/>
10. Yatan Pal Singh Balhara. Diabetes and psychiatric disorders. *Indian J Endocrinol Metab*. 2011 Oct-Dec; 15(4): 274–283. doi: 10.4103/2230-8210.85579 <http://www.ijem.in/article.asp?issn=2230-8210;year=2011;volume=15;issue=4;spage=274;epage=283;aulast=Balhara>
11. Ellen F. Charles, Christophe G. Lambert, and Berit Kerner. Bipolar disorder and diabetes mellitus: evidence for disease-modifying effects and treatment implications. *Int J Bipolar Disord*. 2016; 4: 13. Published online 2016 Jul 7. DOI: 10.1186/s40345-016-0054-4 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4936996/>
12. Benjamin M Leon and Thomas M Maddox. Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations, and future research. *World J Diabetes*. 2015 Oct 10; 6(13): 1246–1258. Published online 2015 Oct 10. DOI: 10.4239/wjd.v6.i13.1246 <https://www.ncbi.nlm.nih.gov/pubmed/26468341>
13. Geographic variation in Medicare spending and mortality for diabetic patients with foot ulcers and amputations. Sargen MR, Hoffstad O, Margolis DJ. *J Diabetes Complications*. 2013 Mar-Apr; 27(2): 128–33. <https://www.ncbi.nlm.nih.gov/pubmed/23062327>
14. Gordois A, Scuffham P, Shearer A, Oglesby A, Tobian JA. The health care costs of diabetic peripheral neuropathy in the US. *Diabetes Care*. 2003; 26: 1790–1795. <https://www.ncbi.nlm.nih.gov/pubmed/12766111>
15. Gordois A, Scuffham P, Shearer A, Oglesby A. The healthcare costs of diabetic peripheral neuropathy in the UK. *The Diabetic Foot*. 2003; 6: 62–73. https://www.woundsinternational.com/uploads/resources/dotn_master/2374/files/pdf/df6-2-62-73.pdf
16. International Working Group on the Diabetic Foot. Epidemiology of Diabetic Foot Infections in a Population Based Cohort. Noordwijkerhout, The Netherlands; 2003. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0124446>
17. Reduction in diabetic amputations over 11 years in a defined U.K. population: benefits of multidisciplinary teamwork and continuous prospective audit. Krishnan S, Nash F, Baker N, Fowler D, Rayman G. *Diabetes Care*. 2008 Jan; 31(1): 99–101. https://www.researchgate.net/publication/5911437_Reduction_in_Diabetic_Amputations_Over_11_Years_in_a_Defined_UK_Population_Benefits_of_multidisciplinary_team_work_and_continuous_prospective_audit