

REVIEW

Surgical Implications in the Pathology of Diabetes Mellitus – Review of the Literature

Florin Teodor BOBIRCA^{1,2}, Dan DUMITRESCU^{1,2}, Teodor Florin GEORGESCU¹, Anca BOBIRCA^{1,3}, Carmen IORGUS³, Mihai GEORGESCU¹, Ionut MELESTEU⁴, Cristina ALEXANDRU³, Traian PĂTRASCU^{1,2}, Dragoș Eugen GEORGESCU^{1,2}

Abstract

Diabetes mellitus brings together several syndromes, all burdened by a high complexity and with the potential to generate vital impairment. The large number of complications result from the association of high blood glucose level with vascular damage, neuropathy, poor healing and overall increased atherosclerosis process. The clinical manifestation of these complications involves a wide range of manifestations from simple lesions to complex pathology, many of them requiring surgical treatment. Surgical implications of diabetes mellitus include diabetic foot syndrome, soft tissue infections, renal impairment and abdominal pathology.

Keywords: diabetes mellitus, diabetic foot, risk factors, screening, surgical treatment

Rezumat

Diabetul zaharat reunește mai multe sindroame, unele fiind caracterizate de un grad ridicat de complexitate cu potențial de risc vital. Numărul mare de complicații rezultă din asocierea valorilor mari ale glicemiei cu leziunile vasculare, neuropatia, vindecarea defectuoasă a leziunilor și accelerarea procesului de ateroscleroză. Expresia clinică a acestor complicații implică o gamă largă de manifestări, de la leziuni simple până la patologii complexe, multe dintre ele necesitând tratament chirurgical. Diabetul zaharat este asociat cu o multitudine de condiții patologice ce prezintă indicație chirurgicală precum: patologia piciorului diabetic, infecțiile de țesuturi moi, insuficiența renală și patologia abdominală.

Keywords: diabet zaharat, picior diabetic, factori de risc, screening, tratament chirurgical.

¹"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

²Surgery Department, Dr Ion Cantacuzino Clinical Hospital, Bucharest

³Internal Medicine and Rheumatology Department, Dr Ion Cantacuzino Clinical Hospital, Bucharest

⁴Gastroenterology Department, Clinical Emergency Hospital, Bucharest

Corresponding author:

Anca BOBIRCA, Dr. Ion Cantacuzino Clinical Hospital, 5-7 Ion Movila Street, Bucharest, 030167, Romania

E-mail: anca.bobirca@umfcd.ro

INTRODUCTION

Diabetes mellitus (DM) is a pathology with an increasing incidence, which leads over time to multiple vital complications, having a significant morbidity and mortality rate worldwide. Age, smoking, DM family history, obesity and a sedentary lifestyle represent major risk factors¹. DM represents a risk factor for various comorbidities such as rheumatoid arthritis, cardiovascular diseases, lung diseases, all of which in turn increase the risk of infections, promotes inflammatory responses and decreased immune system². Moreover, DM is a major, independent risk factor for surgical site infection, a nowadays real health care burden³. The most common multiorgan diseases induced by glycemic disorder, with the worst outcomes are caused by vascular and nerve damage, including damage to the heart, kidneys, and eyes, as well as diabetic foot syndrome.

A patient with DM has an increased vulnerability to infections. The alteration of immune defense mechanisms is what causes this sensitivity, with the hyperglycemic environment serving as a contributing factor. The suppression of the antioxidant system and humoral activity, as well as changes to neutrophil function, are all described⁴.

Epidemiological data show that approximately 50% of diabetic foot syndrome develops from neuropathy alone. Peripheral arterial disease accounts for only 15% of cases, whereas foot ulcers occur in 35% as a combination of neuropathy and vascular disease⁵. Ulcerative diabetic foot has a complex and multifactorial etiology, with multiple causes conspiring to create pathogenic pathways associated with the development of foot ulcers in diabetic patients⁶. Other factors such as trauma caused by arteriopathy, neuropathy, infections, and



Figure 1. Calcanean necrosis (Dr Ion Cantacuzino Hospital Collection)

various methods (inappropriate footwear, fungal infections, etc.), patient activity levels, and deficiencies in the health care system contribute to the prevalence of diabetic foot disease. It is the main factor of the result.



Figure 2. Toe fistulised osteoarthritis (Dr Ion Cantacuzino Hospital Collection)

Diabetic nephropathy is the leading cause of end-stage renal disease due to the increasing prevalence of diabetes, affecting 20-30% of patients with this condition. It first appears in microalbuminuria (early nephropathy) that progresses to end-stage renal disease. Elevated blood sugar levels, long-term diabetes, hypertension, obesity, dyslipidemia are factors that can be modified by antidiabetic medication, antihypertensives, lipid-lowering treatments, and lifestyle changes⁷.

Soft tissue infections are one of the main causes of morbidity and mortality in diabetic patients.

Systemic complications such as: arteriopathy, peripheral nerve damage, the disruption of metabolism, result in the predisposition to infections, studies showing that there is a risk twice as high for diabetics to develop soft tissue infections. The most frequently encountered pathogen in soft tissue infections is *Staphylococcus aureus*, present both in outpatients and to those hospitalized³.

The surgical abdominal pathology of the diabetic patient is important to know because it associates several essential characteristics: poor symptomatology, varying degrees of vascular and neurological damage, slow and inadequate healing, increased risk of anesthetic and surgical complications. Colorectal cancer and DM are two important public health issues. There is a consensus



Figure 3. Back anthracoid (Dr Ion Cantacuzino Hospital Collection)

in the literature regarding the role of type II diabetes as an independent risk factor for colorectal cancer⁸.

The surgery of the diabetic patient requires a close collaboration between the surgeon and the diabetologist because the postoperative outcome of these patients depends on a correct compensation of the diabetic disease and a rigorous control of the imbalances associated with it. The surgery of the diabetic patient is special due to the fact that diabetic neuropathy often causes low pain syndrome. Thus, acute abdominal conditions, which in usual practice are very noisy, in a diabetic patient are associated with mild symptoms, usually making it difficult to make an adequate, promptly positive diagnosis.

For the patient with diabetes, the preoperative period, that of compensating the associated diseases, is important because the patient with diabetes frequently associates renal failure, acido-base imbalances, anemia, infections, cardiological and cerebro-vascular diseases, therefore the usefulness of a multidisciplinary team in the treatment of these fragile patients is mandatory.

DIABETIC FOOT SYNDROME SURGERY

The diabetic foot is one of the most serious consequences, with 15% of diabetic patients requiring significant amputations. This is a complex disorder with mul-

ti-ple etiology, arteriopathy, neuropathy, and infection being the key processes causing foot deformities and reduced joint motion.^{9,10} Due to the growing number of patients who are being diagnosed with DM and the serious problems that could develop, diabetic foot therapy is a significant public health issue. Foot biomechanics is imparted as a consequence of increased local inflammation caused by microtrauma. Thus, the pathophysiology of the diabetic foot can be divided into two groups: those that are mostly neuropathic and those that are primarily arteriopathy. Neuropathy is defined as a nervous system disorder affecting somatic and vegetative components and it can be a clinical or subclinical condition in diabetic patients. Along with other general risk factors including age, smoking, dysmetabolic syndrome, and cardiovascular diseases, hyperglycemia and the length of diabetes are two significant factors that influence the likelihood of developing polyneuropathy in people with DM⁴.

Neuropathic involvement of the diabetic foot has a better outcome of this condition because a substantial amputation is unlikely. This is so that the infection site may be reached by antibiotics because to the little vascular damage, and the circulatory support encourages the growth of granulation tissue and wound healing^{11,12}.

Over the past years, increasing research has focused on preventing foot neuroarthropathy and, consequently, amputations. The best approach involves evaluating patients who are at higher risk and further improving glycemic management. In a recent review, the new prognostic biomarkers for diabetic Charcot foot were emphasized. Important inflammatory biomarkers TNF-, IL-6, and IL-1, as well as bone markers RANK/RANKL, osteoprotegerin, Sclerostin, Dkk-1, and Wnt-1, were discovered. These biomarkers present a fresh opportunity not only to avoid a poor outcome, but also new therapeutic option targeting these immune pathways¹³.

Minor intervention

Ulcers are the main cause of amputations in diabetic foot. Avoiding drastic surgery in ulcerous patients can be done, when a periodical screening is performed, and rapid intervention is made. Before resorting to amputation, several procedures can be accomplished, revascularization and negative pressure wound therapy having great results when applied early [14].

If the wound is small, direct closure can be used. Skin grafts are the most successful treatment option for

big lesions, but they frequently result in caved-in, repulsive closures. Along with flap reconstruction, negative pressure wound therapy is a very helpful procedure that offers patients a number of advantages. It is also possible to use adjacent tissue transfers to stitch up wounds⁹. Additionally, for DM patients surgent seldom resort to flaps due to peripheral arterial disorder which leads to a high rate of failure⁹.

In cases of mainly arteriopathy lesions, surgical intervention by revascularization is the primary therapeutic approach, in case of unfavorable results major amputation will be performed¹⁵. Revascularization is not always possible, in a recent study, only 39 out of 71 DM patients with arteriopathy had a beneficial outcome and didn't require further surgical treatments¹⁴. In those cases, the surgical procedures were desobstructions and by-pass techniques. Moreover, only patients with abscess of the foot needed minor surgical management including incision, evacuation and debridement, all cases of wet and ischemic gangrene requiring minor or major amputations.

In a large local study, the authors analyzed 251 subjects diagnosed with DM who required surgical treatment for diabetic foot, of which the majority 85.8% had a minor procedure, osteitis and ulcer being the most common diagnosis among them¹².

Major intervention

The most crippling complication for a patient with diabetes foot is a major amputation. The risk for a severe amputation can be significantly reduced by tight control of glycemic levels as well as proper prophylaxis of lesion and infection.

The types of lesions described in arthropathic foot are ischemic and wet gangrene and abscess of the foot.

In a study realized on 188 patients with arthropathy, amputation of the calf and thigh was identified in approximately 20% of cases¹⁴. In another study the prevalence of major surgery for a diabetic foot was 14.2%, major surgery being defined as amputation of the foot, above and below the knee. Moreover, for those patients, the cause of this severe course of treatment was a gangrenous foot¹².

SOFT TISSUE INFECTION SURGERY

The infections localized in the soft parts (skin, aponeurosis, subcutaneous tissue, muscular system) at a patient diagnosed with DM can require aggressive sur-

gical treatment, hydro-electrolytic balancing and sustained antibiotic therapy¹⁶.

Thus, a diabetic patient has the risk of a develop various pathological consequences: infections, ulcerations, soft tissue injuries that are associated with complex peripheral neurological and vascular changes¹⁶.

Soft tissue lesions can be easily unnoticed by DM patients, due to lack of pain brought on neuropathy. As a consequence, they frequently become chronic wounds that are difficult to treat, necessitate a complex therapy regimen, involving a multidisciplinary team over time. Peripheral artery disease is frequently present in these patients, which worsens the prognosis³.

Furthermore, due to DM patients compromised immune systems, localized infections frequently worsen, necessitating surgical intervention. Soft tissue infections are often the primary cause of hospitalization for these patients. In surgical compartment, the rate of DM patients presenting for an infected lesion, necessitating a surgical procedure as treatment are over 35%¹². DM patients are hard to manage due to multiple complications, most of them having at least renal and heart diseases concomitant with arteriopathy and neuropathy.

In a study realized on 155 DM patients admitted in a surgical department, almost half of the admission was fasciitis, with an impressive frequency of necrotizing fasciitis¹⁶. Other types of minor lesions that needed surgical approach were fluid collection, skin fistulae with persistent purulent secretions¹⁶.

Fournier gangrene, also known as necrotizing fasciitis of the perineum and genitals, is a serious complication that is frequently present in diabetes patients who are also often obese and have radically impaired immunity. Due to the condition's discrete clinical appearance, surgical therapy can be postponed with disastrous results¹⁶. Regarding the treatment, large excisions, debridement, necrectomies and fasciectomy are the urgent surgical techniques used along with aggressive antibiotic therapy, administered initially empirically and then according to the antibiogram.

ABDOMINAL SURGERY

Surgical Renal involvement - Peritoneal Acces

One of the most serious complications for diabetic patients is end-stage renal failure, which is caused by small arterial vessels damages. It has a higher death rate and affects a growing number of young people—roughly 25–35% of those under the age of 30 years old [17]. An

increased number of DM patients are requiring aggressive treatment, finally turning to dialysis, the last resort before kidney transplant. This method of replacing renal function offers multiple advantages: patient autonomy, decreases the number of hospital visits, better preservation of residual renal function; but like any other method it also has disadvantages such as the increased risk of infections¹⁸. In the case of peritoneal dialysis (PD), abdominal wall complication, infectious and non-infectious often need repeated surgical treatment. In contrast to tunnel infections and peritonitis, which are more serious infectious complications, catheter obstruction or malfunction, external leakage, abdominal wall defect, ultrafiltration failure, and encapsulated peritoneal sclerosis are non-infectious complications. Peritonitis is a major medical issue, particularly for people with diabetes who have weakened immune systems¹⁹. In a 2018 study conducted on a sizable cohort, the rate of this severe consequence was over 43%. Additionally, in this study, more than half of the patients who experienced complications from peritoneal dialysis had lost their ability to continue PD¹⁸.

Colorectal cancer in DM

Recent research has shown a significant link between diabetes and colorectal cancer⁸. A current study, analyzing a large sample of colonoscopies, has proved substantial evidence supporting the association not only between DM and polyps with high grade dysplasia, but also DM and colorectal cancer. Furthermore, they showed that in cases of the patients with uncontrolled serum glycemic levels, colorectal cancer was more frequent²⁰. Patients with DM have a 30% increased likelihood of developing colorectal cancer, according to a meta-analysis²¹. Although more research is needed to fully understand this issue, the possibility of increased colorectal carcinogenesis related to insulin resistance is not contestable⁸. This can increase awareness and recommend a better screening for DM patients, with periodical colonoscopy, in order to identify lesions in early stages, that can benefit from endoscopic or surgical curative treatment. Ultimately, it can not only improve the patient's prognosis and lifetime but release the pressure of complex surgical procedures in advanced colorectal cancer.

Acute cholecystitis in DM

Diabetes mellitus is a risk factor for gall stones which can lead to acute cholecystitis and a higher rate of

post-operative complications due to the vulnerability of DM patients to infections²². Although the exact involvement of diabetes in the physiopathology of cholecystitis is unknown, the factors implicated described so far include a bigger gallbladder, impaired function without appropriate emptying, and diabetic neuropathy²³. Moreover, alithiasis cholecystitis is a serious condition that is more common in people who are already suffering from a chronic illness, including DM. It has poor clinical symptomatology but a significant mortality rate in the absence of urgent surgical treatment. Diabetes mellitus is a risk factor for developing alithiasis cholecystitis, due to the microangiopathy lesions and through vegetative denervation²⁴. In terms of complications, DM patients are more likely to experience bacteriemia, gangrenous cholecystitis and perforation, conditions that usually lead to a more complex surgical approach²⁵.

CONCLUSION

Diabetes mellitus is a debilitating disease with an increased prevalence, affecting younger patients. This pathology can advance quickly since sometimes it lacks obvious symptoms and frequently causes major consequences that configure true challenges for the surgical team. Secondly, diabetic patients require additional post-operative care due to their delayed healing period and higher frequency of further long-term complications.

References

1. Romesh Khardori. Type 2 Diabetes Mellitus; <https://emedicine.medscape.com/article/117853-overview>.
2. Bobirca, F.; Smarandache, C.G.; Bobirca, A.; Alexandru, C.; Dumitrescu, D.; Stoian, A.P.; Bica, C.; Brinduse, L.A.; Musetescu, A.; Gheoca-Mutu, D.-E.; Isac, S.; Ancuta, I. The Outcome of Surgical Treatment for the Neuropathic Diabetic Foot Lesions—A Single-Center Study. *Life* 2022, 12, 1156. <https://doi.org/10.3390/life12081156>
3. Martin ET, Kaye KS, Knott C, Nguyen H, Santarossa M, Evans R, et al. Diabetes and Risk of Surgical Site Infection: A Systematic Review and Meta-analysis. *Infect Control Hosp Epidemiol*. 2016 Jan 27;37(1):88–99.
4. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, Bril V, Russell JW, Viswanathan V. Diabetic neuropathy. *Nat Rev Dis Primers*. 2019 Jun 13;5(1):42. doi: 10.1038/s41572-019-0097-9. PMID: 31197183.
5. Volmer-Thole M, Lobmann R. Neuropathy and Diabetic Foot Syndrome. *Int J Mol Sci*. 2016 Jun 10;17(6):917.

6. Harris RC, Fang W. Transmetatarsal Amputation Outcomes When Utilized to Address Foot Gangrene and Infection: A Retrospective Chart Review. *The Journal of Foot and Ankle Surgery*. 2021 Mar;60(2):269–75.
7. Tziomalos K, Athyros VG. Diabetic Nephropathy: New Risk Factors and Improvements in Diagnosis. *The Review of Diabetic Studies*. 2015;12(1–2):110–8.
8. Agache A, Mustățea P, Mihalache O, Bobîrca FT, Georgescu DE, Jauca CM, Bîrligea A, Doran H, Pătrașcu T. Diabetes Mellitus as a Risk-factor for Colorectal Cancer Literature Review - Current Situation and Future Perspectives. *Chirurgia (Bucur)*. 2018 Sept-Oct;113(5):603-610. doi: 10.21614/chirurgia.113.5.603.
9. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. *Ann N Y Acad Sci*. 2018 Jan;1411(1):153-165. doi: 10.1111/nyas.13569.
10. Sapra A BP. Diabetes Mellitus. [Updated 2022 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK551501/>.
11. Brownrigg JRW, Schaper NC, Hinchliffe RJ. Diagnosis and assessment of peripheral arterial disease in the diabetic foot. *Diabetic Medicine*. 2015 Jun;32(6):738–47.
12. Florin Bobirca, Anca Bobirca, Cristina Jauca, Anca Florescu, Anca Musetescu, Dan Dumitrescu, Andra Birligea, Andreea Schveninger, Traian Patrascu, Particularities of Surgical Treatment for the Neuropathic Diabetic Foot. *Modern Medicine*, 2021, Vol. 28, No. 4, 447-451.
13. Bobircă, A.; Musetescu, A.E.; Bordianu, A.; Pantea Stoian, A.; Salmen, T.; Marinescu, D.-C.; Alexandru, C.; Florescu, A.; Radu, R.; Isac, S.; Patrascu, T.; Serban, D.; Bobircă, F. Novel Biomarkers Predictive of Diabetic Charcot Foot – An Overview of the Literature. *Life* 2022, 12, 1944. <https://doi.org/10.3390/life12111944>
14. Pătrașcu et al "Particularitati ale chirurgiei la diabetici", Editia a II-a, Ed.Niculescu, 2016, 32-41.
15. Lipsky BA, Berendt AR, Deery HG, Embil JM, Joseph WS, Karchmer AW, et al. Diagnosis and Treatment of Diabetic Foot Infections. *Plast Reconstr Surg*. 2006 Jun;117(SUPPLEMENT):212S-238S.
16. Polk C, Sampson MM, Roshdy D, Davidson LE. Skin and Soft Tissue Infections in Patients with Diabetes Mellitus. *Infect Dis Clin North Am*. 2021 Mar;35(1):183-197. doi: 10.1016/j.idc.2020.10.007. Epub 2020 Dec 7.
17. Ghaderian SB, Hayati F, Shayanpour S, Beladi Mousavi SS. Diabetes and end-stage renal disease; a review article on new concepts. *J Renal Inj Prev*. 2015;4(2):28–33.
18. Gorsane I, Ben Hamida S, Ben Hamida F, Ounissi M, Harzallah A, Ben Abdallah T. Peritoneal dialysis in diabetes patients. *Tunis Med*. 2019 Aug-Sep;97(8-9):1017-1020.
19. Li PKT, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, et al. Peritoneal Dialysis-Related Infections Recommendations: 2010 Update. *Perit Dial Int*. 2010 Jul 1;30(4):393–423.
20. Miłek T, Forsyński K, Myrcha P, Ciostek P. Diabetes association of polyps and colon cancer. *Polish Journal of Surgery*. 2019 Jun 28;91(3):1–5.
21. Larsson SC, Orsini N, Wolk A. Diabetes Mellitus and Risk of Colorectal Cancer: A Meta-Analysis. *JNCI: Journal of the National Cancer Institute*. 2005 Nov 16;97(22):1679–87.
22. Abraham S, Rivero HG, Erlikh I v, Griffith LF, Kondamudi VK. Surgical and nonsurgical management of gallstones. *Am Fam Physician*. 2014 May 15;89(10):795–802.
23. Łącka M, Oblój P, Spsychalski P, Łaski D, Rostkowska O, Wieszczy P, et al. Clinical presentation and outcomes of cholecystectomy for acute cholecystitis in patients with diabetes - A matched pair analysis. A pilot study. *Adv Med Sci*. 2020 Sep;65(2):409–14.
24. Doran H, Mihalache O, Bobircă F, Bugă C, Pătrașcu T. Colecistita acută alitiazică--dificultăți de diagnostic și tratament [Acute acalculous cholecystitis--difficulties of diagnosis and treatment]. *Chirurgia (Bucur)*. 2010 Jul-Aug;105(4):465-8. Romanian.
25. Bourikian S, Anand RJ, Aboutanos M, Wolfe LG, Ferrada P. Risk factors for acute gangrenous cholecystitis in emergency general surgery patients. *The American Journal of Surgery*. 2015 Oct;210(4):730–3.