

## REVIEW

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

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## 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.

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## 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 factors<sup>1</sup>. 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 system<sup>2</sup>. Moreover, DM is a major, independent risk factor for surgical site infection, a nowadays real health care burden<sup>3</sup>. 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 described<sup>4</sup>.

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 disease<sup>5</sup>. 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 patients<sup>6</sup>. 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 changes<sup>7</sup>.

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 hospitalized<sup>3</sup>.

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 cancer<sup>8</sup>.

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.<sup>9,10</sup> 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 DM<sup>4</sup>.

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<sup>11,12</sup>.

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 pathways<sup>13</sup>.

### *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 wounds<sup>9</sup>. Additionally, for DM patients surgent seldom resort to flaps due to peripheral arterial disorder which leads to a high rate of failure<sup>9</sup>.

In cases of mainly arteriopathy lesions, surgical intervention by revascularization is the primary therapeutic approach, in case of unfavorable results major amputation will be performed<sup>15</sup>. 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 treatments<sup>14</sup>. 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 them<sup>12</sup>.

### **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 cases<sup>14</sup>. 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 foot<sup>12</sup>.

## **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 therapy<sup>16</sup>.

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 changes<sup>16</sup>.

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 prognosis<sup>3</sup>.

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%<sup>12</sup>. 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 fasciitis<sup>16</sup>. Other types of minor lesions that needed surgical approach were fluid collection, skin fistulae with persistent purulent secretions<sup>16</sup>.

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 results<sup>16</sup>. 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 infections<sup>18</sup>. 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 systems<sup>19</sup>. 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 PD<sup>18</sup>.

#### ***Colorectal cancer in DM***

Recent research has shown a significant link between diabetes and colorectal cancer<sup>8</sup>. 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 frequent<sup>20</sup>. Patients with DM have a 30% increased likelihood of developing colorectal cancer, according to a meta-analysis<sup>21</sup>. Although more research is needed to fully understand this issue, the possibility of increased colorectal carcinogenesis related to insulin resistance is not contestable<sup>8</sup>. 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 infections<sup>22</sup>. 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 neuropathy<sup>23</sup>. 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 denervation<sup>24</sup>. 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 approach<sup>25</sup>.

## **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.

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