"OVIDIUS" UNIVERSITY OF CONSTANŢA

DOCTORAL SCHOOL OF MEDICINE

MEDICAL FIELD

Surgical implications in the evolution and treatment of patients with Diabetes Mellitus

DOCTORAL THESIS ABSTRACT

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The doctoral thesis includes:

- 217 pages (General Part – 44 pages, Personal Part – 134 pages), 127 figures, 119 tables, 236 bibliographic references;
- 2 articles published in BDI as the principal author.

Keywords: diabetes mellitus, peripheral ischemia, diabetic foot, diabetic gangrene, ulceration, prevention.

MOTIVATION FOR CHOOSING THE SCIENTIFIC RESEARCH TOPIC

Over time, there has been a significant delay in understanding the pathogenesis of diabetes mellitus, which remains unrecovered even today.

Our research is explained by the significant presence of diabetic peripheral ischemias, which, in surgical stages, lead to necrectomies, amputations, or associations of these sacrifices with arterial revascularization surgical methods. For this purpose, we aimed to investigate the factors that differentiate surgical cases with severe ischemia from medical ones.

Certainly, there should be an increase in the deepening understanding of groups of patients who have reached vascular failure stages to prevent the hypothesis of such an evolution.

In this regard, we designed a reevaluation of patient groups in light of current knowledge about the mechanisms and evolution of the condition, aiming for optimized therapeutic protocols and as minimal or anatomically limited surgical sanctions as possible.

The informational board about diabetes has changed significantly from classical data, both in terms of physiopathological explanations and staged diagnostics based on advanced investigations, as well as in the therapy of the disease itself. Additionally, in selected surgical cases, it aims to predict the significant reduction in the direction towards surgery for this pathology.

I. CURRENT STATE OF KNOWLEDGE

Diabetes mellitus can be defined as a pathological condition, representing an extremely important pathological entity [1], with a major impact on cardiovascular mortality and morbidity. The risk of cardiovascular mortality is 2-4 times higher than in non-diabetics, with approximately 80% of diabetic patients dying due to cardiovascular events [9].

Peripheral vascular disease also presents an incidence 2 to 4 times higher compared to individuals without diabetes mellitus [13], being the main cause of non-traumatic amputations in developed countries [14]. Among diabetics, peripheral vascular disease represents one of the most significant causes of chronic complications, including chronic pain syndromes, chronic ulcers, and amputations. Neuropathies hold a prominent place among the chronic complications of diabetes mellitus, significantly impacting patients' quality of life and life expectancy, leading to substantial healthcare costs [13,17].

The treatment of this complex pathology is burdened by the presence of complications that patients often exhibit in various degrees, ranging from optimizing lifestyle and therapies with oral antidiabetic medications or insulin therapy to surgical treatment in cases of advanced complications [1,32,33].

Diabetes mellitus itself represents an independent risk factor for atherosclerotic pathology. Major clinical manifestations of atherosclerosis [49], such as ischemic coronary disease, cerebrovascular disease, and peripheral vascular disease, occur at a higher incidence in diabetic patients [49,50], against a backdrop of premature and extensive atherosclerosis [11,46,47]. Clear evidence of established vascular changes is revealed by the presence of medial calcifications in diabetic patients, which predict subsequent vascular events [11,47,49,50].

Moreover, diabetes mellitus significantly increases not only the incidence of developing arteriopathy but also the severity of lower limb ischemia [53,54]. Diabetes mellitus plays a crucial role in atherogenesis through both functional abnormalities of the arterial wall [55] and conditions of hyperinsulinemia and hyperglycemia [52,56,57].

Within the context of generalized atherosclerosis in diabetics [57], peripheral vascular disease remains an important indicator, necessitating careful examination of carotid and coronary arteries since patients with obliterative arterial disease of the lower limbs are at risk even if asymptomatic [61].

Consequently, diabetic patients present an increased associated risk of developing peripheral arterial disease, directly proportional to aging, different degrees of association with

neuropathy, and insulin treatment. This is correlated with a significant increase in the incidence and severity of lower limb ischemia [62].

Vascular changes are often present before the diagnosis of diabetes mellitus and worsen in parallel with its duration, particularly with poorer glycemic control. Early diagnosis of peripheral arterial disease allows prevention of its extension throughout the lower limb [71,72].

The evaluation of peripheral arterial disease is likely the most challenging in diabetic patients. Their presentation to healthcare providers is often delayed, including the late diagnosis of diabetic disease, frequently occurring several years after the first recording of above-normal blood glucose levels [79]. This indicates a silent and secure progression of diabetes toward its vascular complications, resulting in patients seeking medical help when trophic lesions are already extensive, infected, presenting total or partial limb compromise [79].

In terms of diagnostics, the evaluation of arteriopathy should be performed from the time of diagnosing diabetic disease. The current methods include ABI (ankle-brachial index), segmental blood pressure, Doppler ultrasound, arteriography, as well as CT angiography and MRI angiography [89].

It's worth noting that although the ankle-brachial index is an important indicator of the degree of arterial obstruction (correlated or not with clinical presentation), its clinical value in diabetic patients is limited. In many cases, it is overestimated (0.9 is a diagnostic criterion; 0.5 represents chronic ischemia) [90]. Arteriography or CT angiography remains the gold standard in exploring occlusive arterial disease, accurately specifying the location of arterial lesions and observing blood circulation [46], being indispensable in any service performing surgical revascularization procedures [46,92].

The diabetic foot syndrome represents a complex pathological entity, a true long-term disabling complication resulting from peripheral polyneuropathy, arteriopathy, minor traumas, superinfections, foot deformities, all sharing a common element: the increased risk for lower limb ulcers and/or amputations.

Prevention and early, correct treatment of lesions can reduce the number of amputations by over 80% [95]. However, late recognition of lesions, presence of visual and gait disorders, peripheral sensory impairment, social isolation, and lack of compliance by some patients are important risk factors for diabetic foot lesions and, consequently, amputations [97].

The progression of this condition is burdened by multiple complications resulting from vascular and nervous lesions, in turn caused by diabetes. Tissue, vascular, and nervous impairment equally depend on the disease's progression, its degree of compensation, as well as the patient's associated conditions. Therefore, the diagnosis needs to be established early to allow for a correct and as "conservative" treatment as possible [97].

The correct treatment of ulcers represents the primary method of preventing amputations. Diabetes mellitus is highly susceptible to infections, with one in two diabetics requiring at least one medical consultation annually for an infectious condition [113].

Diabetic gangrene represents the most severe and disabling complication of diabetic foot. The mortality rate of patients with diabetic gangrene ranges between 0.5-6%, according to numerous studies [131], and is determined by multiple associated weaknesses in these patients [139].

The management of diabetic foot complications is complex and requires close collaboration between the diabetologist and surgeon, as metabolic rebalancing plays an essential role in the healing stages of these patients. Infectious factors, most frequently associated with diabetic foot lesions, as well as hyperglycemia, are in a vicious circle, where both factors sustain each other [157,158].

Vascular surgery is important in the progression of diabetic foot lesions and involves as a primary step the completion of a complete angiography. Diabetic foot revascularization through bypass/deobstructions often results in partial favorable outcomes and moderate efficiency over time [62,92]. The necessity of performing amputations in diabetic patients depends on two categories of factors: vascular status and the type of lesion [175].

The optimal way to improve the prophylaxis and treatment of patients with diabetic foot is a multidisciplinary approach [207]. Monitoring according to a clinical algorithm of changes occurring at the foot level identifies, in due time, the optimal moment for surgical intervention [202,207].

II. PERSONAL CONTRIBUTION

Purpose and Objectives of the Work

The purpose of the work is to research the correlation between blood sugar levels and the degree of arterial ischemia to improve the treatment outcomes of patients with diabetes mellitus and specific diabetic foot lesions, as well as for the implementation of optimal multidisciplinary treatment measures with well-defined surgical tactics.

Objectives of the work:

1. Identification of causes and factors (external/internal) contributing to the complications of diabetes mellitus and their mitigation;
2. Study of limited surgical interventions and minimally invasive treatment to reduce the number of patients reaching amputations or invasive surgical interventions, with significant economic impacts;
3. Study of the presence of dyslipidemia and atherogenesis in diabetic patients with peripheral vascular disease;
4. Identification of associated pathologies and comorbidities of metabolic nature: cardiac, pulmonary, dyslipidemia, and others, as well as determining their influence on the interventions to be performed;
5. Correlation of lesion severity with diabetes severity (blood sugar levels, dyslipidemia, etc.).

Materials and Methods

The work's objectives were pursued on a group of 303 patients, 152 of whom were from the Medical Section (Diabetes, Nutrition, and Metabolic Diseases compartment) of the "Sf. Apostol Andrei" County Emergency Clinical Hospital in Constanța, while the remaining 151 came from the Surgery II section of the same hospital. The study was conducted over a period of 4 years, between 2015-2019.

Following the analysis of the observed cases, we drew relevant conclusions, which were compared with existing data in specialized literature and specialty protocols.

The patients admitted to the two sections were divided into two groups: the first group (Group A) comprised diabetic patients without surgical complications (medical lot),

and the second group (Group B) comprised diabetic patients with surgical complications (surgical lot). Hence, among the myriad complications associated with diabetes mellitus, we followed the presence of lower limb peripheral arteriopathies, which generate chronic ischemic diabetic foot in patients from Group B.

Within this group, we encountered two categories of situations: some patients presented purely diabetic arteriopathy, while others had associated complications due to a predilection for small vessels, such as diabetic and atherosclerotic arteriopathy. For this latter category of patients, having both diabetes mellitus and atherosclerosis, the necessity of performing a revascularization procedure is absolutely essential to avoid major amputations (thigh amputations, for example). In other words, this category addresses both vascular reconstructive surgery and amputations, as in the case of the diabetic foot.

A vital contribution to the accurate diagnosis of arteriopathy was provided by performing CT angiography or MRI angiography, allowing us to visualize the femoral and external iliac arteries and accurately indicating the site of obstruction, which subsequently led to establishing the indication for revascularization as the optimal treatment method.

The data required for this work were taken from clinical observation sheets from the General Surgery sections, Vascular Surgery, and the Clinic of Diabetes, Nutrition, and Metabolic Diseases at the Constanta Emergency Clinical Hospital. Patients were followed and investigated both preoperatively and postoperatively.

On another note, the parameters monitored in the study were included in a work sheet (template) to facilitate data collection, utilized as a monitoring scheme for the data entered. The template was entered into a medical data management program, which was later statistically analyzed in MS Excel 2016 and SPSS. Statistically, the studies are descriptive, inferential, and also employ comparison methods. To support the conclusions, it was deemed appropriate to present 3-4 representative case studies for this work. Therefore, the main data obtained were specified, which are in agreement or differ in relation to those mentioned in the specialized literature or which are not mentioned in it.

The primary target group remains patients with arteriopathy, as these patients ultimately undergo surgeries. Simultaneously, we also studied the relationship between surgery, results and diabetes evolution.

Sequential Research Results

The study analyzed data for patients requiring specialized medical assistance, either in the medical section, namely the Diabetes, Nutrition, and Metabolic Diseases Clinic, or in the surgical section, namely the Surgery Section of the Constanta County Emergency Clinical Hospital.

According to patient gender, we observed significant differences in proportions between the two admission sections. Specifically, for patients treated in the medical section, the proportion of females was 58.6%, while for patients treated in the surgical section, the percentage of females was 33.1%, indicating an almost twice lower proportion of female patients requiring surgical specialty treatment (Table 2.3).

Table 2.3. Distribution by patients gender

			Department of Admission		Total
			Diabetes,Nutrition and Metabolic Diseases	Surgery	
Gender	Male	Number	63	101	164
		% of Admission Section	41.4%	66.9%	54.1%
	Female	Number	89	50	139
		% of Admission Section	58.6%	33.1%	45.9%
Total number		Number	152	151	303
		% of Admission Section	100.0%	100.0%	100.0%

In essence, a higher proportion of male diabetic patients are admitted for surgical treatment of lower limb issues within diabetes.

Regarding secondary diagnoses highlighted in discharge papers, for patients admitted to the Diabetes, Nutrition, and Metabolic Diseases department, the average was 4.93 diagnoses. Meanwhile, for the Surgery section, the average number of secondary diagnoses was 3.46. This indicates a tendency for a lower number of secondary diagnoses reported on discharge in the Surgery department (Figure 2.6).

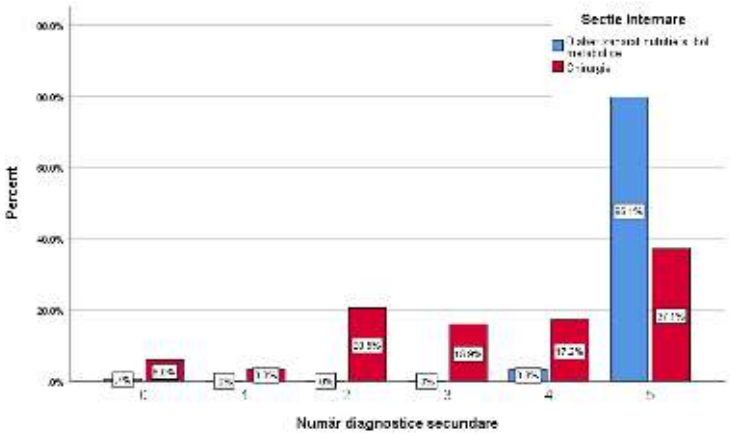

Fig. 2.6. Distribution by number of secondary diagnoses

Peripheral neurovascular involvement represents a significant complication of diabetes. It was identified in more than half of the study patients (57.4%).

Comparing data by gender, similar percentages were observed between genders for patients admitted to the medical section, but significant differences were noted for patients admitted to the surgical section. There was a significantly higher proportion of male patients with a diagnosis of peripheral neurovascular involvement compared to female patients (43.6% versus 36%).

Gangrene of the lower limbs was observed in patients admitted to both the medical and surgical sections, approximately 2.6% in medical and predominantly 93.4% in the surgical section. The differences are significant both clinically and statistically ($p<0.001$), primarily explained by section specifics (Table 2.18).

Table 2.18. Association between gangrene diagnosis and department of admission

			Department of Admission		Total
			Diabetes,Nutrition and Metabolic Diseases	Surgery	
Gangrene	***No***	Number	148	10	158
		% of Admission Section	97.4%	6.6%	52.1%
	Yes	Number	4	141	145
		% of Admission Section	2.6%	93.4%	47.9%
Total number		Number	152	151	303
		% of Admission Section	100.0%	100.0%	100.0%

From the total patients in both study groups, 10 patients had a history of amputation, with 90% being admitted to the Surgery department, a statistically significant difference, p=0.01 (Table 2.24).

Table 2.24. Distribution by history of amputations and department of admission

			Department of Admission		Total
			Diabetes,Nutrition and Metabolic Diseases	Surgery	
History of amputations	***No***	Number	151	142	293
		% of Admission Section	99.3%	94.0%	96.7%
	Yes	Number	1	9	10
		% of Admission Section	0.7%	6.0%	3.3%
Total number		Number	152	151	303
		% of Admission Section	100.0%	100.0%	100.0%

Conclusively, it can be stated that males were much more predisposed to require subsequent interventions on lower limbs in the surgical section compared to females, partly due to the presence of amputations in their history and their tendency to develop various surgical complications.

To highlight the evolution of blood sugar levels during hospitalization, a new variable was created: the evolution of blood sugar. It appears that there was an average drop in blood sugar twice as high in patients admitted to the medical section (average drops of 107.65 mg/dl for medical section versus 52.51 mg/dl for the surgical section) (Table 2.39).

Table 2.39. Descriptive statistical analysis of blood sugar evolution

	Department of Admission		
	Diabetes,Nutrition and Metabolic Diseases	Surgery	Total
N	117	89	206
Mean	-107.65	-52.51	-83.83
Standard Deviation	86.32	84.96	89.80
Minimum	-414.00	-341.00	-414.00
Median	-91.00	-39.0000	-72.00
Maximum	38.00	182.00	182.00
Skewness	-1.114	-5.79	-7.70
Kurtosis	1.417	9.21	1.243

To emphasize is the fact that, the blood glucose values are influenced not only by increased blood sugar but also by numerous intrinsic and extrinsic factors that equally contribute to its alteration, both in terms of increase and decrease.

The difference in the elevated values of the leukocyte count between the two sections, namely 31% (Figure 2.45), concludes that patients in the surgical section were more exposed to infections and had a much slower recovery due to lowered immunity, where glucose fluctuations, as mentioned earlier, played a decisive role in the subsequent development and maintenance of infections.

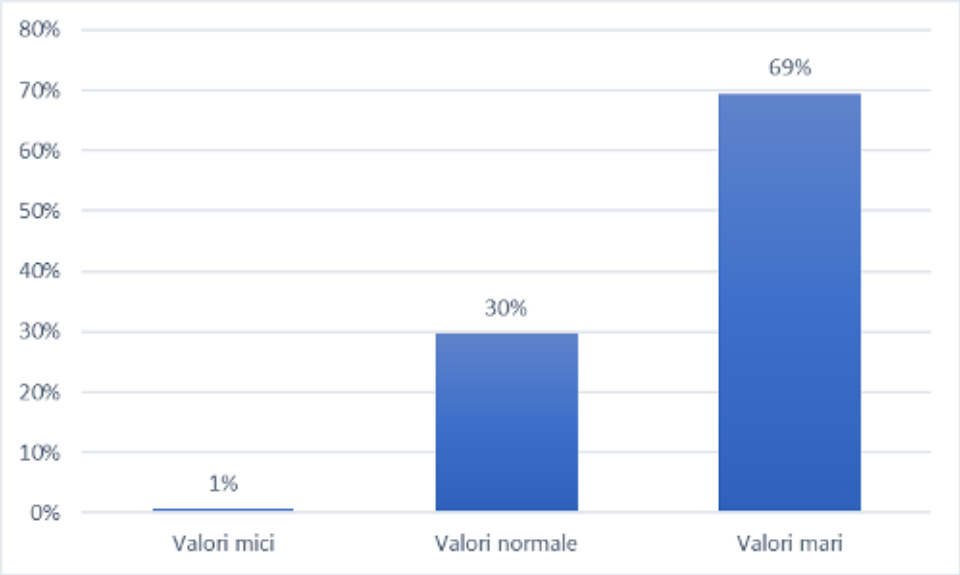

Fig. 2.45. Normal distribution of leukocyte count in diabetic patients, surgically treated.

Following the descriptive statistical analysis of the LDL cholesterol fraction, it was observed (Table 2.97) that there is a moderate difference between the two groups of patients (103.5 versus 129.0), a statistically significant difference, demonstrating higher values of LDL cholesterol fraction in the group of surgical patients compared to the medical group.

Table 2.97. Descriptive statistical analysis of LDL cholesterol fraction

LDL cholesterol	**Department of Admission**		
	Diabetes, Nutrition, andMetabolic Diseases	Surgery	Total
N	130	114	244
Mean	109.94	129.77	119.20
Standard Deviation	4.3646	5.1039	4.8176
Minimum	23	10	10
Median	103.50	129.00	113.50
Maximum	220	231	231
Skewness	4.91	1.89	3.90
Kurtosis	-3.19	-6.60	-4.99

Regarding the glycosylated hemoglobin indicator, it is observed from Figure 2.70 that within the medical group, the majority proportion consists of high values, at 87%, much higher than in the case of the surgical patient group (68%), representing a risk factor for this category of patients.

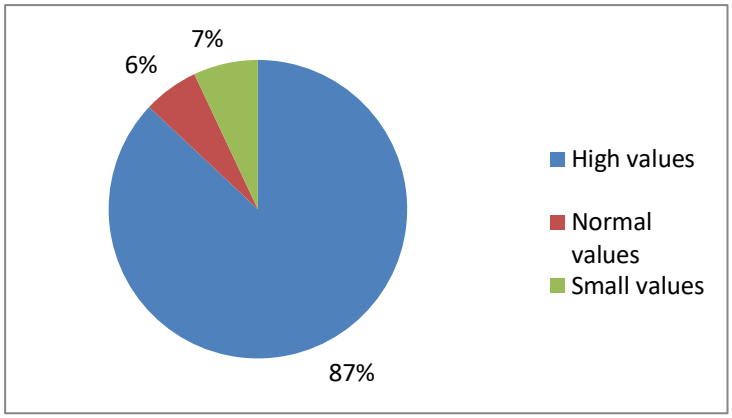

Figure 2.70. Normality distribution of HbA1c for patients in the medical section

However, concerning IGB (ankle-brachial index) values, it was noticed that low values of IGB represent the highest proportion (85%) for diabetic patients treated surgically, compared to the group of diabetic patients in the medical section (73%). (Figure 2.73.).

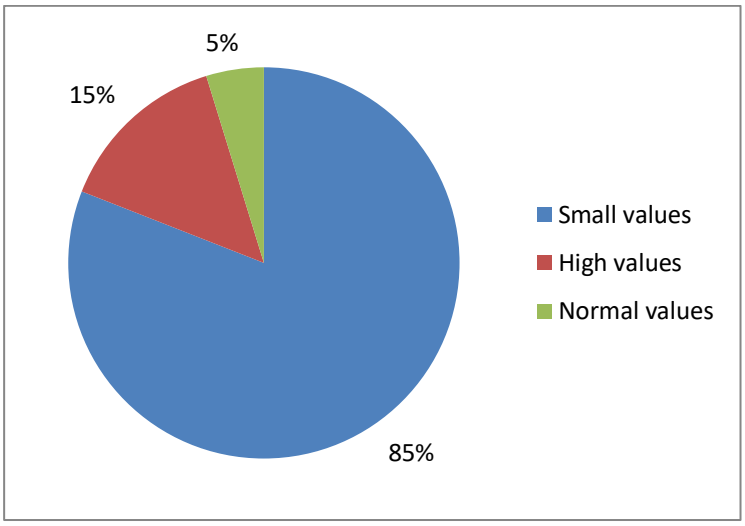

Figure 2.73. Normality distribution of IGB in diabetic patients, surgically treated

Results

At the population level, numerous observational studies demonstrate that both average and higher incidence rates are found in the male category compared to females, while in populations with lower incidence, women seem to have a higher risk. Thus, within our study, we obtained the same results, namely a smaller proportion of females needing interventions in the surgical field.

If we specifically refer to peripheral arteriopathy, as an integral part of peripheral neurovascular impairment, it represents one of the most important causes for the appearance of persistent ulcers, painful syndromes, as well as amputations, both among diabetic patients and non-diabetic individuals.

The involvement of risk factors in the development of different types of lesions or ulcers that can lead to the appearance of gangrene in the lower limbs is well-known, especially their elimination (glycemic control, blood pressure control, maintaining an ideal body weight, quitting smoking, combating sedentary lifestyle).

This difference between genders in the total cases of lower limb gangrene is quite significant, approximately 36.5%, highlighting that men bear a significantly higher risk of developing ulcers in the lower limbs compared to women, which may eventually lead, through the involvement of the aforementioned risk factors, to the appearance of lower limb gangrene. These results also underline that the amputation rate tends to be much higher in male patients.

Currently, the risk of a patient with diabetes developing an ulceration and later requiring an amputation has become much higher than the risk of losing sight or reaching the final stage of chronic renal failure.

Finally, comparing the percentages obtained from the statistical analysis between the two sections, medical and surgical, we can support the fact that the shorter duration of hospitalization and the absence of the need for surgical interventions for patients hospitalized in the medical section, as well as their condition at discharge, significantly improved compared to that of patients hospitalized in the surgical section (99.3% versus 64.5%), is due to both better glycemic control and adherence to implemented treatment regimens.

In light of the above, it is of major importance to define glycemic control as an integral part of long-term metabolic balance, as the glycemic homeostasis of a diabetic patient is significantly different from that of a non-diabetic individual.

In this work, as presented in the previous chapter, there was a statistically significant difference in terms of LDL cholesterol fraction, explained by higher values of this indicator in patients admitted to the Surgery section, giving these patients a higher implicit risk of developing cardiovascular and atherothrombotic events, through the existence of an advanced atherosclerosis process, affecting blood vessels and circulation. As for the HDL cholesterol and triglyceride indicators, they do not represent an additional cardiovascular risk factor.

In our study, we observed that the highest incidence is that of normal values, specifically 73%, for the group of diabetic patients in the medical section, with low values as well as high ones (15% and 12%, respectively) being much lower in incidence in this group of patients compared to diabetic patients treated surgically, where low values of IGB represent the highest proportion (85%), followed by a significantly lower incidence of high and normal values (15% and 5%, respectively). Therefore, measuring IGB is mandatory for all diabetic patients, accurately indicating the risk of patients developing different degrees of arteriopathy, subsequently, angiography-CT should be performed to confirm the location of the obstruction and the degree of arteriopathy.

Treatment and management of diabetic foot complications within the investigated group

The treatment of diabetic foot complications includes the combination of both medical and surgical treatment.

In this chapter, to support the working hypothesis, four case presentations suggestive of our pathology were chosen, addressed both medically and surgically.

Thus, in the first two presentations of this scientific work, the cases of two patients who underwent surgical intervention were addressed, performing arterial revascularization procedures to prevent traumatic amputations as much as possible. In the next two case presentations, their approach and management were predominantly medical, as these patients had optimal metabolic control during the study, ultimately not requiring surgical procedures, either arterial revascularizations or traumatic amputations, due to the control of all associated risk factors.

Therefore, the importance of the degree of metabolic balance, both in the short and long term, in diabetic foot complications management is emphasized.

Discussions

Regarding the age of patients in both medical and surgical groups, although the statistically obtained differences were minimal, patients admitted to the medical section were younger (under 40 years old), compared to those admitted to the Surgery section, with the clarification that in the surgical patient group, there were no patients under the age of 40.

In terms of patient gender, there were significantly different proportions between the two admission sections, so in the case of patients treated in the medical section, the proportion of females was 20% higher than in surgical patients, while in the case of patients treated in the surgical section, there was approximately twice the proportion of female patients who required surgical specialty treatment.

Essentially, a higher proportion of male diabetic patients end up being hospitalized in the Surgery department for the surgical management of lower limb complications in diabetes compared to female patients.

Regarding the frequency of types of complications or comorbidities associated with diabetes observed in patients from both study groups, different percentages were found between the two sections, regarding cardiovascular impairment, higher for female patients hospitalized in the Medical section, where more patients also present a higher number of secondary diagnoses, while at the same time, there is a tendency for the number of secondary diagnoses reported at discharge to be smaller.

If we refer to the peripheral neurovascular impairment, we obtained similar results. Namely, when comparing the data by gender, we found similar percentages between genders for patients admitted to the Medical section. However, there were significant differences for patients admitted to the Surgical section, where a significantly higher proportion of male patients with a diagnosis of peripheral neurovascular impairment was observed compared to female patients (43.6% and 36%, respectively).

Lower limb gangrene was observed in both patients admitted to the Medical section, in approximately 2.6% of cases, and the Surgical section, where it represented the majority of cases, specifically 93.4%. These differences were significant both clinically and statistically. Regarding each gender, diabetic gangrene was diagnosed in 61% of male patients compared to female patients (32.4%).

Out of the total patients in both study groups, we observed a number of 10 patients with a history of amputation, with 90% of them being admitted to the Surgery section. Thus, concluding the obtained results, we can affirm that men were much more predisposed to

require subsequent interventions at the lower limb level in the Surgical section compared to women. This predisposition is partly due to the existence of amputations in their medical history and their tendency to develop various complications in the surgical sphere.

It was observed that the average decrease in blood glucose was twice as high in patients admitted to the Medical section (average decreases of 107.65 mg/dl for the Medical section and 52.51 mg/dl for the Surgical section). This significant difference in favorable glycemic evolution concerning the Medical section is attributed, on the one hand, to the optimal control of both blood glucose and other biological parameters, and on the other hand, to the patients' adherence to the initiated therapy from the beginning of the hospitalization period until discharge.

Regarding the inflammatory status, specifically the value of fibrinogen, in both groups of patients, although the value of this inflammatory marker is often elevated in diabetic patients, its prevalence was observed more among surgical patients. This explains the subsequent unfavorable evolution towards surgical complications.

The observed differences in bleeding time (aPTT) within the study groups indicate that patients in the Surgical study group have a moderate, even higher risk of developing hemorrhagic complications compared to the comparative Medical group.

Regarding the lipid profile, the observed difference between the two groups is statistically significant, demonstrating higher values of the LDL cholesterol fraction in the Surgical patient group compared to the Medical group. Therefore, this difference indicates that patients in the Surgical study group have a higher risk of cardiovascular incidents compared to patients in the Medical group. The same difference was not observed, however, in the case of HDL cholesterol and triglyceride fractions, indicating that these do not necessarily represent an additional risk factor for patients in both study groups.

The observed values of glycosylated hemoglobin in both groups were significantly higher in patients from the Diabetes, Nutrition, and Metabolic Diseases section compared to those observed in the Surgery section. Thus, this result indicates that patients in the Diabetes section have higher HbA1c values due to long-term glycemic decompensation compared to the Surgical group.

Changes in the ankle-brachial index (ABI) values in both study groups revealed a much higher proportion of low values, specifically 85%, in diabetic patients treated surgically compared to the diabetic patients in the Medical section, where the proportion of low ABI values represented only 15% of the total values. This underscores the higher risk of developing various degrees of arteriopathy in diabetic patients in the surgical group

Conclusions

1. Diabetes mellitus, despite therapeutic advancements, remains a serious condition with a significant surgical patient group, caused by the vascular complications of the disease.
2. Research on medical and surgical cases of this condition has highlighted numerous elements specific to the surgical group, particularly in diabetic foot cases. These elements need to be monitored in modern therapeutic protocols to de-surgicalize diabetic patients, which is the proposed goal, as well as the contribution of the conducted study.
3. Correlating surgical complications with the aging of patients demonstrates the association of classic diabetic microangiopathies with an obstructive load on large femoropopliteal vessels. This necessitates arterial imaging investigations for all patients over 40 years old, especially males, where a significant surgical burden was found.
4. Surgical complications occur approximately 20% more frequently in men, indicating a lesser adherence to therapeutic guidelines, dietary measures, risk factor abstinence, essentially a lack of stable glycemic values.
5. Diabetic gangrene is much more prevalent in men (68% compared to only 32% in women), suggesting a specific endocrine protection that should be the subject of further dedicated research.
6. Re-amputations are not very frequent and are usually limited but involve prolonged hospitalizations, aligning with existing literature data.
7. Paradoxically, in our study, blood glucose values were higher in the medical group than in the surgical group. In-hospital determinations are associated with the scope of an intervention, which doesn't present a long-term picture of the evolution leading to ischemic and irreversible complications.
8. Balancing and "normalizing" blood glucose levels occurred much faster in the non-surgical cases, which is extremely valuable compared to the diminishing response to hypoglycemic therapy with the prolongation of the evolutionary interval.
9. It's paradoxical that numerically, comorbidities in our studied groups are more frequent in women, which, correlated with more frequent gangrene in men, leads to the conclusion that diabetes in men represents a more severe vascular condition than in women. This somewhat partially confirms the classic concept that at menopause, there

is a collapse of women's vascular protection, coinciding with the fulfillment of their biological (divine) mission to perpetuate the human species.

10. Neurovascular impairment was equal in both the surgical and medical groups, indicating the independence of this complication and its lack of correlation with other factors, including the patients' gender.
11. Among the laboratory elements studied in our groups, we found a parallelism and fidelity of the leukocyte count with the course of the cases, significantly correlating with superinfections and predicting irreversible ischemic complications. In contrast, we observed a significant change in the platelet count in the surgical group, behaving similarly to blood fibrinogen.
12. The ankle-brachial index represents a fairly faithful parameter, yet inexplicably, it is not applied and researched, being overshadowed by glycemic determinations, CT scans, angiographies, glycosylations, etc.

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