IMPACT OF COVID-19 ON THE COURSE OF DIABETIC FOOT SYNDROME

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Keywords:
diabetic foot syndrome,
neuro ischemia,
angiopathia,
foot ulcers,
amputation,
complications of amputations,
coronavirus infection.

Abstract
It is known that diabetes mellitus (DM) complicates the course of many diseases, since it affects almost all systems of the human body. As the practice of 2020 has shown, this phenomenon also applies to infectious diseases. The work analyzes the clinical and laboratory values and results of treatment of patients with purulent-necrotic complications of DFS. All of these patients had a history of COVID-19 in 2020. In the majority of patients with purulent-necrotic complications of DFS, treatment ended with amputation of the hip. A mathematical model was developed, which was the basis of the software module - a program for predicting the likelihood of limb amputation in ulcerative-necrotic lesions of DFS. Due to the careful selection of the main parameters of the state of blood circulation in the limb and the degree of generalization of the purulent-necrotic process, this program allows, in the conditions of a non-specialized multidisciplinary medical institution, to predict the likelihood of limb amputation.

ISSN 2181-3175

INTRODUCTION

Diabetes mellitus (DM) is known to complicate the course of many diseases as it affects almost all human body systems [1]. As practice of 2020 showed, this phenomenon also affects infectious diseases [2]. According to the WHO recommendations, people with diabetes are a category of patients at high risk of a severe course of COVID-19 [3]. Evidence is available as to why coronavirus infection is not favorable in this patient population [2-5]. The main argument is the important role of hyperglycemia, which is seen in patients without control of their diabetes mellitus [6]. Accordingly, at present, we note a tendency of special course of complications of DM, in particular diabetic foot syndrome (DFS), in patients who have undergone COVID-19.

MATERIAL AND METHODS OF RESEARCH

We have analyzed clinical and laboratory values and treatment results of 126 patients with purulent-necrotic complications of DFS. All these patients had a history of COVID-19 in 2020. In 82 patients with purulent-necrotic complications of DFS, treatment resulted in amputation of the thigh.

The degrees of tissue damage in diabetic foot syndrome were determined according to the Wagner F. criteria developed in 1979. [7]: 0 - no ulcerous defect, but there is dry skin, beak-like deformity of fingers, protrusion of metatarsal bone heads, other bone, joint abnormalities;

I - superficial ulcer without signs of infection;

II - deep ulcer, usually infected, but without involvement of bone tissue in the process;

III - deep ulcer with abscess formation, involving bone tissue;

IV - limited gangrene (toe or part of the foot);

V - gangrene of the entire foot.

To determine the qualitative composition of the microflora, the wound exudate was inoculated on selective nutrient media for aerobic and anaerobic microorganisms. Identification of Gram-negative bacteria was performed by studying the biochemical activity of these microorganisms using a number of differential diagnostic tests and media. In order to predict the development and course of DFS, the degree of wound contamination, or the number of microorganisms per 1 gr of tissue, was quantified by microbiological examination.

Assessment of regional microhemodynamics by determining the partial pressure of oxygen in the skin ($TcPO_2$) made it possible to estimate indirectly the state of the microcirculatory blood flow in the tissues of the area under study.

RESULTS OBTAINED AND THEIR DISCUSSION

The analysis of the dependence of the frequency of high amputations on the degree of ulcerous lesion according to Wagner showed that in the patients with degree I the outcome of treatment was without amputation of the limb at the thigh level. The low proportion of thigh amputations was noted in patients with grade II and grade III ulcerous lesions (33,3% and 39,3%, respectively). A high percentage of thigh amputations was noted in patients with grade IV and grade V ulcerous lesions. It should be noted that this picture of treatment outcomes appears to fit the logic of the de-

pendence of high rate of thigh amputations on the depth of ulcerous lesion in patients with different clinical and pathogenetic forms of DFS [8,9]. However, this analysis, as mentioned above, included patients with both neuropathic and neuroischemic forms of DFS (Table # 1).

Table # 1

Dependence of the frequency of high amputations on the degree of ulcerous lesions according to Wagner

DEGREE OF ULCEROUS LESION	ANALYSED PATIENT POPULATION			
	Number of patients		Of these, thigh amputations	
	n	%	n	%
I	2	1,6	-	-
II	15	11,9	5	33,3
III	28	22,3	11	39,3
IV	56	44,4	42	75
V	25	19,8	24	96
TOTAL	126	100	82	65,1

A retrospective analysis of the microbiological characteristics of the ulcerous-necrotic process in patients with various forms of DFS showed a close correlation with the number of microbes in 1 gr of tissue. In particular, if in patients subjected to thigh amputation, the microbial semination of foot ulcers was in the order of 105 CFU/ml or higher, then the number of patients with lower parameters of microbial semination of thigh amputation actually was not.

We determined the features of the wound process course by the nature of the necrobiotic process in the wound bed, the tissue type in the wound bed, the extent of the affected area, the amount and nature of the wound exudate, its consistency, colour, and odour (Table #2).

The analysis of the frequency dependence of high amputations on the nature of the necrobiotic process in the wound showed that these operations were performed to a greater extent in patients with mixed wound necrosis (63,4%). In the presence of dry or moist wound necrosis, thigh amputations were performed in 3,7% and 25,6% of cases, respectively. In 31 patients with inflammatory process in the wound without wound necrosis the proportion of amputations was 7,3% (6 patients). Patients without an inflammatory process in the wound (1,6%) all managed to preserve the supporting function of the limb.

Tissue types in the wound bed included granulation tissue (in 47,27% of cases), fibrous tissue (14,79% of cases), fibrinous film and scab (37,94% of cases). Granulation tissue was red, dense and lumpy. Its fragility indicated the presence of bacterial contamination. Fibrous tissue was yellow and dense in 98,9% of cases. The fibrinous film was often friable and had a yellow to grey-green colour gradation. At the same time, the scab was black in colour, indicating the presence of necrotic tissue. The scab could be soft and moist or hard and dry. The extent of the lesion area was from the tip of the toe to the heel and the entire foot.

Pain syndrome was another important feature in the evaluation of the wound condition. An increase in pain and destruction is known to be the most significant sign of a wound [10].

The presence of a fragile granulation tissue and an unpleasant odour was as diagnostic as a purulent effusion. However, the exudate of an infected defect was odourless in 32,7% of cases.

The following scale was used to assess odour during bandage changes: no odour near the wound, a faint odour near the wound, a faint odour in the room, a strong odour in the room [11]. On the other hand, direct inspection of the wound bed was a simple and quick procedure, and it helped in obtaining information about the etiology of the lesion, making an accurate diagnosis, and developing goals and a treatment plan. Subsequent monitoring helped to determine the degree of efficacy of the therapy.

Evaluation of the wound bed appearance included a description of its colour, structure and the presence of any deeper structures in the wound (pockets and effusions). Coloration was varied in 97,4% of cases: black, yellow, red, pink and white. Black or dark brown staining of the wound appeared due to thickening of the dehydrated necrotic tissue, which was most common in sacral necrosis. This necrosis, or scab, appeared as a result of deep tissue destruction and could completely or partially cover the wound bed. It delayed healing, so we removed it whenever possible during treatment.

A yellow colour of the wound bed in 46% of cases indicated of fibrous tissue or fibrin. Fibrous tissue was dense and appeared in the wound before granulation developed. At the same time, the fibrinous film consisted of cellular detritus and could adhere tightly to the wound bed or be loose. If a large number of leukocytes were present, it was creamy yellow, and if necrotized fascia was involved, the colour changed from yellow to grey-green. If the fibrinous film was associated with connective tissue, it was removed carefully to avoid additional trauma to the wound and prolong the inflammatory response. A red colour of the wound bed indicated the presence of granulation tissue. A bright

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ISSN 2181-3175

A bright red, moist wound surface was a sign of healthy granulation tissue, while a paler, bleeding surface could be due to ischemia, infection or comorbidities such as anaemia. Dark red or hypertrophic granulations in 72,2% of cases were a sign of infection. A pink color indicated the beginning of epithelialisation. At this stage, pink, white or translucent patches of epithelium migrating from the edges of the wound or hair follicles into the wound were usually seen above the granulation tissue. However, these cells may be obscured by effusion or fibrin, or mistaken for macerated skin at the wound edges [12,13]. Depending on the severity of the wound process, its color usually changed from initial black or yellow to red and then to pink as it healed.

Table #2

The dependence of the frequency of high amputations on the nature of the necrobiotic process in the wound

THE NATURE OF THE PROCESS IN THE WOUND	ANALYSED PATIENT POPULATION			
	Number of patients		Of these, thigh amputations	
	n	%	n	%
No inflammatory process	2	1,6	-	-
Inflammatory process without necrosis	31	24,6	6	7,3
Dry necrosis	10	7,9	3	3,7
Moist necrosis	25	19,8	21	25,6
Mixed necrosis	58	46,1	52	63,4
TOTAL	126	100	82	37,6

In patients with the neuroischemic form of DFS, the dynamics of changes in characteristic indices of blood circulation assessment in the limb, had different correlation characteristics. In particular, changes of ankle brachial index (ABI) in relation to resting $TcRO_2$ (r=0,970), whereas Purcellot and Gosling indices (r=-0,915) had high inverse correlation coefficients.

The finger-brachial index (FBI) and $TcPO_2$ orthostatic (r=0.912) were in direct correlation, while the $TcPO_2$ orthostatic and Purcellot index were in inverse correlation (r=-0,914). Less dependent in change were the correlation coefficients between the ABI /$TsPO_2$ and resting $TcPO_2$/$TsPO_2$ orthostatic indices, which were characterized by an exclusively direct relationship (r=0.874 and r=0.850, respectively).

We found an absolutely identical level of correlation coefficient between such Doppler indices as resting PPI/$TsPO_2$, resting PPI/Gosling index and resting $TcPO_2$/Purcellot index. However, whereas in the first two cases the correlation coefficient had a direct value (r=0.845), in the latter case it was the opposite (r=-0.845). The ABI and FBI indices also had a direct correlation relationship. Their correlation in arithmetic value was equal to r=0,815.

Less sensitive direct correlation was observed for such indices as: resting Gosling index/$TsPO_2$ (r=0.768), orthostatic Gosling index/$TsPO_2$ (r=0.718), and resting Gosling index/$TsPO_2$ (r=0.619). Similarly, only the Purcellot/ABI index (r=-0.795) and Purcellot/FBI index (r=-0.746) were in inverse correlation.

The level of wound microbial contamination and the number of SIRS signs were in direct correlation with the Purcellot index (r=0.914 and r=0.974 respectively) and in inverse correlation with the other analysed parameters. The mean value of the correlation coefficient for these parameters was r=-0.857±0.102.

Statistical analysis of the data array allowed us to identify the most characteristic indicators, which formed the basis for the construction of linear integral data on the probability of amputation of the hip in patients with DFS. The most informative 9 indicators are involved in predicting the probability of limb amputation in ulcerative-necrotic lesions of DFS. Among the clinical and laboratory indexes characterizing prognostic probability of the completion of treatment measures by amputation at the thigh level there were especially distinguished: degree of ulcerous lesion according to Wagner, wound microbial semination, presence and quantity of the signs of systemic inflammatory reaction syndrome. The following indices obtained by means of Doppler ultrasound of the lower limbs vessels are also important in patients with the neuroischemic form of DFS: ABI and ABI, TcPO2 at rest and in orthostasis, Purcellot and Gosling indices.

The picture of their transformation depending on the probability of thigh amputation has a different shape. In particular, 5 indices have a decreasing gradation and 4 have an increasing gradation.

When constructing models of probability of thigh amputation in patients with DFS by the method of least squares, the condition of their positive dynamics was imposed on the parameters of the values not lower than the p<0,05 level by the t-criterion. Based on the graphical construction of the above data and identification of their correlation, we developed a software model to assess the course of the purulent-necrotic process in DFS patients who undergone COVID-19.

When constructing the prediction rule using the least-squares method, the weighting coefficient values were determined from the original data sample, and they were the best in the class of linear functions.

This made it possible to take into consideration

ISSN 2181-3175

more objectively the contribution of each investigated feature to the prognosis of the further course of the pathological process (Table #3).

Table #3

Program for assessing the dynamics of the purulent-necrotic process in DFS patients who have undergone COVID-19

CRITERIA	POSITIVE	NEGATIVE
Degree of ulcerous lesion according to Wagner (grade)	I-II	III-V
Microbial contamination of the wound (lg/ml)	≤10^4	10^5≤
Presence and number of signs of SIRS	≤2	3≤
ABI (mmHg)	0,7-1,0	≤0,6
FBI (mmHg)	0,4-0,7	≤0,3
Nature of necrotic process	Dry	Moist
Presence of granulation in the wound	Available	Not available
Presence of purulent discharge from the wound	Not available	Available
Presence of morbid obesity	Not available	Available

The variation of digital arithmetic values in the dynamics of the course of DFS in patients who undergone COVID-19 had a graphical type of compaction within the framework of the variants of the development of this pathological process that we identified. It should be noted that the characteristic changes in the progression of the ulcerous-necrotic process, which led to the need for amputation of the thigh, directly depended on the severity of the laboratory and instrumental parameters obtained in the dynamics of examination of patients with DFS. All of them were pre-evaluated in the starting position. This study approach is most typical for assessing the likelihood of amputation of the thigh in patients with DFS who have undergone COVID-19.

The developed mathematical model was the basis of the software module, a program for predicting the probability of limb amputation in ulcerative-necrotic DFS lesions. Due to careful selection of the basic parameters of blood circulation condition in a limb and the degree of generalization of a purulent-necrotic process, the given program makes it possible to make a prognosis of amputation probability in conditions of a non-specialized multi-specialized medical institution. This, in turn, makes it possible to make an appropriate and correct decision on further treatment tactics of patients with this pathology.

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ISSN 2181-3175