ALGORITHM FOR TREATMENT OF COMPLICATED DIABETIC FOOT SYNDROME

Summary. Diabetes mellitus (DM) is the most common endocrine pathology, which ranks third in the general structure of morbidity after cardiovascular and oncopathology. DM is recognized by the WHO as an epidemic of non-infectious origin, which allows us to talk about the globalization of the problem.

We monitored 2,024 patients with complicated SDS who were treated in the purulent-septic center with diabetic foot beds, Municipal Hospital No. 3, Zaporizhzhia, during the period 2008-2022. In the article, we present the classification and algorithm for the treatment of complicated SDS developed by us, which, in our opinion, will contribute to the progress of specialized medical care for purulent-inflammatory processes of the diabetic foot.

The difficulty of creating and adopting a single surgical classification of complicated SDS is caused, first of all, by the combination of several pathogenetic mechanisms of the development of the pathology.

Modern disease classifications should be: clear and accessible; clearly classify diseases according to the degree of severity; facilitate clinical decision-making; take into account modern diagnostic and treatment methods; increase the economic efficiency of medical care; contribute to the simplification of statistical processing.

The distribution of patients thanks to the proposed classification creates conditions for statistical processing and registration of forms of complicated SDS, as well as the volume of surgical assistance. Allows to determine surgical tactics depending on the specific complication of SDS. The use of a controlled approach to ABT allowed to reduce the number of cases associated with antibacterial resistance from 23% to 11%. Optimization of the complex treatment of patients with complicated SDS made it possible to increase the number of patients with preserved supporting function of the lower limb from 21.9 to 36.5% (χ²=11.2; P<0.05), reduce the number of «high» amputations from 24.5 to 15.1% (χ²=4.8; P<0.05). The distribution of patients according to the proposed classification substantiates the actual terms of arrival at the hospital, taking into account all stages of treatment. A comprehensive approach, priority areas of treatment and a mandatory sequence of actions allow to improve the final results of treatment, reduce mortality from 25.8 to 5.3% (χ²=3.92; P<0.05).

Key words: diabetes mellitus, diabetic foot syndrome, lower limb support function, unified surgical classification

Introduction

Diabetes mellitus (DM) is the most common endocrine pathology, which ranks third in the general structure of morbidity after cardiovascular and oncopathology. DM is recognized by the WHO as an epidemic of non-infectious origin, which allows us to talk about the globalization of the problem.

According to official data of the Center for Medical Statistics of the Ministry of Health, more than 1.9 million patients with diabetes were registered in Ukraine at the end of 2020, but the actual number of patients is 2.5-3 times more. According to WHO experts, the number of patients with diabetes in developing countries is forecast to increase from 6.3 to 8.4 % on average in 2030, from 4.6 to 6.4 % in developed countries, and the total number of patients will reach 366 million people. According to world statistics, the number of patients with diabetes doubles every 13-15 years.

Diabetic foot syndrome (DFS) is one of the most socially significant complications of diabetes, which develops in 10-50% of patients and is the cause of early disability and mortality.

In ICD-10, SDS is not distinguished as a separate nosological unit, but at the Geneva International Conference on Diabetes (1987), the diabetic foot was distinguished as an independent complication. It has been established that the risk of amputation of the lower limb in patients with SDS is 25 times higher, and mortality during the first 5-7 years after
amputation is 50%. Therefore, prevention of amputation is the most important task in the treatment of patients with SDS.

In the publications on this topic, we did not find standardized schemes for the treatment of complicated diabetic foot syndrome, which gave the impetus for an in-depth study.

Materials and methods

We monitored 2,024 patients with complicated SDS who were treated in the purulent-septic center with diabetic foot beds, Municipal Hospital No. 3, Zaporizhzhia, during the period 2008–2022. All patients had type II diabetes. its average duration was (13.6±2.7) years. The average age of the patients was (63.5±2.9) years. There were 972 (48%) men, 1052 (52%) women.

In the article, we present the classification and algorithm for the treatment of complicated SDS developed by us, which, in our opinion, will contribute to the progress of specialized medical care for purulent-inflammatory processes of the diabetic foot.

Prerequisites for creating a classification of complicated diabetic foot syndrome

The difficulty of creating and adopting a single surgical classification of complicated SDS is caused, first of all, by the combination of several pathogenetic mechanisms of the development of the pathology.

Modern disease classifications should be: clear and accessible; clearly classify diseases according to the degree of severity; facilitate clinical decision-making; take into account modern diagnostic and treatment methods; increase the economic efficiency of medical care; contribute to the simplification of statistical processing.

The main requirements include the ability to determine an accurate clinical diagnosis for choosing a treatment method and making a prognosis. We offer an overview of the existing classifications of SDS.

The most well-known and practically applicable classification of SDS Wagner R.M. (1979), which includes determining the depth (prevalence) of the development of the infectious-inflammatory process and reflects the degree (from 0 to 5) of tissue damage. However, this classification does not take into account the etiological features of the development of SDS, it is «conditional» in nature, since it does not distinguish the entire variety of tissue damage. In addition, this classification does not reflect the clinical features and differences in complications of SDS.

Classification of chronic arterial insufficiency of the lower extremities according to Fontaine–Pokrovsky (1972), based on the determination of ischemia of the tissues of the lower extremity. However, with the neuroischemic form of SDS, the pain syndrome and the syndrome of «intermittent» lameness mask polyneuropathy, so certain difficulties arise when using this classification.

In the classification of the diabetic foot of the University of Texas (1996), 12 gradations are provided for the stage and degree of severity, which clearly distinguish the etiological components. However, it does not reflect the level and localization of the purulent-necrotic lesion, which complicates differential approaches to surgical treatment.

The classification of SDS «Redis» (2003) does not allow to assess the level of damage to the tissues of the foot.

The international classification adopted at the consensus conference on diabetic foot problems in 2000 divides it into neuropathic, neuroischemic, and ischemic forms. However, this classification does not reflect specific complications of SDS, which does not allow to determine surgical tactics.

Thus, unfortunately, to date there is no classification of complicated SDS that would satisfy the requirements of specialists.

Classification of complicated diabetic foot syndrome

At the XXII Congress of Surgeons of Ukraine (Vinnitsia, 2010), we proposed a classification of complicated SDS, which provides for the creation of diagnostic and treatment algorithms from the standpoint of evidence-based medicine and substantiates the actual terms of the patient’s stay in the hospital.

The proposed surgical classification of complicated SDS is defined as the «CZE system». It takes into account the clinical form - Clinical form (C), anatomical localization (zone) - Anatomy zona (Z), etiological factor - Etiological factor (E).

At the IV Congress of Angiologists and Vascular Surgeons of Ukraine (Uzhgorod, 2012), this classification was approved and recommended for wide implementation.

The clinical form involves the identification of a specific complication of SDS and is denoted by symbols from C1 to C6.

The prevalence of the local pathological process is assessed according to anatomical criteria, which are denoted by symbols from Z1 to Z6 and reflect the increasing severity of foot tissue damage.

The etiological factor is taken into account as the presence of infection - E1, the presence of ischemia - E2, the presence of infection and ischemia - E3 (Table 1).

Taking into account the clinical form, anatomical localization and etiological factor, the symbolic designation of the clinical diagnosis of complicated SDS according to the «CZE system» can have the following four main groups of options (Table 2).
Classification of complicated diabetic foot syndrome Clinical form

<table>
<thead>
<tr>
<th>Group</th>
<th>Symbolic definition of the diagnosis</th>
<th>Clinical form</th>
<th>Anatomical localization</th>
<th>Etiological factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C_{1,2}Z_{1-3}E_{1,2}</td>
<td>C_{1,2}</td>
<td>Z_{1-3}</td>
<td>E_{1-3}</td>
</tr>
<tr>
<td>II</td>
<td>C_{2-3}Z_{2-3}E_{2-3}</td>
<td>C_{2-3}</td>
<td>Z_{2-3}</td>
<td>E_{2-3}</td>
</tr>
<tr>
<td>III</td>
<td>C_{3-4,5}Z_{3-5}E_{3-5}</td>
<td>C_{3-4,5}</td>
<td>Z_{3-5}</td>
<td>E_{3-5}</td>
</tr>
<tr>
<td>IV</td>
<td>C_{4-5,6,7}Z_{4-5,6,7}E_{4-5,6,7}</td>
<td>C_{4-5,6,7}</td>
<td>Z_{4-5,6,7}</td>
<td>E_{4-5,6,7}</td>
</tr>
</tbody>
</table>

The classification is clinical, allows to determine the surgical tactics depending on the specific complication of SDS, creates conditions for unification and single registration of the form and severity of complicated SDS, as well as the scope of surgical assistance.

Treatment of patients with complicated SDS

Treatment of patients with complicated SDS at all stages should be comprehensive and interdisciplinary. We present the tasks and their sequence.
2. Correction of metabolic disorders and acid-base status.
3. Correction of ischemia.
4. Surgical treatment of purulent-necrotic foci of the foot followed by plastic wound closure.
5. Antibacterial therapy (ABT) taking into account the sensitivity of the microflora.
6. Unloading or immobilization of the diseased limb with the use of orthopedic means of correction.
7. Anticoagulant and antiplatelet therapy.
8. Antioxidant therapy.
9. Local treatment of wounds.
10. Correction of depressive disorder.
11. Physiotherapy.

Algorithm of complex treatment of various forms of complicated SDS

1. Compensation for diabetes occurs due to the transfer of all patients (regardless of the type of diabetes) to short-acting insulin according to the principle of «intensive insulin therapy». Intensive insulin therapy involves subcutaneous or intravenous administration of small doses (8-10 units) of short-acting insulin four or more times a day, with glycemic control during the day.
2. Correction of metabolic disorders and acid-base status.

Violations of carbohydrate metabolism due to insulin deficiency lead to metabolic acidosis and diabetic ketoacidotic coma. A decrease in the volume of circulating fluid and deterioration of kidney function lead to electrolyte disturbances. To correct these disorders, infusion therapy is used: Ringer-Locke solution, isotonic solution, 5% glucose solution, 4% soda solution.
3. Correction of ischemia (for E2-3).

In the presence of arterial insufficiency of the limb and damage to the arteries of the foot, the decision on the type and volume of surgical intervention is made only after performing dopplerography, computer laser fluometry and contrast angiography.

Possible options for ischemia correction are surgical correction, endovascular or indirect revascularization. Preference is given to endovascular methods, in the absence of conditions, other possible methods are used.
4. Surgical treatment of purulent-necrotic foci of the foot followed by plastic wound closure.

The goal of therapy is maximum preservation of the area of foot support, therefore, if necessary, operative interventions should be used in a 2-3 stage approach.

Closure of the postoperative wound is performed using secondary sutures, skin-musculoplasty or dermatoplasty with a free skin flap.

Technical features of performing surgical interventions and plastic wound closure in complicated SDS:
- in the case of damage to the toes, amputations are performed with the preservation of a part of the proximal phalanx and the metatarsophalangeal joint, using a plantar flap to close the wound;
- in the case of destruction of the bones of the fingers and metatarsals, amputations are performed with resection of the head or the entire metatarsal
bone with the formation of a «narrow foot» and closing the wound with a front or lateral plantar flap;
- in case of damage to the metatarsal bones, amputation is performed at the level of the Lisfranc joint with the removal of all metatarsal bones, while the tendon of the anterior tibial muscle is split and fixed to the sphenoid bone;
- for small, up to 5 cm in diameter, wound defects of the middle parts of the plantar and back surfaces of the foot, plastic surgery is performed with local skin-fascial flaps;
- with widespread defects of the middle parts of the foot, it is advisable to perform plastic surgery using rotated lateral or medial skin-muscle flaps;
- in the case of wound defects of the rear parts of the foot, plastic surgery is performed with rotated skin-muscle flaps with preliminary treatment of the affected bones of the metatarsal and heel bones;
- in case of total defeat of the heel, amputation of the foot is performed with resection of the tibial bones above the level of the bones and closing of the surgical defect with a plantar flap with its fixation to the tendon of the anterior tibial muscle to prevent further migration.

5. ABT taking into account the sensitivity of the microflora.

In the presence of sensitivity to several antibacterial drugs, the sequence should be used - from weaker to stronger:

a) for group I (tablet forms are used for convenience):
- amoxicillin/clavunate (per os, 1 g. 2 times a day);
- cephalexin (per os, 0.5 g. 4 times a day);
- cefuroxime (per os, 0.5 g. 2 times a day);
- clindamycin (per os, 0.3 g. 4 times a day).

If methicillin-resistant Staphylococcus aureus (MRSA) is isolated:
- linezolid (per os, 0.6 g 2 times a day) or co-trimoxazole (per os, 0.96 g 2 times a day).

b) for II and III groups (treatment begins with intramuscular or intravenous methods of administration):
- amoxicillin/clavunate (in/in, 1.2 g. 4 times a day);
- ampicillin/sulbactam (in/in, 3 g. 4 times a day);
- cefazolin (in/m, 2 g. 3 times a day);
- cefuroxime (intravenous, 1.5 g. 3 times a day);
- clindamycin (in/in, 0.3-0.6 g. 3-4 times a day);

c) for III and IV groups:
- levofoxacin (in/in, 1 g once a day) + metronidazole (in/in, 0.5 g. 3 times a day);
- moxifloxacin (in/in, 0.4 g once a day);
- ofloxacin (in/in, 0.4 g 2 times a day) + clindamycin (in/in, 0.6 g. 3 times a day);
- ertapenem (in/in, 1 g once a day).

If MRSA is isolated - linezolid (in/in 0.6 g 2 times a day) or co-trimoxazole (in/in 0.96 g 2 times a day) before any therapy regimen.

d) for II, III, IV groups with the development of sepsis:
- levofoxacin (in/in, 0.75g-1g once a day) or ciprofloxacin (in/in, 0.4g 2-3 times a day) + metronidazole (in/in, 0.5g 3 times a day);
- piperacillin/tazobactam (in/in, 4.5 g. 3-4 times a day);
- cefoperazone/sulbactam (in/in, 4 g. 2-3 times a day);
- ertapenem (in/in, 1 g once a day);
- imipenem/cilastatin (in/in, 1 g 3-4 times a day);
- meropenem (IV, 1-2 g. 3-4 times a day).

At risk of MRSA:
- linezolid or vancomycin before any therapy regimen.

d) for II, III, IV groups with the development of septic shock or multiple organ failure (PON):
- imipenem/cilastatin (IV, 1 g 3-4 times a day) or meropenem (IV, 1-2 g 3-4 times a day) + linezolid (IV, 0.6 g 2 times a day) or vancomycin (in/in, 15 mg/kg. 2 times a day).

6. Unloading or immobilization of the diseased limb with the possible use of orthopedic means of correction.

- unloading of the limb by immobilization, with the possible use of orthopedic means, which allows to exclude load and traumatization of the foot, eliminate peripheral edema and prevent the spread of the infectious process.

7. Anticoagulant and antiplatelet therapy:

a) for group I (tablet forms are used):
- sulodexide (per os 600 units per day for 3-6 weeks) or
- pentosan polysulfate (per os 50-75 mg. 2-3 times a day for 2 weeks, then 50-75 mg. 1-2 times a day for 3-6 weeks).

b) for II, III, IV groups:
- sulodexide (in/m 600 units - 1 ampoule for 14-20 days followed by oral administration for 1-3 months) or
- pentosan polysulfate - (in/m 100 mg once a day for 7 days followed by oral administration for 1-3 months);
- low molecular weight heparins - (p/sh 1750 - 2500 ME 1 year per day for 7-10 days).

8. Antioxidant therapy:

a) for group I (tablet forms are used):
- preparations of alpha-lipoic acid 600 mg each. per day for 1 dose for 2-3 months;

b) for II, III, IV groups:
- preparations of alpha-lipoic acid 600 mg each. per day intravenously for 2-3 weeks;
- benfotiamine 300 mg. per day for 1 dose for 2-3 weeks;
71. Gabriapentin in a dose of 100 mg. up to 300 mg. three times a day for 2-3 months, the dosage must be selected gradually. After achieving the desired effect, the dose can be reduced.

9. Local wound treatment:
   a). in the I stage of the wound process:
      - daily treatment of the wound using ultrasonic cavitation or necrootomy using surgical instruments;
      - antiseptics (povidone-iodine, iodoform, dioxidin, miramistin);
      - sorbent fabrics on a carbon base;
      - preparations of proteolytic enzymes (trypsin, chymotrypsin);
      - ointments on a hydrophilic basis according to the gram-positive or gram-negative landscape of the microbial isolate.
   b). in the II stage of the wound process:
      - wound coverings based on collagen;
      - hydrogels;
      - xenoskin.
   c). in the III stage of the wound process:
      - atraumatic oil-based dressings.

10. Correction of depressive disorder.
    When a depressive disorder occurs, antidepressants from the group of selective serotonin reuptake inhibitors are prescribed as monotherapy:
    - Escitalopram 10 mg each. in the morning regardless of food or
    - venlafaxine in a dose of 37.5-75-150 mg. in the morning and 30-60 mg of mirtazapine. 1 time a day.

11. Physiotherapy.
    Laser therapy, magnetotherapy, and diadynamic currents, which are applied to the lumbar region, in the direction of the vascular-nerve bundle of the lower limb and foot, are the most effective in the treatment of complicated SDS.

The study of patients with complicated SDS made it possible to identify four main groups, coordinate treatment measures and calculate the actual terms of inpatient treatment (Table 3).

**Conclusions**

1. The distribution of patients thanks to the proposed classification creates conditions for statistical processing and registration of forms of complicated SDS, as well as the volume of surgical assistance. Allows to determine surgical tactics depending on the specific complication of SDS.

2. The use of a controlled approach to ABT allowed to reduce the number of cases associated with antibacterial resistance from 23% to 11%.

3. Optimization of the complex treatment of patients with complicated SDS made it possible to increase the number of patients with preserved supporting function of the lower limb from 21.9 to 36.5% ($\chi^2=11.2; P<0.05$), reduce the number of «high» amputations from 24.5 to 15.1% ($\chi^2=4.8; P<0.05$).

4. The distribution of patients according to the proposed classification substantiates the actual terms of arrival at the hospital, taking into account all stages of treatment.

5. A comprehensive approach, priority areas of treatment and a mandatory sequence of actions allow to improve the final results of treatment, reduce mortality from 25.8 to 5.3% ($\chi^2=3.92; P<0.05$).

### Table 3

<table>
<thead>
<tr>
<th>Items of the treatment program</th>
<th>Groups of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
</tr>
<tr>
<td>1</td>
<td>●</td>
</tr>
<tr>
<td>2</td>
<td>●</td>
</tr>
<tr>
<td>3</td>
<td>●</td>
</tr>
<tr>
<td>4</td>
<td>●</td>
</tr>
<tr>
<td>5</td>
<td>●</td>
</tr>
<tr>
<td>6</td>
<td>●</td>
</tr>
<tr>
<td>7</td>
<td>●</td>
</tr>
<tr>
<td>8</td>
<td>●</td>
</tr>
<tr>
<td>9</td>
<td>●</td>
</tr>
<tr>
<td>10</td>
<td>●</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Term of arrival at inpatient treatment</th>
<th>from 8 to 12 days</th>
<th>from 14 to 22 days</th>
<th>from 24 to 32 days</th>
<th>from 14 to 18 days or more (depending on the severity of PON).</th>
</tr>
</thead>
</table>

**Notes:** ● — mandatory measures; ○ — if needed.
ПЕРЕЛІК ПОСИЛАНЬ


REFERENCES

Резюме. Цукровий діабет (ЦД) - найпоширеніша ендокринна патологія, яка посідає третє місце в загальній структурі захворюваності після серцево-судинної та онкопатології. ЦД визнаний ВООЗ епідемією неінфекційного походження, що дозволяє говорити про глобалізацію проблеми. Під нашим спостереженням перебували 2024 пацієнти з ускладненим СДС, які лікувалися в гнійно-септичному центрі з ліжками діабетичної стопи КУ "Міська лікарня № 3" м. Запоріжжя за період 2008-2022 рр. У статті представлені розроблені нами класифікація та алгоритм лікування ускладнених СДС, які, на нашу думку, сприятимуть прогресу спеціалізованої медичної допомоги при гнійно-запальних процесах діабетичної стопи. Складність створення та прийняття єдиної хірургічної класифікації ускладненого СДС зумовлена, насамперед, поєднанням декількох патогенетичних механізмів розвитку патології. Сучасні класифікації хвороб повинні бути: зрозумілими і доступними; чітко класифікувати захворювання за ступенем тяжкості; полегшувати прийняття клінічних рішень; враховувати сучасні методи діагностики та лікування; підвищувати економічну ефективність медичної допомоги; сприяти спрощенню статистичної обробки. Розподіл пацієнтів за запропонованою класифікацією створює умови для статистичної обробки та обліку форм ускладненого СДС, а також обсягів хірургічної допомоги. Дозволяє визначити хірургічну тактику в залежності від конкретного ускладнення СДС. Використання контрольованого підходу до АБТ дозволило зменшити кількість випадків, пов'язаних з антибактеріальною резистентністю, з 23% до 11%. Оптимізація комплексного лікування хворих з ускладненим СДС дозволила збільшити кількість пацієнтів зі збереженою опорною функцією нижньої кінцівки з 21,9 до 36,5% ($\chi^2=11,2; P<0,05$), зменшити кількість "високих" ампутацій з 24,5 до 15,1% ($\chi^2=4,8; P<0,05$). Розподіл пацієнтів за запропонованою класифікацією обґрунтовує реальні терміни надходження в стаціонар з урахуванням усіх стапів лікування. Комплексний підхід, пріоритетні напрямки лікування та обов'язкова послідовність дій дозволяють покращити кінцеві результати лікування, знизити летальність з 25,8 до 5,3% ($\chi^2=3,92; P<0,05$).

Ключові слова: цукровий діабет, синдром діабетичної стопи, опорна функція нижньої кінцівки, єдина хірургічна класифікація