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Rehabilitation and limb restoration in patients with traumatic osteomyelitis

S.N. Krivenko

Gorky Donetsk National Medical University, Donetsk, Ukraine

Purpose To improve the treatment effectiveness of long-bone posttraumatic osteomyelitis through the development and implementation of pathogenically substantiated surgical and medication measures according to the stages of multiple organ dysfunction syndrome. **Materials and methods** Group 1 consisted of 176 (69 %) patients who required large-volume surgical interventions (debridement of fistulae and bone sequestrae, segmental resection). Group 2 consisted of 79 (31 %) patients with traumatic osteomyelitis who required small-volume surgical interventions (debridement of fistulae and bone sequestrae by removing a smaller portion of bone tissue, parietal resection). **Results** Hemodynamical, immunological, biochemical, and rheovasographic changes revealed allowed us to consider traumatic osteomyelitis as a syndrome of polyorganic dysfunction in stages I-II. Average period of inpatient stay for patients with traumatic osteomyelitis of the tibia was 44.6 ± 0.7 days while in the control group it was 54.4 ± 0.7 days. An increase in the number and duration of remission periods was also observed (the participation of patients with traumatic osteomyelitis in working activity after a complex of rehabilitative and restorative treatment was 77.4 %). **Conclusion** According to the author’s observation, the proposed complex of measures for treatment of pyogenic complications due to injuries, in view of the current opinions on the pathogenesis of the multiple organ dysfunction syndrome, contributed to a more favorable course of the postoperative period and reduction in the number of recurrences. Therefore, the periods of inpatient treatment decreased.
Keywords: traumatic osteomyelitis, treatment, polysystemic dysfunction

INTRODUCTION

For several decades, posttraumatic osteomyelitis remains a challenging problem for contemporary traumatology due to a steady increase in the number of patients with this pathology. To date, one can state that traumatic osteomyelitis, being an infectious and inflammatory process, is an integral interaction between microorganisms and the macro-organism, determined by the individual characteristics of the latter. In addition, traumatic osteomyelitis is also associated with the emergence of antibiotic-resistant microorganisms and a deterioration of the immune status [1-3]. However, despite extensive and multidirectional therapeutic measures, the recurrence rate of the osteomyelitic process remains rather high, ranging from 6 % to 50 %. Most frequently, the recurrence of purulent and necrotic processes is observed in the lower leg (up to 45 %). High level of poor outcomes after treatment of posttraumatic osteomyelitis is considered by a number of researchers to be associated with an insufficiently radical debridement, incorrect antibiotic therapy, and the development of postoperative inflammation [4-6]. Some authors associated the development of complications after an adequate debridement with several soft tissues conditions in the osteomyelitic focus area such as their scar transformation, disorders in the peripheral blood supply to the affected limb, changes in the immune status, and disturbance of metabolic processes. In general, these factors result in secondary sequestration and recurrent osteomyelitis that requires a revision surgery [7–10].

Despite the importance of studying the wound process during the postoperative period in patients with posttraumatic osteomyelitis, few studies were devoted to this problem. The available literature that describes the peripheral circulation and the immune status of patients with posttraumatic osteomyelitis is scarce and often contradictory. There are no published reports describing the dynamic changes in blood circulation of the affected limb, the condition of the immune system, or metabolic processes in patients with posttraumatic osteomyelitis during the postoperative period. Furthermore, a detailed analysis of the relationship between these functional and morphological disturbances and the development of postoperative complications or the outcomes of posttraumatic osteomyelitis treatment has not been performed. Moreover, no pathogenically justified complex of therapeutic measures exists for optimizing the course of the wound process in the postoperative period of posttraumatic osteomyelitis [10–12].

Therefore, the objective of this study was to improve treatment efficiency in patients with posttraumatic osteomyelitis of limb long bones through the development and implementation of pathogenically substantiated surgical and medical measures aimed at correction of the disorders in regard to the stages of multiple organ dysfunction syndrome (MODS).

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MATERIALS AND METHODS

To achieve the study objectives, the results of 255 patients (50 % aged 15–50 years; 50 % aged 51–70 years) treated between 2010 and 2014 at the Department of Traumatology and Orthopedics of Gorky Donetsk National Medical University with posttraumatic osteomyelitis of long bones were analyzed. Duration of the disease was more than one year. Patients were grouped according to surgical methods used.

The first group consisted of 176 (69 %) patients with severe osteomyelitis in which large-volume surgical interventions such as debridement of fistulae and bone sequesters of the segmental resection type were required. The second group consisted of 79 (31 %) patients with moderate traumatic osteomyelitis requiring small-scale surgical interventions (debridement and removal of a smaller portion of bone, or parietal resection).

The type of intervention was determined based on the degree of damage. If less than one third of the diameter was damaged, the main intervention was a parietal resection of the affected parts within the healthy tissues with smoothing of the bone edges. The preserved part of the bone remained fairly strong and allowed full weight-bearing.

In cases where more than one half of the diameter was damaged, even in the presence radiographic and clinical (lack of pathological mobility) consolidation, the affected bone area along the entire bone diameter was resected to create a defect. These patients were not able, as we assumed, to fully use the limb while walking as far as the thinnest and weakest bone part would fracture. In addition, prolonged immobilization with splints of various designs would not ensure full weight-bearing as well. In cases of segmental resection, we performed Ilizarov bone transport to restore the bone tissue and full weight-bearing ability of the limb.

Among the injured patients, there were 4.4 times more men (81.6 %) than women (18.4 %). The majority (70.6 %) were of working age. According to social occupation, 92 (36.1 %) patients were workers, 78 (30.6 %) were employees, 49 (19.2 %) were unemployed; 20 (7.8 %) were retired persons and 16 (6.3 %) were students.

By the type of injury, 103 patients (40.4 %) sustained injuries in road accidents, 60 (23.5 %) in industrial accidents, 48 (18.8) due to falls, and 44 (17.3 %) patients had accidents at home.

In most cases, the mechanism of trauma was a direct impact in road accidents that then resulted in long bone traumatic osteomyelitis.

Due to the geological conditions in the Donbass mines and the specifics of their production sites, injuries sustained in coal mines have their peculiar characteristics. In the Donetsk region, 18.3 % of total coal-mining is performed in mines with steep slopes (up to 45°). Work is carried out in most of the mines at a depth of more than 900 m in poor conditions for miners. **Table 1** shows the causes of injuries and rates of posttraumatic limb bone osteomyelitis in miners.

Table 1

Causes of traumatic osteomyelitis
of limb long bones in miners

Causes of injuries	Number of patients	%
Pressed down by a combine	2	6.3
Blast wave	3	9.4
Pressing with a pan, drum	14	43.7
Stroke with a rack, winch	13	40.6
Total:	32	100

Thus, among the mechanisms of traumatic osteomyelitis of limb long bones in miners, direct trauma was the most dominant, representing 29 (90.6 %) patients.

Immune and biochemical parameters were examined in all patients in dynamics. The levels of total protein, urea, creatinine, and uric acid were studied. Lipid metabolism was assessed by values of cholesterol, triglycerides, lipoproteins of alpha, pre-beta, and beta classes, as well as metabolic products of diene conjugates of fatty acids and malonic aldehyde (KONE, Finland). Triglyceride levels were analyzed with the use of microbial lipase (KONE, Finland). The metabolism of electrolytes and macroelements was evaluated by the content of potassium, sodium, calcium, magnesium, phosphorus, and chlorine in blood serum. The activity of enzymes, including amylase, lactate dehydrogenase, acid phosphatase, acidic RNAase, acid DNAase, and cathepsin D, was also evaluated. Total and direct bilirubin was determined by Indrashik (KONE, Finland).

Evaluation of the immunological reactivity of the injured patients included the analysis of certain aspects of the immune system, including the T- and B-lymphocyte systems, a subpopulation of T-cells with helper (theophyllin-resistant) and suppressor (theophyllin-sensitive) activity. In this case, a fluorescent method was used for determining monoclonal antibodies. The total number of white blood cells and the relative and absolute number of lymphocytes was determined. Circulating immune complexes were determined by selective precipitation of antigen-antibody complexes in 3.75 % polyethylene glycol, followed by photometric measurement of the precipitate density. The functional activity of the phagocytic system was evaluated in terms of the phagocytic activity of neutrophils and the phagocytic index. To study the functional activity of neutrophils, the nitro blue tetrazolium reduction reaction was used (i.e., the NBT test).

Biomechanical characteristics were assessed based on the support ability of the lower extremities (i.e., studying the rhythm of walking and standing stability). Podography was used to evaluate walking parameters on a metal track in special shoes. The posturography method enabled the quantitative and qualitative analysis of the duration of body fluctuation in two planes - frontal and sagittal.

The inclusion criteria were age between 15 and 70, no disorders in consciousness and absence of hypotension, acidosis, or coagulopathy; as well as ISS scale of injury severity ≥14 points, and stable compensatory condition according to the severity scale.

The study was approved by the ethics committee of Gorky Donetsk National University, and was conducted in accordance with the ethical standards of the Helsinki Declaration of the World Association “Ethical principles for medical studies involving human subjects” (2000).

Statistical analysis of the results was performed using the software package Statistica 12. Assessment of the significance level of the data was performed on the basis of multifactorial disperse nonparametric analysis ANOVA (multi-way ANOVA). Quantitative variables are presented as M ± SD, where M is the arithmetic mean and SD is the standard deviation. Qualitative characters are presented as absolute and relative (%) values. Depending on the distribution type of quantitative variables, Student’s t-test was used to evaluate differences. The critical level of significance when testing statistical hypothesis was set at $p < 0.05$ [14].

RESULTS AND DISCUSSION

Surgery takes the central role in the treatment of posttraumatic osteomyelitis and is aimed at the removal of necrotic tissues. In our opinion, surgical treatment should be performed as early as possible from the onset of the process and should be radical (removal of devitalized bone within the healthy tissue) and low-traumatic. In addition, the restoration of limb integrity as an organ should begin as early as possible. The debridement and subsequent bone plasty should be performed with minimal time interval between them.

The extent of debridement was determined by necrotic tissue. It was parietal resection or segmental resection. The mandatory condition is removal of the focus to healthy tissues.

In the immediate postoperative period, bone and soft tissue plasty was performed according to indications. The most sparing interventions were performed; optimal conditions were created for a favorable postoperative rehabilitation.

Semi-closed osteotomy, Piler therapy with the use of Curiosin, and surgical prevention of inverted scar were performed for these purposes. In the study group, the leading (n = 176; 69 %) method of treatment was segmental bone resection within healthy tissues. In 70.6 % of 423 closed fractures of long bone diaphysis complicated by the osteomyelitis process, we implemented transosseous osteosynthesis with use of the Ilizarov external fixator (**Fig. 1, 2**).

In 45.7 % of 274 open long bone fractures complicated with osteomyelitis, osteosynthesis was performed using external fixation only, regardless of fracture location (**Fig. 3**).

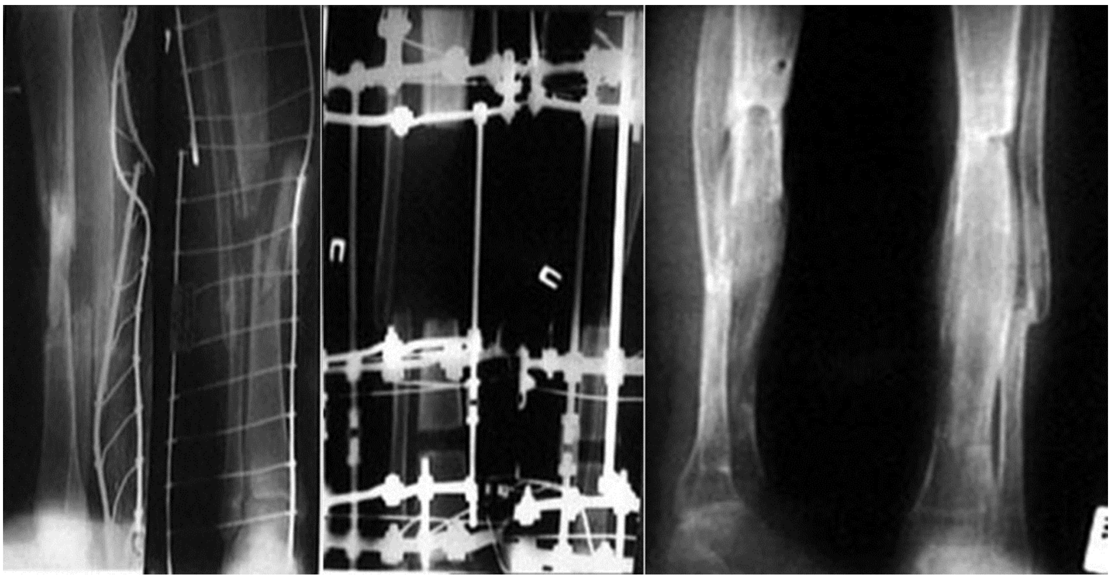

Fig. 1 X-rays of the right tibia of a patient with traumatic osteomyelitis

Fig. 2 Clinical photograph of the right lower leg at the end of treatment

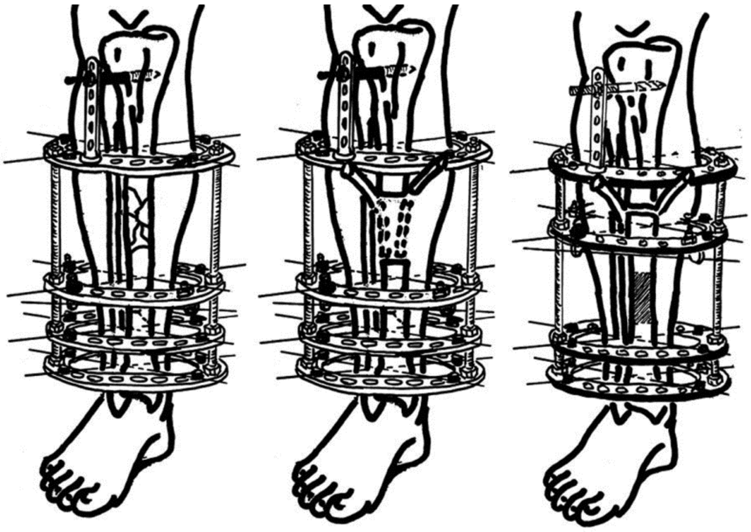

Fig. 3 Diagrams of tibial defect management with external fixation

Surgical tactics in the control group (n = 79, 31 %) of patients included parietal resection of the affected parts within the healthy tissues with smoothing of the bone edges and transosseous osteosynthesis of fractures in all the segments complicated by the osteomyelitic process. External fixators of wire and half-pin type were used in all patients, regardless of the nature and location of fractures.

Such an aggressive surgical tactics was possible and was applied along with a mandatory complex of conservative therapy proposed by us. A full complex of conservative therapy was prescribed after surgical intervention. We assumed that debridement of the necrotic tissues and reconstruction of the limb on the background of an existing chronic purulent inflammation results in the destruction of the metabolic barriers in the focus. Surgery is a traumatic factor that inevitably leads to the aggravation of chronic inflammatory processes. At the same time, delivery of medications to the focus is facilitated and significantly increases the efficacy of their action.

The presence of the infection focus, with the concomitant release of cytokines, results in local and generalized reactions in the body. The clinical course of osteomyelitis is an interaction of several main syndromes, including disorders of organ blood flow, reperfusion injury to tissues, and shortage of oxygen. The main factors aggravating the “mediator-cytokine storm” are hypoxia, deep microcirculatory disorders, abnormally high levels of intermediate and end products of metabolism, circulating immune complexes, biogenic amines, and peroxidation products.

Properties of biogenic amines, cytokines, tumor necrosis factor alpha, and nitric oxide, in combination or separately, are also the basis for the development of metabolic changes in the syndrome of multiorgan dysfunction. The development of the latter, as a rule, is accompanied by manifestations of hypermetabolism. In this situation, the satisfaction of the energy needs occurs from the destruction of the body’s own cellular structures (autocannibalism) and includes the redistribution of proteins for gluconeogenesis, the synthesis of acute phase proteins, and the release of cytokines. Despite increased protein synthesis, the decay of protein substances predominates. In addition, carbohydrate metabolism is impaired, which is determined by an increase in the tolerance of peripheral tissue cells to insulin and glucose, an increase in the rate of glucose production by hepatocytes, and the mobilization of amino acids from myocytes of skeletal muscles and visceral cells for gluconeogenesis.

These hemodynamic, immunological, biochemical and rheovasographic changes revealed by us enabled to consider traumatic osteomyelitis as the first and second stages of multiorgan dysfunction syndrome.

Use of the identified patterns in the treatment of traumatic osteomyelitis has met a number of difficulties. Thus, the process has staged and dynamic characteristics. There are no generally accepted treatment regimens. The number of medications administered is restricted and there are no systematic data on their interaction in these specific conditions. New understanding of the processes associated with posttraumatic osteomyelitis as the first and second stages of multiorgan dysfunction syndrome allows for the treatment of this complex pathology at the contemporary level.

The first and most important direction, which involves the elimination of the trigger factor initiating and maintaining a violent impact on the body of the patient, was solved surgically and with the use of antibacterial preparations. The antibacterial therapy was performed with antibiotics active to major causative agents of purulent infections at an early stage of treatment and, later, according to antibiograms.

The second direction identified in the study process involves the correction of metabolic disorders in the segment and the body of the injured patient with traumatic osteomyelitis, including the restoration of the oxygen-delivery function of the blood, the arrest of hemorheology disorders, and the treatment of biochemical and immune disorders.

A full complex of conservative therapy was indicated after surgical intervention. We preceded from the supposition that debridement of the infection focus and reconstruction of the limb on the background of existing chronic purulent inflammation results in the destruction of the generated barriers. Surgery is a traumatic factor that inevitably leads to the aggravation of the chronic inflammatory process. At the same time, delivery of medications to the focus is facilitated and significantly increases the efficacy of their action

Correction of identified hemodynamic disorders started with the restoration of blood rheological properties and improvement of its gas transportation function to the affected segment. To do this, we used colloidal solutions (e.g., Refortan, Stabisol, and Rheopolyglucin) with simultaneous use of proteolysis inhibitors (e.g., Contrykal and Gordox). In parallel, for the suppression of inflammatory mediator activity (TNF-α and IL-1), and in order to protect the vessels of the endothelium from those already circulating, we used Pentoxifylline. For treatment of tissue deoxy in the segment, we considered it justified to use antioxidants and antihypoxic drugs, including vitamins E and C. The therapy of edematous-pain syndrome was conducted using L-lysine aescinat. The rheological properties of blood were adjusted by administration of nonsteroidal anti-inflammatory drugs (e.g., Aspirin, Acelyzin, and Meloxicam).

An important step in the treatment of traumatic osteomyelitis is the correction of hypermetabolic disturbances. These, in turn, were divided into two components – correction of protein metabolism and correction of glucose metabolism.

The rapid decay of proteins was the indication for protein preparations such as albumin, as well as a diet rich in easily digestible proteins. In addition, medications with anabolic effects were administered.

Due to disturbances in glucose metabolism, a glucose solution (in combination with insulin to prevent hyperosmolar syndrome) was administered.

Immune correction was performed with Polybiolin and Cycloferon. During surgical interventions and wound dressing, interferon was administered into the wound.

Disintoxication therapy included transfusion of Ringer's solution, saline solutions, Neo-hemodez, and, more recently, Sorbilact.

Desensitizing therapy involved administering antihistamine preparations to patients, including Diazolin, Suprastin, and Tavegyl.

The efficiency of the proposed complex treatment regime was confirmed by comparative biochemical and immunological data in the study and the control groups.

Thus, the reaction to conservative treatment in the injured patients and control groups was characterized by activation of lymphocytes in the period of 1-3-7 days and phagocytic activity of neutrophils in the period of 14 days. The reaction of the immune system to surgical treatment in the group of “low-volume” intervention was characterized by a tendency towards leucocytosis and high phagocytic activity of neutrophils. Surgical treatment in the group with “high volume” intervention was accompanied by normal values of leukocytes in peripheral blood for the entire study period. The phagocytic activity of neutrophils in this group of patients increased in comparison with the baseline in a period of 7 days and had a tendency to decrease by Day 14 after surgery.

Surgical treatment, combined with the use of activators of the humoral component of the immune system, did not result in the development of the leukocytic reaction in the postoperative period in patients with a large amount of surgical intervention. Rather, in the period of 1–14 days, these patients maintained the content of B-lymphocytes at the normal level while in patients of the control group by Day 14, a 2.5 fold decrease in IL_{19} was measured compared to baseline.

It was also found that the immune status was characterized by increased activity of the phagocytosis system and the development of cell type immune deficiency in the first day after surgical treatment in the study and control groups, which was compensated by humoral factors of protection. The degree of the immune deficiency severity was higher in the injured patients of group 1 and was due to a large amount of surgical intervention.

On Day 7 after surgical treatment in the injured patients of group 1, the activation of the lymphoid component and, consequently, normalization of values of the T-system and leuko-T-index was registered. In addition, an increased activity of humoral factors, which generally can be regarded as predictively favorable in the course of traumatic disease related to immune system changes.

At the same time, in the injured patients of group 2, the immunity status was characterized by the preservation of immune deficiency, the severity of which was greater than on the first day (**Table 2**).

The presence of cell type immune deficiency in injured patients for such a long period is due, in our opinion, is due to the peculiarities of surgical treatment. During the period of 14–21 days, immunity indices in the injured patients of group 1 were characterized by normal values of leukocytes and lymphocytes, T-lymphocytes and B-lymphocytes, and a decrease in the degree of sensibilization. At the same time, there was a tendency to activation of humoral factors of protection, which was due to the active processes of antibody formation.

In patients of group 2, leukocytosis and the value of immune deficiency (the leukocyte to T-lymphocyte ratio) reached normal values only on Day 21 after surgery.

Comparative analysis of the biochemical parameters of the analyzed groups revealed that for the injured patients of group 2, lower values of cholesterol and glucose and higher activity of serum amylase was characteristic as compared to patients of group 1. This pattern was observed in the patients of this group from the first day of surgical treatment until the end of the examination (**Table 3**).

Table 2

Changes in the immune status of patients with different methods of surgical treatment

Test parameters	Patient groups	Terms of examination of patients (day)			
		1	7	14	21
Leukocytes, g/L	1	8.26 ± 0.85	7.97 ± 0.75	6.27 ± 0.87	5.29 ± 0.67
	2	7.74 ± 0.93	8.16 ± 0.98	7.29 ± 0.74	6.68 ± 0.81
Lymphocytes, cells/μL	1	1580 ± 215	2080 ± 305	1570 ± 441	1560 ± 437
	2	1600 ± 263	1410 ± 511	1680 ± 364	1710 ± 667
T-lymphocytes, cells/μL	1	960 ± 149	1530 ± 261	1250 ± 229	1130 ± 639
	2	1120 ± 398	1080 ± 597	1190 ± 363	1310 ± 255
B-lymphocytes, cells/μL	1	610 ± 136	900 ± 191	510 ± 197	720 ± 245
	2	500=59	460=364	600=221	480 ± 153
TGF (helper-inducing), cells/μL	1	750 ± 189	1420 ± 356	1020 ± 465	1110 ± 364
	2	1030 ± 249	820 ± 567	840 ± 427	1060 ± 258
Theophylline-sensitive lymphocytes (suppressor-cytotoxic), cells/μL	1	160 ± 53	110 ± 61	160 ± 73	70 ± 38
	2	80 ± 42	170 ± 35	370 ± 105	300 ± 85
Leukocyte to T-lymphocyte ratio (leuko-T-index)	1	8.6 ± 0.42	5.2 ± 0.71	5.0 ± 0.21	4.7 ± 0.68
	2	6.9 ± 0.68	7.5 ± 1.53	6.12 ± 1.74	5.1 ± 1.02
Phagocytic activity of neutrophils (%)	1	1.89 ± 5.87	73.33 ± 3.63	72.28 ± 4.54	73.85 ± 5.34
	2	8.38 ± 3.46	67.38 ± 5.00	77.25 ± 3.72	70.88 ± 3.91
Phagocytic index, un.	1	11.33 ± 16	11.82 ± 1.05	9.72 ± 2.66	12.07 ± 13
	2	11.76 ± 01	9.06 ± 1.84	11.39 ± 0.98	10.15 ± 1.52
NBT test (spontaneous; %)	1	31.83 ± 7.31	33.73 ± 6.87	34.42 ± 5.78	34.38 ± 7.12
	2	32.29 ± 9.89	20.57 ± 8.23	32.71 ± 3.97	37.75 ± 6.98

Significance level is $p < 0.05$

Table 3

Changes in biochemical parameters in patients with different methods of surgical treatment

Test parameters	Terms of examination of patients (day)			
	1	7	14	21
Potassium, mmol/L	5.1 ± 0.2	5.0 ± 0.2	5.2 ± 0.2	5.1 ± 0.2
	4.5 ± 0.5	5.1 ± 0.1	5.0 ± 0.2	4.6 ± 0.1
Sodium, mmol/L	140.5 ± 1.2	143.0 ± 2.0	141.0 ± 1.1	141.8 ± 1.3
	151.2 ± 8.7	150.8 ± 7.9	142.3 ± 2.0	142.6 ± 1.6
Calcium (tot.), mmol/L	2.4 ± 0.02	2.3 ± 0.03	2.4 ± 0.03	2.3 ± 0.07
	2.4 ± 0.08	2.3 ± 0.03	2.4 ± 0.04	2.3 ± 0.03
Calcium (dec.), mmol/L	0.98 ± 0.02	0.99 ± 0.02	0.94 ± 0.06	0.94 ± 0.01
	1.0 ± 0.04	1.0 ± 0.05	1.0 ± 0.04	1.0 ± 0.05
Phosphorus, mmol/L	1.2 ± 0.05	1.2 ± 0.05	1.3 ± 0.05	1.3 ± 0.05
	1.0 ± 0.09	1.4 ± 0.1	1.3 ± 0.09	1.2 ± 0.08
Magnesium, mmol/L	0.9 ± 0.02	0.9 ± 0.01	0.9 ± 0.02	0.9 ± 0.02
	1.0 ± 0.05	0.9 ± 0.03	0.9 ± 0.03	0.9 ± 0.03
Chlorine, mmol/L	102.9 ± 0.9	101.3 ± 0.74	102.1 ± 0.69	101.8 ± 0.52
	100.5 ± 0.6	102.1 ± 0.3	100.6 ± 0.6	100.9 ± 1.4
Protein (tot.), g/L	62.2 ± 1.3	67.3 ± 1.6	67.9 ± 1.7	69.5 ± 1.4
	57.4 ± 3.8	60.8 ± 2.2	64.8 ± 0.8	70.6 ± 2.7
Albumins (%)	47.2 ± 0.7	48.6 ± 0.5	49.4 ± 0.7	49.1 ± 0.5
	48.2 ± 1.4	47.2 ± 1.2	48.9 ± 0.9	50.0 ± 0.6
Globulins (%)	52.5 ± 0.9	51.0 ± 0.6	49.9 ± 1.0	50.6 ± 0.8
	51.7 ± 0.17	52.6 ± 0.9	49.9 ± 1.0	49.5 ± 0.7
α1- globulins (%)	5.2 ± 0.3	4.4 ± 0.2	4.1 ± 0.2	3.8 ± 0.1
	4.6 ± 0.3	4.9 ± 0.4	4.3 ± 0.3	3.6 ± 0.2
α2- globulins (%)	11.9 ± 0.3	11.4 ± 0.3	10.7 ± 0.3	11.0 ± 0.3
	11.9 ± 0.7	11.8 ± 0.6	10.7 ± 0.4	10.1 ± 0.2
Β- globulins (%)	14.6 ± 0.4	14.0 ± 0.3	14.3 ± 0.2	14.6 ± 0.6
	14.3 ± 0.6	14.3 ± 0.5	13.6 ± 0.9	15.5 ± 0.7
Y- globulins (%)	20.9 ± 0.6	21.5 ± 0.4	21.8 ± 0.5	21.9 ± 0.3
	21.2 ± 0.5	22.3 ± 0.8	22.4 ± 0.6	21.0 ± 0.9
Urea, mmol/L	6.3 ± 0.5	6.4 ± 0.3	5.6 ± 0.2	5.0 ± 0.4
	6.8 ± 0.9	6.0 ± 0.8	7.0 ± 1.0	5.7 ± 0.6
Uric acid, mmol/L	266.4 ± 20.7	247.3 ± 16.3	246.8 ± 21.2	283.8 ± 19.7
	301.0 ± 45.3	220.6 ± 33.9	247.8 ± 61.8	276.2 ± 96.3
Creatinine, μmol/L	81.8 ± 3.6	82.4 ± 3.7	80.1 ± 3.2	77.3 ± 2.8
	82.0 ± 9.3	82.4 ± 8.0	77.4 ± 9.2	80.8 ± 7.2
Glucose, mmol/L	6.0 ± 0.3	7.7 ± 2.3	6.8 ± 1.5	5.3 ± 0.3
	5.7 ± 0.5	4.3 ± 0.3	4.5 ± 0.4	4.2 ± 0.4
Bilirubin (total), μmol/L	10.1 ± 0.9	9.3 ± 0.9	8.6 ± 0.6	7.3 ± 0.6
	18.8 ± 8.1	7.2 ± 1.3	7.1 ± 1.7	7.4 ± 1.3
Bilirubin (unconjugated), μmol/L	3.8 ± 0.2	4.5 ± 0.3	4.1 ± 0.2	3.9 ± 0.2
	5.0 ± 0.7	3.9 ± 0.3	3.5 ± 0.4	3.9 ± 0.5

Continuation of Table 3

Changes in biochemical parameters in patients with different methods of surgical treatment

Test parameters	Terms of examination of patients (per day)			
	1	7	14	21
Triglycerides, μmol/L	1.1 ± 0.1	1.3 ± 0.1	1.1 ± 0.1	1.1 ± 0.1
	1.05 ± 0.4	1.0 ± 0.2	1.1 ± 0.2	0.85 ± 0.1
Cholesterol, mmol/L	4.1 ± 0.2	4.6 ± 0.2	4.6 ± 0.3	4.8 ± 0.4
	3.1 ± 0.3	3.4 ± 0.4	3.6 ± 0.3	3.2 ± 0.6
α-lipoproteins (%)	31.3 ± 0.5	30.7 ± 0.8	30.6 ± 0.5	31.0 ± 0.6
	29.7 ± 2.3	30.4 ± 0.6	30.4 ± 1.0	32.0 ± 1.9
pre-B-lipoproteins (%)	25.3 ± 0.4	25.1 ± 0.5	25.3 ± 0.2	25.6 ± 0.4
	25.2 ± 0.7	24.3 ± 0.9	25.5 ± 0.4	24.6 ± 0.8
B-lipoproteins (%)	43.4 ± 0.6	44.1 ± 0.8	44.1 ± 0.6	42.9 ± 0.8
	45.0 ± 2.9	44.7 ± 0.7	44.0 ± 0.8	43.4 ± 2.4
Diene conjugates, un. E	1.7 ± 0.07	1.7 ± 0.05	1.6 ± 0.05	1.5 ± 0.04
	1.5 ± 0.1	1.8 ± 0.1	1.5 ± 0.1	1.5 ± 0.1
Aspartate aminotransferase (AST), un. E	84.5 ± 15.6	44.0 ± 6.1	26.4 ± 2.0	24.5 ± 2.3
	98.8 ± 26.4	65.4 ± 21.2	31.0 ± 8.7	23.6 ± 5.2
Alanine aminotransferase (ALT), un. E	67.0 ± 10.4	69.1 ± 14.1	39.5 ± 8.4	39.2 ± 9.4
	80.2 ± 26.5	71.6 ± 27.9	37.4 ± 13.0	19.0 ± 3.4
Acid phosphatase, un. E	3.6 ± 0.14	4.1 ± 0.12	3.6 ± 0.15	3.6 ± 0.08
	4.3 ± 0.5	3.7 ± 0.2	4.3 ± 0.2	3.9 ± 0.1
Alkaline phosphatase, un. E	142.7 ± 8.8	208.9 ± 13.1	267.2 ± 22.7	279.1 ± 24.9
	147.2 ± 20.3	211.6 ± 37.1	259.6 ± 43.3	283.8 ± 2.6
Y- glutamyltransferase (GGT), un. E	68.1 ± 17.6	111.0 ± 19.8	104.2 ± 16.0	91.4 ± 23.3
	52.4 ± 14.1	83.0 ± 23.5	74.8 ± 20.5	95.6 ± 39.6
Creatine kinase, un. E	794.9 ± 33.6	157.6 ± 18.7	108.0 ± 12.2	94.4 ± 10.3
	542.2 ± 25.4	250.0 ± 16.3	81.2 ± 7.6	93.2 ± 26.4
Lactic dehydrogenase (LDH), un. E	651.5 ± 70.4	532.8 ± 32.0	473.3 ± 32.0	386.8 ± 26.0
	748.2 ± 76.3	646 ± 96.7	422.4 ± 51.4	394.2 ± 45.5
Amylase, un. E	27.4 ± 2.3	40.2 ± 2.9	39.7 ± 3.7	43.8 ± 3.5
	72.8 ± 20.6	67.8 ± 16.3	48.2 ± 9.3	52.4 ± 8.2
RNAase, un. E	0.22 ± 0.02	0.18 ± 0.01	0.16 ± 0.01	0.13 ± 0.004
	0.22 ± 0.03	0.15 ± 0.02	0.16 ± 0.01	0.14 ± 0.007
DNAase, un. E	0.16 ± 0.01	0.13 ± 0.01	0.11 ± 0.01	0.08 ± 0.04
	0.13 ± 0.02	0.11 ± 0.02	0.10 ± 0.01	0.10 ± 0.01
Cathepsin D, un. E	2.3 ± 0.18	1.7 ± 0.13	1.5 ± 0.09	1.2 ± 0.05
	2.0 ± 0.4	1.6 ± 0.2	1.2 ± 0.1	1.3 ± 0.1

The critical level of significance is $p < 0.05$.

On Day 14, in the patients of group 2, the concentration of urea in the serum was found to be higher when compared to group 1, which was generally indicative of a protracted catabolic reaction to trauma. The observed increase in acid phosphatase was considered by us a result of the release of lysosomal membranes on the one hand and as the risk of degenerative-dystrophic changes in joints, on the other.

The characteristic features of the changes in biochemical parameters of the injured patients in group 2 reflected, in general, the inflammatory reactions occurring on the background of the protracted oxidizing phase of the metabolic processes in the body of patients.

Thus, the results of clinical and laboratory studies enabled us, on the one hand, to evaluate the efficacy of the surgical treatment methods used, and on the other, to identify the causes of unsatisfactory results.

Special investigations, particularly the analysis of the chronometric characteristic of walking, showed that in the presence of clinical and radiological consolidation, the absence of pain, and moderately pronounced restriction of movements in adjacent joints, a more rational type of walking was observed. In patients with an osteomyelitis process in both lower limbs, the sum of the reference time was 61.2 %–61.8 %, which indicated it was slightly reduced as compared with the norm (65 %). Accordingly, there was a slight increase in transferred time from 38.2 to 38.8 %, with the norm being 37 %. The phase characteristic of the time of support on different parts of the foot in our patients was very variable and depended both on the nature of compensatory and adaptive processes developed as a result of the trauma, and the state of the neuromuscular system of the limbs. It became possible to distinguish two basic types of movement, which are characterized, in one case, with a decrease in time of rolling through the toe of both feet by means of increasing the time of support on the heel and the whole foot. An increase in time of support on the whole foot of one limb and reduction of this time of the second limb was registered. At the same time, a decrease in time of rolling through the toe was less pronounced. The time of support on the heel exceeded the norm significantly. However, the available changes to the support difference, given the symmetry of the injury, slightly influenced walking. And the latter remained rhythmic; the rhythm index was within the normal range both in the first and second type of movement. Unsatisfactory clinical and radiological effects of the treatment, in particular, a pronounced restriction of movements in adjacent joints, resulted in a violation of the walking rhythm, with the rhythm index being 0.79 while the norm is 1.0. The support function of the limb was not impaired, which was due to the damage in both lower limbs.

Regardless of the clinical and radiological results of treatment in patients, there were virtually no disorders of blood circulation in the limbs, which was confirmed by oscillography and skin thermometry data. In two patients, the reduction of lower limb vessel oscillations was associated with a concomitant disease – osteochondrosis of the lumbar spine, which was accompanied by neurotrophic disorders, as evidenced by the marked reduction in the excitability of nerve trunks of the lower limbs. Oscillation of the vessels on the dorsal artery of foot on the right was two times lower than that on the left. The condition and degree of the restoration processes in the skeletal muscles and the peripheral nervous system in patients is indicative of the duration of the normalization of the neuromuscular system function in almost all patients. At the time of the examination, a moderate decrease in the bioelectrical activity in the muscles of the damaged limb was, on average, 1.5 times.

CONCLUSION

It was found that the early acute period (Day 1) was characterized by acute-phase processes, which resulted in the mobilization of the energy reserves, such as proteins and lipids. This process was accompanied by hyperenzymemia with a predominance of phosphorylation processes. The integral indicators of the internal structure of biochemical reactions were acute phase proteins and transaminases. The late acute period (Day 7) was characterized by active oxidative processes and the catabolism of proteins with the purpose of metabolic sanogenesis. The integral indicators of the internal structure of the metabolic processes at this stage were proteins and lysosomal enzymes. The early period (Day 14) was characterized, by an activation of anabolic processes. This manifested in an increase in total protein concentration in blood serum and a decrease in the final products of their metabolism. The integral indicators of the metabolic processes were albumins and globulins. The early period of the restoration of metabolic processes (Day 21) was characterized by normalization of protein metabolism and activity of transaminases and lysosomal enzymes. The internal structure of the metabolic processes was characterized by processes of bone tissue regeneration. The integral indicators of this condition were acid phosphatase as a major enzyme of osteoclasts, and the free fraction of bilirubin, and also alkaline phosphatase, phosphorus, alpha class lipoproteins, and DNAase. This is the period of resorption and bone tissue regeneration. This balance is provided between active processes of lipid synthesis and phosphorylation. An important role in these processes belongs to the functional state of the liver. As for the correlation of transaminases, their identical nature and focus of relations with other biochemical parameters should be noted. In the main group of the injured patients, positive correlation relationships were found between ALT and AST and creatinine ($r = 0.61$; $r = 0.63$), uric acid ($r = 0.585$; $r = 0.69$), creatine kinase activity ($r = 0.67$; $r = 0.56$), RNAase ($r = 0.59$; $r = 0.60$), and cathepsin D ($r = 0.51$). The physiological significance of the relationships determined in the acute period can be explained by the fact that the damage to cell structures with the release of enzymes occurs as a result of injury. Hyperenzymemia results in increased production of α1-globulins, which, being transport proteins, contribute to the binding and inactivation of enzymes.

The important role of ensuring homeostatic reactions in the body of the injured patients belongs to the hepatobiliary system, to maintain disintoxication and protein synthesis functions to which the drug therapy should be directed.

Having analyzed all clinical cases, periods of inpatient stay, and duration of remission, we made the following conclusions.

The proposed complex of measures to treat infection complications due to trauma taking into account the current views on the pathogenesis of multiorgan dysfunction syndrome, according to our observations, contributed to a more favorable course of the postoperative period, and enabled a reduction in the number of relapses. Therefore, the duration of inpatient stay decreased. Thus, the average hospital stay of the patients in the main group was 44.6 ± 0.7 bed-days compared to 54.4 ± 0.7 in the control group. An increase in the duration of remission periods was also observed. The patients with posttraumatic osteomyelitis that returned to their work activities after treatment according to this complex of rehabilitation and restoration measures made 77.4 % of the total treated.

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Information about the authors:

Sergei N. Krivenko, M.D., Ph.D., Professor, Donetsk Gorky National Medical University, Donetsk, Professor at the Department of Traumatology and Orthopaedics