

Burianov Olexandr, Dubrov Sergii, Omelchenko Taras, Lianskorunskyi Volodymyr. The impact of certain factors on complications development in patients with multiple long bone fractures of lower extremities and severe associated trauma. *Journal of Education, Health and Sport*. 2020;10(4):317-332. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2020.10.04.035>
<https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2020.10.04.035>
<https://zenodo.org/deposit/4381252>

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.
© The Authors 2020;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland
Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike.
(<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.
The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 06.04.2020. Revised: 23.04.2020. Accepted: 30.04.2020.

THE IMPACT OF CERTAIN FACTORS ON COMPLICATIONS DEVELOPMENT IN PATIENTS WITH MULTIPLE LONG BONE FRACTURES OF LOWER EXTREMITIES AND SEVERE ASSOCIATED TRAUMA

Olexandr Burianov, Sergii Dubrov, Taras Omelchenko, Volodymyr Lianskorunskyi

Bogomolets National Medical University

Burianov Olexandr, Traumatology and Orthopedics Department Bogomolets National Medical University, 13 T. Shevchenko blvd., Kyiv, Ukraine, 01601
ORCID: <https://orcid.org/0000-0002-2174-1882>
kaftraum@ukr.net

Dubrov Sergii, Anesthesiology and Intensive Care Department Bogomolets National Medical University, 13 T. Shevchenko blvd., Kyiv, Ukraine, 01601; Intensive Care Unit, Kyiv City Clinical Hospital №17, 14-20 Laboratornyi str., Kyiv, Ukraine, 01133
ORCID: <https://orcid.org/0000-0002-2471-3377>
sergii.dubrov@gmail.com

Omelchenko Taras, Traumatology and Orthopedics Department Bogomolets National Medical University, 13 T. Shevchenko blvd., Kyiv, Ukraine, 01601
ORCID: <https://orcid.org/0000-0003-1722-0803>
tnomelchenko@gmail.com

Lianskorunskyi Volodymyr, Traumatology and Orthopedics Department Bogomolets National Medical University, 13 T. Shevchenko blvd., Kyiv, Ukraine, 01601; Polytrauma Department Kyiv City Clinical Hospital №17, 14-20 Laboratornyi str., Kyiv, Ukraine, 01133
+38 098 824 48 66
<https://orcid.org/0000-0002-1288-0688>
lyanskorynsky@gmail.com

Abstract

The aim: to determine the influence of individual factors on the development of complications in patients with polytrauma and multiple long bone fractures of lower extremities.

Materials and methods: a prospective study conducted in Kyiv City Clinical Hospital №17 from December 2016 to January 2020. The study included 57 patients with polytrauma and multiple long bone fractures of lower extremities, treated according to the proposed algorithm.

Results: the most common complications were: pneumonia (21.1%), acute respiratory distress syndrome (ARDS) (15.8%), multiple organ failure (MOF) (15.8%), sepsis (8.8%), mortality (12.3%). A number of factors influenced the development of complications in patients with multiple long bone fractures of lower extremities and polytrauma were identified and the correlation analysis was conducted. These factors included: age; sex; the Injury Severity Score (ISS); the Glasgow Coma Scale (GCS); the severity of a general condition of a patient according to the Clinical Grading Scale (CGS); trauma to the head, and neck, chest, abdomen, pelvis; head and neck, chest, abdomen, pelvis trauma in accordance with the Abbreviated Injury Scale (AIS); the number of segments of damaged limbs; Gustilo-Anderson fracture type; blood loss volume; massive blood transfusions; respiratory index; duration of mechanical ventilation (MV); treatment tactics; osteosynthesis method; conversion phasing.

Conclusion: the analysis allowed to identify the most significant factors that lead to complications in patients with multiple long bone fractures of lower extremities and polytrauma. Informative parameters were:

- for pneumonia: GCS and CGS; chest injury; AIS head and neck, chest ≥ 4 ; duration of MV; treatment tactics; conversion phasing (IC = 1.0-2.1).
- for ARDS: GCS and CGS; AIS chest ≥ 4 ; fractures > 2 long bones; blood loss volume; massive blood transfusions; respiratory index; duration of MV; treatment tactics (IC = 1.2-4.6).
- for sepsis: GCS; trauma to the chest, abdomen; AIS head and neck, abdominal cavity ≥ 4 ; fractures > 2 long bones; conversion phasing (IC = 1.1-3.2).
- for MOF: GCS and CGS; abdominal trauma; AIS abdominal cavity ≥ 4 ; fractures > 2 long bones; massive blood transfusions; conversion phasing (IC = 1.2-2.2).

– for mortality: age, ISS, GCS and CGS; abdominal trauma; AIS head and neck; chest, abdomen, pelvis ≥ 4 ; blood loss volume; massive blood transfusions; duration of MV (IC = 1,1-5,9).

Among the factors there were those for which the diagnostic and treatment process:

– affected: the choice of treatment tactics (IC = 1,1-1,3); use of massive blood transfusions (IC = 1.8-4.8); duration of MV (IC = 1,2-2,1); conversion of the fixation method (IC = 1.2-1.8).

– did not affect: GCS (IC = 1,2-3,1), CGS (IC = 1,1-1,3), AIS (IC = 1,0-6,2).

Keywords: polytrauma; long bone fractures; definitive osteosynthesis; complication; outcomes.

Introduction

Nowadays polytrauma is an actual problem, because it is one of the leading causes of mortality in young people [1, 2].

Treatment of patients with severe trauma is a difficult task of modern medicine. Controversial issues are to determine the priority of medical care, the choice of treatment tactics, in particular the method and term of stabilization of long bone fractures of lower extremities, as one of the most common localizations of injuries [3-5].

The right choice of treatment tactics at the early hospital stage gives a patient a chance to survive, but does not provide recovery and complete restoration of all organ and system functions, as severely injured patients from the first minutes after injury and during inpatient treatment develop numerous complications, including pneumonia, acute respiratory distress syndrome (ARDS), sepsis, multiple organ failure (MOF), fat embolism syndrome, thromboembolism [6-11].

An important issue in the diagnosis and treatment of this category of patients is the prevention of complications at the remote period of treatment, which can be achieved by identifying factors influencing their development and by predicting the treatment outcome, which dictate the need for further research.

The aim of the research: to determine the influence of individual factors on the complication development in patients with polytrauma and multiple long bone fractures of lower extremities.

Materials and methods

Study design: a prospective study conducted in Kyiv City Clinical Hospital №17 (KCCH No17) from December 2016 to January 2020.

Inclusion criteria: age ≥ 18 years; the presence of closed and open multiple long bone fractures 2 and more segments of lower extremities, one of which is the femur; diagnosed polytrauma (associated injury of two or more anatomical regions, the severity of damage of each one corresponds to ≥ 3 points according to the Abbreviated Injury Scale (AIS); the presence of at least one of the five parameter changes: hypotension (systolic blood pressure (sBP) ≤ 90 mmHg), impaired consciousness in accordance with Glasgow Coma Scale (GCS) ≤ 8 points, acidosis (base excess (BE) ≤ -6.0 , coagulopathy (activated partial thromboplastin time ≥ 40 s or international normalized ratio ≥ 1.4); age ≥ 70 years) [12]; patients treated according to the developed treatment algorithm [13].

Exclusion criteria: refusal of a patient or his/her legal representatives to participate in the study; the presence of severe concomitant chronic pathology, preventing the stabilization of a patient's condition for surgery; open type III fractures (Gustilo-Anderson); neoplasm; pregnancy.

Medical care for all patients included in the study was provided according to the proposed algorithm [13].

All patients were transported to KCCH No17 by an ambulance. In order to prepare a team of medical staff and necessary services for the admission of a patient with polytrauma, the admission department of the Kyiv City Center for Emergency Care warned the polytrauma department doctors of KCCH No17 in time. On admission the primary examination was performed according to the CABABCDE algorithm (Fig.1, 2).

A patient was transported to the operating room providing at least one of the following criteria: sBP < 90 mm Hg; signs of tension pneumothorax; $10 / \text{min} > \text{respiratory rate} > 30 / \text{min}$; "positive" ultrasound diagnostics Focused Assessment with Sonography for Trauma; GCS < 13 points. In the operating room, medical team took measures to stop bleeding, performed decompression of the pleural cavities, resuscitation measures, cardiopulmonary resuscitation.

If the above measures were successful and a patient was transported to the whole body computer tomography, then to the operating room to continue resuscitation measures and stabilization of injuries, in particular long bone fractures of lower extremities.

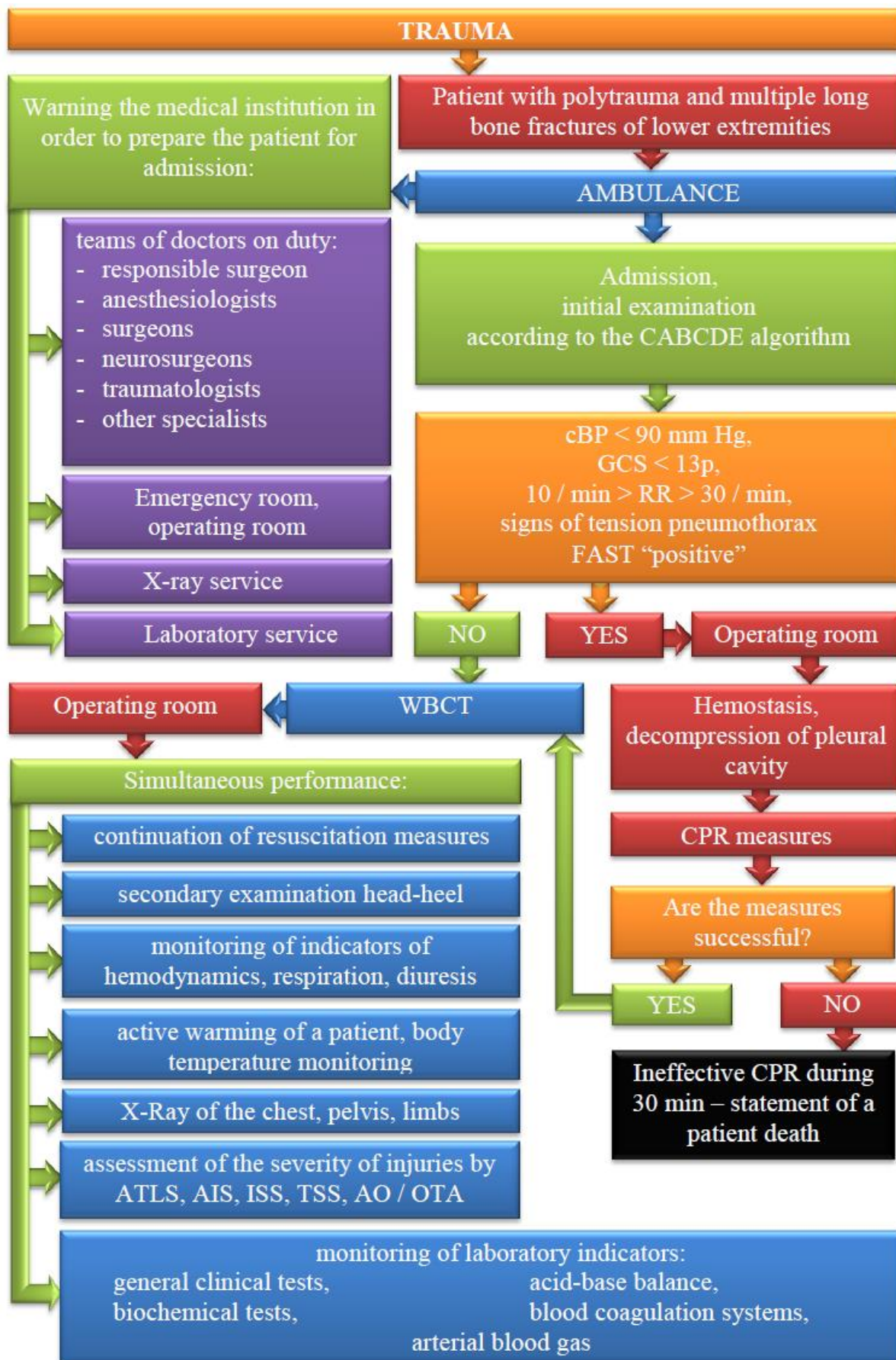


Fig. 1 Algorithm for the treatment of patients with polytrauma and multiple long bone fractures of lower extremities (part I)

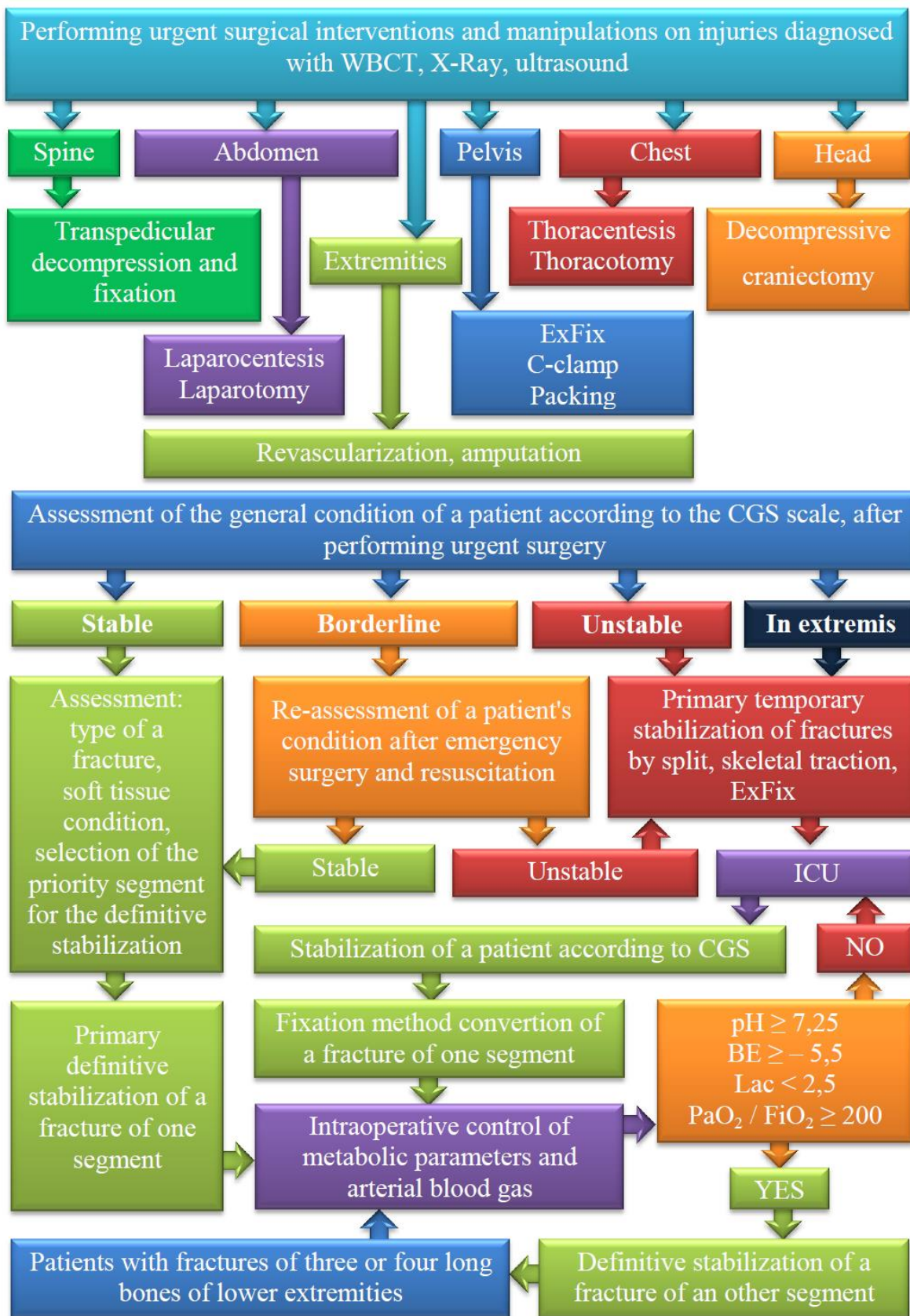


Fig. 2 Algorithm for the treatment of patients with polytrauma and multiple long bone fractures of lower extremities (part II)

All measures in the operating room were performed simultaneously under the leadership of the responsible surgeon, including: continuation of resuscitation with control of hemodynamics, respiration, diuresis; active warming of a patient with a thermoblanquet, infusion therapy only with warm solutions; monitoring of laboratory parameters: the blood coagulation system, general clinical, biochemical parameters, acid-base balance, arterial blood gas; secondary examination of the whole body from head to toe, diagnostics of injuries and appointment of additional or repeated examinations; assessment of a general condition of a patient and the severity of the injury on known scales.

In order to assess the severity of a patient's general condition the Clinical Grading System (CGS) score was used, divided patients into stable, borderline, unstable and in extremis. The severity of lesions according to the anatomical criterion was assessed by the AIS [15] and the Injury Severity Score (ISS) [16]. Impairment of consciousness was assessed by the GCS [17]. The type of bone fracture was classified according to the Arbeitsgemeinschaft für Osteosynthesefragen / Orthopedic Trauma Association (AO / OTA) [18], and an open fracture according to the Gustilo-Anderson classification [19].

After diagnostic measures for revealed lesions, urgent surgical interventions were performed, after which the severity of a patient's condition was re-assessed by CGS.

Patients in stable condition underwent primary definitive osteosynthesis of one segment, according to the recommendations of AO / OTA, depending on a location and type of a fracture and after assessment of a condition of soft tissues. Priority was given to the primary definitive osteosynthesis of the femur fracture.

In patients in unstable and in extremis conditions primary temporary stabilization of fractures was provided by external fixation, splints and skeletal traction. Subsequently, these patients continued treatment in intensive care unit (ICU) for general condition stabilization, and required conversions of the method of primary temporary fixation to the definitive.

Criteria for the readiness for conversion of the fixation method of long bone fractures of lower extremities from the temporary to the definitive were: the shock management; stabilization of vital functions, hemodynamics and no need for vasopressor support; and following parameters: $\text{Lac} < 4.0 \text{ mmol / l}$, $\text{BE} \geq - 5.5$ and $\text{pH} \geq 7.25$, $\text{PaO}_2 / \text{FiO}_2 \geq 200$.

Patients in a borderline condition after urgent surgery and resuscitation were re-evaluated for the severity of a general condition. Under a patient's stable condition, the definitive osteosynthesis of one segment was performed, if a patient wasn't in a stable condition he continued treatment as unstable.

The decision to convert the temporary fixation of the fracture of another long bone to the definitive osteosynthesis was made on the basis of intraoperative control of metabolic parameters and gas composition of arterial blood. Under the level of indicators: Lac < 4.0 mmol / l, BE \geq - 5.5, pH \geq 7.25 and PaO₂ / FiO₂ \geq 200, the definitive osteosynthesis of another segment was performed. If at least one indicator did not correspond to the above parameters, the definitive osteosynthesis of another segment was postponed until their normalization.

The treatment effectiveness was assessed by "endpoints": pneumonia, which was assessed by the criteria of the Clinical Pulmonary Infection Score (CPIS) \geq 6 points [20]; ARDS, defined on the basis of the "Berlin Definition" criteria from 2012 [21]; sepsis, diagnosed according to the "Sepsis-3" criteria from 2016 [22]; MOF defined according to the Sepsis-related Organ Failure Assessment (SOFA) [23]; pulmonary embolism (PE) of the pulmonary artery defined by the results of angiopulmonography; fat embolism syndrome diagnosed according to the Gurd and Wilson scale [24], and mortality; duration of mechanical ventilation (MV); length of stay (LOS); hospital length of stay (HLOS).

Statistic

The distribution for normality was checked using the Shapiro-Wilk test. Given the normal distribution the data presented in the medium value, the standard deviation \pm (SD). The Information Coefficient (IC) for each clinical sign in general was defined as the sum of the IC of separate subgroups of the clinical parameter. The IC, determined in the study, presented in their actual values. The comparison assessment of the informativeness of clinical factors is based on the comparison of the absolute values of the IC. For this study, it was found that the IC above 1.0 determines the possibility of priority use of these parameters to assess the condition of patients considering the probability of developing certain complications. Statistically significant differences were considered at levels $p < 0.05$. The analysis is performed using statistical software STATA 12.

Results and discussions

The study included 57 patients with polytrauma and multiple long bone fractures of lower extremities.

Among the contingent of patients included in the study, young people (40.6 ± 16.1) and males (75.4%) predominated. The main cause of injury was traffic accidents (77.2%), resulting in high rates of injury according to AIS, ISS, GCS and CGS (Table 1).

Table 1 Characteristics of demographic indicators, injury severity and general patient's condition, limb injuries and treatment tactics

Characteristics	Patients (n = 57)
Age (years)	40.6 ± 16.1
Male (n / %)	43 / 75.4
Traffic accidents (TA) (n / %)	44 / 77.2
Catatrauma (n / %)	10 / 17.5
Others (n / %)	3 / 5.3
GCS (point)	9.1 ± 3.6
ISS (point)	31.1 ± 12.3
Stable (n / %)	4 / 7.0
Borderline (n / %)	16 / 28.1
Unstable (n / %)	25 / 43.9
In extremis (n / %)	12 / 21.1
Bone fractures (n)	125
Femur (n / %)	68 / 54.4
Tibia (n / %)	57 / 45.6
Diaphyseal (n / %)	99 / 79.2
Closed fractures (n / %)	84 / 67.2
Open fractures (n / %)	41 / 32.8
Early Total Care (ETC) (n / %)	10 / 17.5
DCO (n / %)	47 / 82.5
Intramedullary nail (IMN) (n / %)	96 / 76.8
Plate (n / %)	29 / 23.2
One-stage replacement (n / %)	32 / 68.1
Replacement in several stages (n / %)	15 / 31.9

In the structure of fractures, femur fractures predominated (54.4%), which were closed (67.2%), and the dominant localization was the diaphyseal region (79.2%).

Most patients were treated according to Damage Control Orthopedics (DCO) tactics (82.5%) and required replacement of the fixation method of long bone fractures of lower extremities. Conversion of the fixation method from temporary to definitive was performed in

47 patients, of which 68.1% of patients underwent one-stage replacement of the temporary fixation method to definitive, and 31.9% of patients - in several stages.

Assessment of the treatment effectiveness of patients with polytrauma and multiple long bone fractures of lower extremities, in accordance with the established "endpoints" of the study is shown in table 2.

Table 2 Treatment outcomes.

Characteristics	Patients (n = 57)
Fatal PE (n / %)	1 / 1.8
Fat embolism (n / %)	4 / 7.0
ARDS (n / %)	9 / 15.8
Pneumonia (n / %)	12 / 21.1
Sepsis (n / %)	5 / 8.8
MOF (n / %)	9 / 15.8
MV duration (days)	10.9 ± 8.3
LOS (days)	15.7 ± 9.7
HLOS (days)	34.2 ± 16.3
Mortality (n / %)	7 / 12.3

In the structure of complications the most frequent ones were: pneumonia, ARDS, sepsis, MOF, mortality. A number of factors that influenced the development of complications in patients with multiple long bone fractures of lower extremities and severe associated trauma were also identified and correlated.

The above factors included: age; gender; ISS; GCS; the severity of a patient's general condition for CGS at the admission; head and neck injury; chest injury; abdominal trauma; pelvic injury; AIS head, neck ≥ 4; AIS chest ≥ 4; AIS abdominal cavity ≥ 4; pelvic AIS ≥ 4; a number of segments of damaged limbs; Gustilo-Anderson fracture type; blood loss volume; massive blood transfusions; respiratory index; duration of MV; treatment tactics; osteosynthesis method; conversion phasing.

One of the most common complications in polytrauma patients with multiple long bone fractures of lower extremities is pneumonia, the incidence of which was 21.1%.

The analysis showed that for the development of pneumonia the most important factors were: severity of injury according to the ISS > 41 points (OR = 7.39 (1.9-28.6), p = 0.002); degree of consciousness in accordance with GCS ≤ 8 points (OR = 3.72 (1.0-14.2), p = 0.047); unstable condition of a patient at the admission according to CGS (OR = 4.81 (1.2-18.4), p = 0.013); severity of chest injury in accordance with the AIS ≥ 4 (OR = 4.72 (1.2-21.3), p = 0.020); duration of MV > 3 days (OR = 7.42 (0.9-65.4), p = 0.031); treatment according to DCO tactics (OR = 6.91 (0.9-59.2), p = 0.044); conversion of the fixation method in several stages (OR = 4.31 (1.0-17.7), p = 0.037).

Accordingly if the patient has: severity of injury according to ISS > 41 points, the risk of pneumonia increases by 7.39 times; with impaired consciousness on the basis of GCS ≤ 8 points, this risk increases by 3.72 times; if the patient is unstable at the admission in accordance with the CGS, the risk of pneumonia increases by 4.81 times; if the patient has a chest injury, the severity of which is ≥ 4 on the basis of the AIS, the risk of pneumonia increases by 4.72 times; if the duration of MV is more than 3 days, the risk of pneumonia increases by 7.42 times; when using DCO tactics, the risk of developing pneumonia increases 6.91 times; with fixation method conversion in several stages, the risk of developing pneumonia increases by 4.31 times.

The incidence of ARDS was 15.8%. The analysis showed that the most important factors for the development of ARDS are: severity of injury according to the ISS > 41 points (OR = 7.87 (1.7-35.2), p = 0.002); in extremis patient condition at the admission in accordance with CGS (OR = 4.55 (1.0-19.3), p = 0.031); severity of chest injury on the basis of the AIS ≥ 4 (OR = 13.16 (1.4-115.2), p = 0.004); fractures > 2 long bones of lower extremities (OR = 7.31 (1.3-36.7), p = 0.007); massive blood transfusions (OR = 20.90 (3.6-124.9), p = 0.0001); respiratory index at the admission < 200 (OR = 9.28 (1.7-49.1), p = 0.003); DCO tactics (OR = 6.13 (0.9-52.8), p = 0.035).

Thus, the risk of ARDS increases: with the severity of the injury according to the ISS > 41 points by 7.87 times; in patients in extremis condition at the admission in accordance with CGS by 4.55 times; with the severity of chest injury on the basis of the AIS ≥ 4 by 13.16 times; if the patient has fractures > 2 long bones of lower extremities by 7.31 times; massive blood transfusions by 20.90 times; with indicators of a respiratory index at the admission < 200 by 9,28 times; when using DCO tactics by 6.13 times.

The incidence of sepsis was 8.8%. The analysis showed that for the development of sepsis the most important factors were: the degree of disturbance of consciousness according to the GCS ≤ 8 points (OR = 9.44 (1.0-93.6), p = 0.025); severity of head injury according to

the AIS ≥ 4 (OR = 5.81 (0.9-37.9), $p = 0.047$); severity of abdominal injury according to the AIS ≥ 4 (OR = 10.18 (1.3-74.5), $p = 0.006$).

Thus, if a patient has: impaired consciousness on the basis of the GCS ≤ 8 points, the risk of sepsis increases by 9.44 times; head injuries, the severity of which on the AIS is more than 4 points, the risk of developing sepsis increases by 5.81 times; abdominal injuries, severity of which on the AIS is more than 4 points the risk of sepsis increases by 10.18 times.

The incidence of MOF was 15.8%. The analysis showed that for the development of MOF the most important factors were: severity of injury according to the ISS > 41 points (OR = 4.38 (1.0-19.2), $p = 0.034$); in extremis condition of a patient at the admission according to the CGS (OR = 7.87 (1.7-38.6), $p = 0.004$); severity of abdominal injury on the AIS ≥ 4 (OR = 5.79 (1.2-27.9), $p = 0.014$); fractures > 2 long bones of lower extremities (OR = 7.22 (1.4-36.3), $p = 0.007$); massive blood transfusions (OR = 5.72 (1.4-28.6) $p = 0.012$).

The obtained data show that: with severity of injury according to the ISS > 41 points the risk of MOF developing increases by 4.38 times; in extremis condition of a patient at the admission on the CGS, the risk of MOF increases by 7.87 times; the severity of injury to the abdominal organs on the AIS ≥ 4 the risk of MOF increases by 5.79 times; the presence of fractures of more than two long bones of lower extremities increases the risk of MOF by 7.22 times; using the protocol of massive blood transfusion, the risk of MOF developing increases by 5.72 times.

Among patients, mortality after definitive long bone osteosynthesis of lower extremities was 12.3%. Correlation analysis showed that mortality was influenced by such factors as: severity of injury according to the ISS > 41 points (OR = 7.44 (1.4-39.8), $p = 0.007$); degree of disturbance of consciousness on the GCS ≤ 8 points (OR = 6.18 (1.1-34.9), $p = 0.024$); in extremis condition of a patient at the admission according to the CGS (OR = 7.31 (1.4-37.9), $p = 0.007$); severity of head injury on the AIS ≥ 4 (OR = 32.91 (3.5-316.7), $p = 0.001$); severity of abdominal injury according to the AIS ≥ 4 (OR = 10.19 (1.9-56.4), $p = 0.003$); massive blood transfusions (OR = 5.67 (1.1-29.5), $p = 0.024$).

Therefore, if a patient has: severity of injury according to ISS > 41 points, it increases the risk of death by 7.44 times; degree of disturbance of consciousness on the GCS ≤ 8 points, increases the risk of death by 6.18 times; in extremis condition of a patient at the admission on the CGS –by 7.31 times; severity of head injury on the AIS ≥ 4 by 32.91 times; severity of abdominal injury on the AIS ≥ 4 by 10.19 times; massive blood transfusion by 5.67 times.

Conclusions

The analysis revealed the most significant factors that lead to complications in patients with multiple long bone fractures of lower extremities with severe associated trauma.

The informative parameters for pneumonia are: the GCS and CGS; chest injury; AIS head and neck ≥ 4 ; AIS chest ≥ 4 ; duration of MV; treatment tactics; conversion phasing (IC = 1.0-2.1).

Informative parameters for ARDS are: the GCS and CGS; AIS chest ≥ 4 ; fractures > 2 long bones; blood loss volume; massive blood transfusions; respiratory index; duration of MV; treatment tactics (IC = 1.2-4.6).

Informative parameters for sepsis are: the GCS; chest and abdominal trauma; AIS head and neck ≥ 4 , AIS abdominal cavity ≥ 4 ; fractures > 2 long bones; conversion phasing (IC = 1.1-3.2).

Informative parameters for MOF are: the GCS and CGS; AIS abdominal trauma ≥ 4 ; AIS abdominal cavity ≥ 4 ; fractures > 2 long bones; massive blood transfusions; conversion phasing (IC = 1.2-2.2).

Informative parameters for mortality are: age, the ISS, GCS and CGS; abdominal trauma; AIS head, neck, chest, abdomen, pelvis ≥ 4 ; blood loss volume; massive blood transfusions; duration of MV (IC = 1,1-5,9).

Among the factors influencing the development of all above complications are those that are affected by the diagnostic and treatment process, namely the choice of treatment tactics (IC = 1,1-1,3), the use of the protocol of massive blood transfusions (IC = 1,8- 4.8), the duration of MV (IC = 1.2-2.1), the conversion of the fixation method (IC = 1.2-1.8). But there are those factors that are not affected by the choice of treatment tactics, in particular the GCS (IC= 1,2-3,1), CGS (IC = 1,1-1,3), AIS (IC = 1,0-6, 2).

Conflicts of interest: the authors declare no conflict of interest.

References:

1. WHO, The top 10 causes of death 24 May 2018 <https://www.who.int/en/news-room/fact-sheets/detail/the-top-10-causes-of-death>
2. WHO, Global Health Observatory (GHO) data. https://www.who.int/gho/mortality_burden_disease/en/
3. Liu, X. Y., Jiang, M., Yi, C. L., Bai, X. J., & Hak, D. J. (2016). Early intramedullary nailing for femoral fractures in patients with severe thoracic trauma: A

systemic review and meta-analysis. Chinese journal of traumatology = Zhonghua chuang shang za zhi, 19(3), 160–163. <https://doi.org/10.1016/j.cjtee.2016.04.001>

4. Nahm, N. J., & Vallier, H. A. (2012). Timing of definitive treatment of femoral shaft fractures in patients with multiple injuries: a systematic review of randomized and nonrandomized trials. *The journal of trauma and acute care surgery*, 73(5), 1046–1063. <https://doi.org/10.1097/TA.0b013e3182701ded>

5. Cantu, R. V., Graves, S. C., & Spratt, K. F. (2014). In-hospital mortality from femoral shaft fracture depends on the initial delay to fracture fixation and Injury Severity Score: a retrospective cohort study from the NTDB 2002-2006. *The journal of trauma and acute care surgery*, 76(6), 1433–1440. <https://doi.org/10.1097/TA.0000000000000230>

6. Blokhuis, T. J., Pape, H. C., & Frölke, J. P. (2017). Timing of definitive fixation of major long bone fractures: Can fat embolism syndrome be prevented?. *Injury*, 48 Suppl 1, S3–S6. <https://doi.org/10.1016/j.injury.2017.04.015>

7. Banerjee, M., Bouillon, B., Shafizadeh, S., Paffrath, T., Lefering, R., Wafaisade, A., & German Trauma Registry Group (2013). Epidemiology of extremity injuries in multiple trauma patients. *Injury*, 44(8), 1015–1021. <https://doi.org/10.1016/j.injury.2012.12.007>

8. Pfeifer, R., Rixen, D., Husebye, E. E., Pardini, D., Müller, M., Dumont, C., Oestern, H. G., Giannoudis, P., Pape, H. C., & EPOFF study group (2012). Do stable multiply injured patients with bilateral femur fractures have higher complication rates? An investigation by the EPOFF study group. *European journal of trauma and emergency surgery : official publication of the European Trauma Society*, 38(2), 185–190. <https://doi.org/10.1007/s00068-011-0147-9>

9. Kobbe, P., Micansky, F., Lichte, P., Sellei, R. M., Pfeifer, R., Dombroski, D., Lefering, R., Pape, H. C., & TraumaRegister DGU (2013). Increased morbidity and mortality after bilateral femoral shaft fractures: myth or reality in the era of damage control?. *Injury*, 44(2), 221–225. <https://doi.org/10.1016/j.injury.2012.09.011>

10. Nahm, N. J., Moore, T. A., & Vallier, H. A. (2014). Use of two grading systems in determining risks associated with timing of fracture fixation. *The journal of trauma and acute care surgery*, 77(2), 268–279. <https://doi.org/10.1097/TA.0000000000000283>

11. Lichte, P., Weber, C., Sellei, R. M., Hildebrand, F., Lefering, R., Pape, H. C., Kobbe, P., & TraumaRegister DGU (2014). Are bilateral tibial shaft fractures associated with an increased risk for adverse outcome?. *Injury*, 45(12), 1985–1989. <https://doi.org/10.1016/j.injury.2014.10.005>

12. Pape, H. C., Lefering, R., Butcher, N., Peitzman, A., Leenen, L., Marzi, I., Lichte, P., Josten, C., Bouillon, B., Schmucker, U., Stahel, P., Giannoudis, P., & Balogh, Z. (2014). The definition of polytrauma revisited: An international consensus process and proposal of the new 'Berlin definition'. *The journal of trauma and acute care surgery*, 77(5), 780–786. <https://doi.org/10.1097/TA.0000000000000453>.
13. Lyanskorunsky, VM, Dubrov, SO, Buryanov, OA, Myasnikov, DV (2020). The influence of the choice of treatment tactics on patients with polytrauma and multiple fractures of the long bones of the lower extremities on the development of complications. *Pain, anesthesia and intensive care / Pain, anesthesia and intensive care*, №2 (91), 76-86. DOI: [https://doi.org/10.25284/2519-2078.2\(91\).2020.205603](https://doi.org/10.25284/2519-2078.2(91).2020.205603)
14. Pape, H. C., Giannoudis, P. V., Krettek, C., & Trentz, O. (2005). Timing of fixation of major fractures in blunt polytrauma: role of conventional indicators in clinical decision making. *Journal of orthopaedic trauma*, 19(8), 551–562. <https://doi.org/10.1097/01.bot.0000161712.87129.80>
15. Rating the severity of tissue damage. I. The abbreviated scale. (1971). *JAMA*, 215(2), 277–280. <https://doi.org/10.1001/jama.1971.03180150059012>
16. Baker, S. P., O'Neill, B., Haddon, W., Jr, & Long, W. B. (1974). The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *The Journal of trauma*, 14(3), 187–196
17. Teasdale, G., & Jennett, B. (1974). Assessment of coma and impaired consciousness. A practical scale. *Lancet (London, England)*, 2(7872), 81–84. [https://doi.org/10.1016/s0140-6736\(74\)91639-0](https://doi.org/10.1016/s0140-6736(74)91639-0)
18. Meinberg, E. G., Agel, J., Roberts, C. S., Karam, M. D., & Kellam, J. F. (2018). Fracture and Dislocation Classification Compendium-2018. *Journal of orthopaedic trauma*, 32 Suppl 1, S1–S170. <https://doi.org/10.1097/BOT.0000000000001063>
19. Gustilo, R. B., & Anderson, J. T. (1976). Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. *The Journal of bone and joint surgery. American volume*, 58(4), 453–458
20. Schurink, C., Nieuwenhoven, C., Jacobs, J. A., Rozenberg-Arska, M., Joore, H., Buskens, E., Hoepelman, A., & Bonten, M. (2004). Clinical pulmonary infection score for ventilator-associated pneumonia: accuracy and inter-observer variability. *Intensive care medicine*, 30(2), 217–224. <https://doi.org/10.1007/s00134-003-2018-2>

21. ARDS Definition Task Force, Ranieri, V. M., Rubenfeld, G. D., Thompson, B. T., Ferguson, N. D., Caldwell, E., Fan, E., Camporota, L., & Slutsky, A. S. (2012). Acute respiratory distress syndrome: the Berlin Definition. *JAMA*, 307(23), 2526–2533. <https://doi.org/10.1001/jama.2012.5669>
22. Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., Bellomo, R., Bernard, G. R., Chiche, J. D., Coopersmith, C. M., Hotchkiss, R. S., Levy, M. M., Marshall, J. C., Martin, G. S., Opal, S. M., Rubenfeld, G. D., van der Poll, T., Vincent, J. L., & Angus, D. C. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, 315(8), 801–810. <https://doi.org/10.1001/jama.2016.0287>
23. Vincent, J. L., Moreno, R., Takala, J., Willatts, S., De Mendonça, A., Bruining, H., Reinhart, C. K., Suter, P. M., & Thijs, L. G. (1996). The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive care medicine*, 22(7), 707–710. <https://doi.org/10.1007/bf01709751>
24. Gurd, A. R., & Wilson, R. I. (1974). The fat embolism syndrome. *The Journal of bone and joint surgery. British volume*, 56B(3), 408–416