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Mathematical modeling of physiological parameters in traumatic shock caused by lower limb blast injury

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ABSTRACT

The aim of this study was to apply integrative physiological mathematical models to simulate physiological parameters in traumatic shock caused by lower limb blast injury.

Materials and methods. At the first stage of mathematical modeling, we applied lumped parameter integrative physiological models, and at the second stage we used neural networks.

Results. We developed a clinical decision support system that allows to determine the intensity of blood loss in lower limb blast injuries according to physiological monitoring data.

Conclusion. The developed approaches make it possible to partially solve the problem associated with the impossibility of accumulating a sufficient amount of medical data for a specific person to create an adequate personalized clinical decision support system.

Keywords: mathematical modeling, traumatic shock, bleeding, clinical decision support systems

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Математическое моделирование физиологических показателей при травматическом шоке, вызванном взрывной травмой нижних конечностей

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РЕЗЮМЕ

Целью настоящего исследования является применение интегративных физиологических математических моделей для моделирования физиологических показателей при травматическом шоке, вызванном взрывной травмой нижних конечностей.

Материалы и методы. На первом этапе математического моделирования использовались интегративные физиологические модели с сосредоточенными параметрами, а на втором этапе – нейронные сети.

Результаты. Разработана система поддержки принятия врачебных решений, позволяющая по данным физиологического мониторинга определять интенсивность кровопотери при минно-взрывной травме нижних конечностей.

Заключение. Разработанные подходы позволяют частично решить проблему, связанную с невозможностью накопления достаточного количества медицинских данных для конкретного человека с целью создания адекватной персонализированной модели поддержки принятия врачебных решений.

Ключевые слова: математическое моделирование, травматический шок, кровотечение, системы поддержки принятия врачебных решений

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

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INTRODUCTION

Assessing the severity and predicting the development of traumatic shock in mine blast injuries is a relevant task of modern military science. Blast injury is a special type of gunshot injury, characterized by a combination of injuries resulting from direct or indirect exposure to an explosion. Blast injury requires a special approach to the assessment of the severity and the condition of the wounded, which is the key to the effectiveness of medical and evacuation measures [1].

The development of traumatic shock is determined by the type of injury, the volume of mechanical damage to tissues and organs, blood loss and hypovolemia, pain intensity and, a body reaction to aggression, and the duration of the pathological condition. From the pathogenic point of view, traumatic shock is a severe multicomponent reaction of the body to severe mechanical damage and is identified by clinicians as the first stage of the so-called traumatic disease. The main pathogenic element of shock is generalized tissue hypoperfusion, which disrupts homeostatic mechanisms and leads to irreversible cellular damage. Tissue hypoperfusion entails the development of irreversible metabolic, biochemical, and enzymatic cellular disorders, and in the absence of adequate treatment – death [2].

The concepts of "severity of injury", "severity of damage", and "severity of condition" are interrelated, but are not synonymous. The severity of the damage depends on its location, the extent of the anatomical damage, and the functional significance of the affected organ or anatomical and functional area. The severity of the condition is associated with the severity of the injury and the severity of functional disorders, time that passed since the injury, the initial condition of the person, and the amount of medical care provided. Methods for assessing the severity of injury using combined approaches, including parameters of the injury severity (morphological signs) and parameters of the condition severity (functional signs), have proven to be extremely effective [3–5]. This article focuses on the assessment of functional signs, which implies further development of the methodology with additional criteria for assessing the injury severity.

Numerous classifications of acute blood loss with the development of shock ultimately come down to a discussion of the role of two components of impaired oxygen-carrying capacity of the blood. The first component is associated with impaired myocardial contractility due to several reasons: hypoxia, myocardial ischemia, the effect of myocardial depression factors of various etiologies, concomitant pathology, intensive care strategy used, etc. The second component which is most discussed and directly caused by blood loss is associated with primary circulatory system disorders due to deficient circulating blood volume (CBV); therefore, with the development of metabolic and microcirculatory disorders, it is called hypovolemic shock. However, the cause of shock due to acute blood loss is of great practical importance only in early stages of the process, since subsequently, due to the convergence of pathophysiological parameters, it loses its specificity associated with the etiological factor [6]. Based on the above, the use of mathematical modeling may be effective for solving problems in developing a clinical decision support system (CDSS) to assess the severity and predict the development of traumatic shock when monitoring the condition of a serviceman at the frontline stages of evacuation, as well as to develop activities for simulation training.

The aim of this study was to use integrative physiological mathematical models to simulate physiological parameters in traumatic shock caused by lower limb blast injury.

MATERIALS AND METHODS

To simulate physiological parameters in traumatic shock caused by lower limb blast injury, we used the Pulse Physiology Engine [7], a multi-platform universal human physiology simulator, modified for work. The system is used to enable accurate and consistent physiology simulation in real time. The structure of the developed engine includes the main core, which is the basic software that manages the engine components using interfaces. Engine components include verified models of physiological mechanisms and pharmacokinetic (pharmacodynamic) models. These models belong to the class of lumped parameter mathematical models and are based on ordinary differential equations (ODEs) taking into account feedback mechanisms.

Unlike systems in which lumped parameter models are typically used to model individual physiological functions and behaviors, the engine is used to examine the physiological state of the body based on physiological functions in each individual subsystem.

The cardiovascular subsystem includes the heart and blood vessels of pulmonary and systemic circulation, and the respiratory subsystem models various components of the airways. These two subsystems interact through the alveolar – capillary barrier to mediate gas exchange. The simulation involves diffusion due to partial pressure between liquid (blood) and gas (air). The result of the simulation is the pressure and volume values in the capillaries and airways. Feedback mechanisms occur through baroreceptors. The baroreceptor mechanism rapidly regulates blood pressure (BP) based on negative feedback. A drop in blood pressure is detected by baroreceptors and leads to an increase in heart rate (HR) and vascular resistance. These changes are needed to maintain constant blood pressure at rest by calculating the sympathetic (1) and parasympathetic (2) responses.

$$\eta_s(P_a) = [1 + P_a / P_{a,s})^{v}]^{-1}, \quad (1)$$

$$\eta_p(P_a) = [1 + P_a / P_{a,s})^{-v}]^{-1}, \quad (2)$$

where v – baroreceptor parameter, P_a – mean blood pressure, $P_{a,s}$ – fixed value of P_a. These values are then used to calculate changes in heart rate (HR) (3), elasticity (E) (4), systemic vascular resistance (R) (5) and compliance (C) (6).

$$dHR / dt = -\tau^{-1}_{HR} (-HR + \alpha_{HR}\eta_s(P_a) + \beta_{HR}\eta_p(P_a) + \gamma_{HR}), \quad (3)$$

$$dE / dt = -\tau^{-1}_{E} (-E + \alpha_E\eta_s(P_a) + \gamma_{HR}), \quad (4)$$

$$dE / dt = -\tau^{-1}_{R} (-R + \alpha_R\eta_s(P_a) + \gamma_R), \quad (5)$$

$$dC / dt = -\tau^{-1}_{C} (-R + \alpha_C\eta_s(P_a) + \gamma_C), \quad (6)$$

Here HR, E, R, and C are relative values of heart rate, elasticity, vascular resistance and compliance, respectively; α, β, γ – model parameters, τ – time parameters of the corresponding processes. These time-dependent changes are introduced into a model of the cardiovascular system by changing components with lumped parameters, scale factors determining vascular resistance, blood volume, and heart rate are defined.

In terms of mathematical modeling, the amount of physiological data generated is limited only by the variations of independent variables. Therefore, it is fundamentally possible to generate an arbitrarily large array of data for subsequent training of the CDSS model. The approach was tested by generating an array of data containing 10,000,000 records including changes in physiological parameters over 20 minutes: diastolic blood pressure, systolic blood pressure, heart rate, respiratory rate, blood oxygen saturation (SpO_2), temperature in lower limb blast injury accompanied by acute blood loss of varying intensity (the modeling step for the rate of blood loss from the lower limb is 10 ml / min). The total volume of generated data was 16.2 GB in CSV format.

RESULTS

The developed CDSS is a cyber physical system (CPS), which implies a set of physical processes and systems, computer and other devices, Internet resources and users coordinately interacting with one another through computer implementation of algorithms (protocols) aimed at solving a wide range of multi-purpose tasks in the field of network technologies. To visualize data in real time, software generating model signals was developed in accordance with the specified initial conditions of the mathematical model (Fig. 1).

a

b

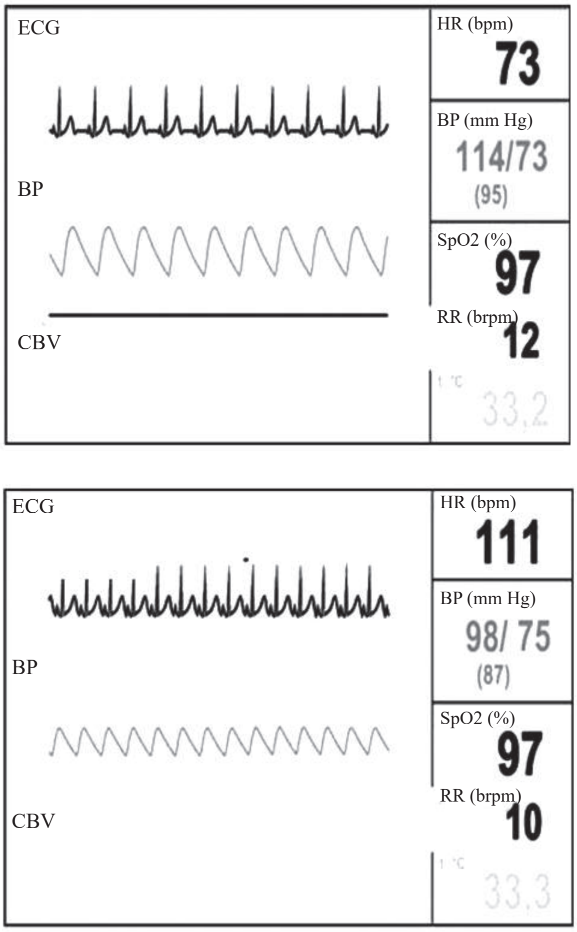

Fig. 1. An example of the results of mathematical modeling of physiological parameters in traumatic shock caused by lower limb blast injury: *a* is the initial state; *b* is the state of compensated traumatic shock

The physiological parameters obtained as a result of solving the direct problem of mathematical modeling represent an array of data in which variations of physiological parameters in dynamics are compared, allowing to identify the most likely combination of vital signs with different blood loss intensity.

The development of the final CDSS includes several stages: 1) building a personalized database (DB) of the examined persons based on the measurement of physiological parameters, modeling a number of physiological conditions in both normal and critical conditions on the basis of a computer simulator of human physiological functions used in the system; 2) training a classifier used in the system that can determine the nature of a person's pathological condition by comparing the flow of measured physiological parameters of a person with a set of records in a personalized database.

The priority task of the CDSS is to monitor data using sensors of vital physiological parameters, create the medical data flow in an established format using software, and use a software component to compare the data flow with a personalized database in order to detect a critical condition (CC). If a critical condition is detected, its type is determined (the CC is indexed), and information about the CC and its type is sent to the person responsible for making a clinical decision.

The general diagram of the developed CDSS is shown in Fig. 2, 3. In this system, module 1 is implemented on the basis of the Pulse Engine software package, which generates a personalized object database. Module 2, which classifies object states, is implemented as a set of deep neural networks trained on the object database. CDSS includes the following interconnected structural elements: array of X vectors of personalized database obtained by measuring state parameters (Fig. 2).

Module 2 monitors the functional states of an object by comparing the input stream of measured physiological parameters of the object, detecting CC and indexing it. In the system under development, module 2 is implemented in the form of neural systems. The training of neural networks, which makes it possible to determine the CC of an object, is carried out using a set of CC from a personalized object database generated by module 1.

The input array consists of X vectors of the patient's primary data. Vector X has the following structure: $X = (X_{1,} X_{2})$. Here X_{1} is a vector of anthropometric parameters, and X_{2} is a vector of physiological parameters of the patient.

The components of vector X_1 include such parameters as height, weight, gender, baseline values of vital signs at rest and on exertion. If necessary, the list of input parameters can be significantly expanded. Currently, most of the input parameters (parameters of the endocrine system, hemostasis, nervous system, etc.) are recorded as average values.

The components of vector X_2 include heart rate (number of contractions / min); SpO_2, the normal level 95%; respiration rate (breaths / min); blood pressure (mm Hg).; physical activity; temperature (°C). Let us consider the structural elements of the CDSS presented in Fig. 2 in more detail.

The vector supplied to the input system (X) consists of the measured parameters of the patient's condition. The list of patient parameters can be adjusted depending on the specific conditions of applying the CDSS.

Module 1 generates a personalized patient database consisting of model vectors (Y) of the patient's condition in a given range of model parameters ($a = (a_{1}, \ldots, a_{k}$). The Pulse Physiology Engine performs this function in the developed CDSS.

For a given set of parameters of model a and input vector X, module 1 generates a time series of vectors $Y(a, t)$ (the information flow of the object data) at the output. The time variable t with sample spacing δ is defined as the characteristic time of the modeled physiological process. For example, a step can be set to 1 minute for blood loss. You make the step δ "small" compared to its consequence, i.e. when the modeled process leads to a change in the state of an object (to a transition from a normal state to a critical one). For example, the time series appears when the process of blood loss does not immediately lead to the transition from a normal condition to a critical one (the effect is accumulated).

In Fig. 3, the "External Expert" block includes the function of configuring the CDSS, which consists in setting the vector of model parameters, $a = a_{(j)}$, at which module 1 generates a vector flow of vectors $Y_{(j)}(a_{(j)}, t)$, representing the j CC of the object . It will be designated as cr. j. Let us assume that the value $j = 1$ corresponds to the patient's CC, which occurs in blood loss at a rate of 10 ml / min.

Module 2. The neural network should perform the function of assessing the state, including the critical condition of the object according to (tested) input vector of the measured parameters of the object's state. The use of neural network machine learning algorithms makes it possible to turn from mathematically complex solutions of inverse problems for dynamical system through multiple integration to solving simple models with a known structure (weighting factors and activation functions). The input vector for the neural network is a time series of vectors $Y(a,t)$ generated by module 1. Accordingly, the output of the network will be a time series of vectors of the form $Z_{cr}(t_{1}) = (h_{1}(t_{1}), h_{2}(t_{1}), \ldots, h_{R}(t_{1}))$.

Here the time variable t_1 changes at a scale different from the time scale t set in module 1. Sample spacing Δ time t_1 is greater than the step δ of a physiological process, for example, blood loss, i.e. t_1 is a "slow" time compared to a "fast" time t.

The values $h_1(t_1)$, $h_2(t_1), \ldots, h_R(t_1)$ – components of vector $Z_{cr}(t_1)$ – represent probabilities, for example, $h_1(t_1)$ – there is a probability that the patient is in CC 1 in the time interval $(t_1, t_1 + \Delta)$.

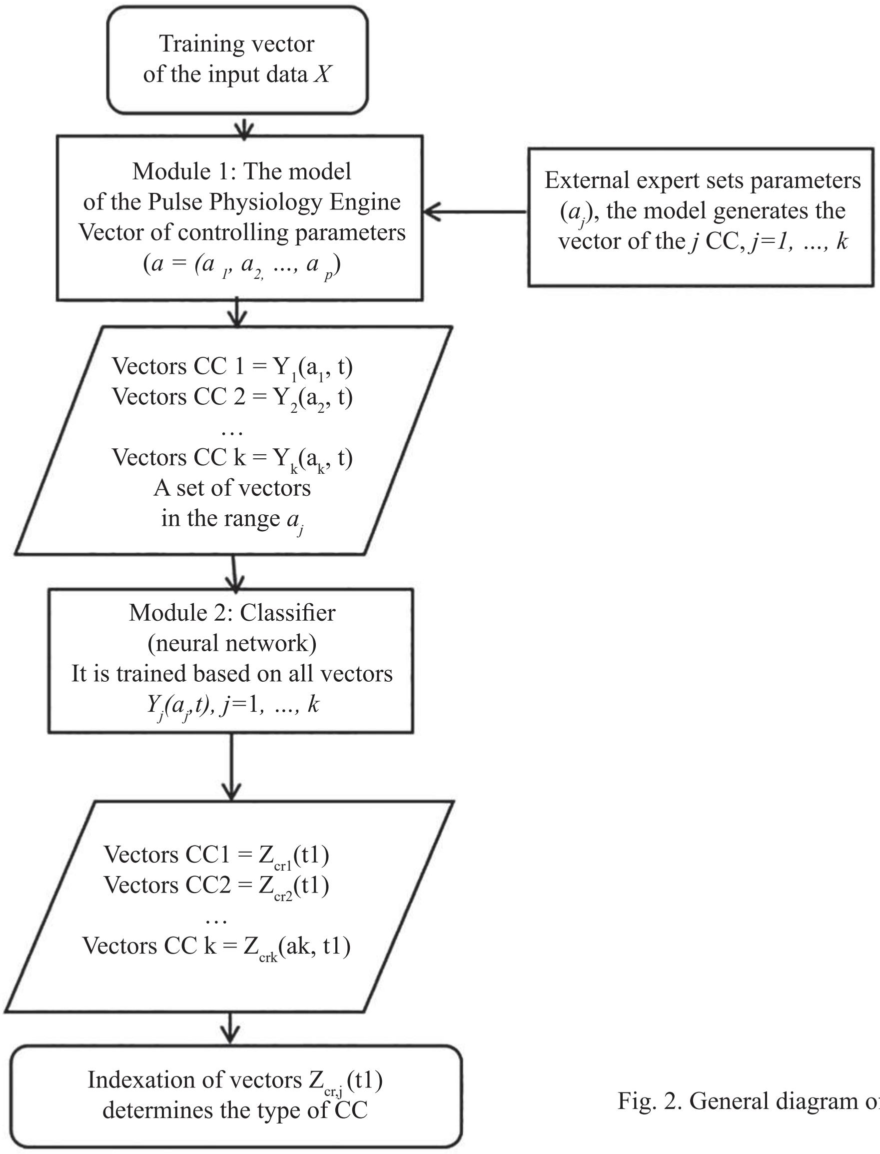

Fig. 2. General diagram of the clinical decision support system

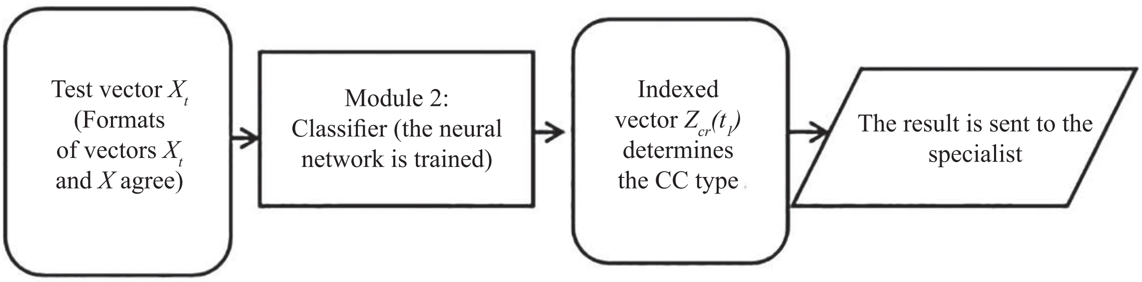

Fig. 3. Decision support system testing scheme

Neural networks are trained through operations with a personalized database object. Based on the results of the work of module 2, CDSS algorithms are obtained, which are “input – output” models. The input of the model consists of an array of data with vital parameters accumulated over a fixed period of time (60 seconds). At the output, the system forms a vector containing information about the state of the object and calculated physiological parameters that are highly informative content for medical specialists (rate of blood loss, volume of blood loss).

A software application in Python was developed to build the final model of the CDSS based on neural network algorithms. Using the annotated data set generated at the previous stage, several neural networks are built including long short-term memory (LSTM), Autoencoder, and convolutional neural network (CNN). The final CDSS algorithm performs the following functions: classification of states according to physiological monitoring (heart rate, systolic BP, diastolic BP, SpO_2, respiration rate, body temperature), restoration of the data array if some of the values are missing. If a patient is bleeding, the system will determine the rate of blood loss, the volume of blood loss and the time of blood loss onset. Several deep neural network architectures have been proposed:

1) LSTM network whose main task is to classify the physiological state. It belongs to recurrent neural networks capable of learning long-term dependencies. LSTM is specifically designed to detect events in a changing process mode.

2) Autoencoder network whose main task is to recreate a data array if there are gaps and predict changes in the trajectory of parameters.

3) CNN network whose main task is to calculate the rate of blood loss, the volume of blood loss, and the time of the bleeding onset. A convolutional neural network is a specialized artificial neural network architecture that promotes efficient image recognition. The developed algorithm makes it possible to calculate a neural network using a sample of simulated parameters in Python. When assessing the quality of the modeled structure, final accuracy was 0.992 (99.1%) and 0.997 (98.9%) according to MSE and MAE, respectively.

CONCLUSION

The developed approaches make it possible to partially solve the problem associated with the inability to accumulate a sufficient amount of medical data for a particular person to create an adequate personalized model to support clinical decision-making. In the future, the proposed algorithm will make it possible to create a hardware solution for assessing the need for medical care in case of lower limb blast injury, which is especially important at the pre-hospital phase and in emergency care during medical evacuation. Criteria for assessing the injury severity remain an important problem. The complexity of including these parameters in the mathematical model does not allow to use the developed methodology alone. In addition, to confirm the results of mathematical modeling, a set of clinical data is required to verify the model.

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