Research Article

Modelling Of Wound Process Dynamics in Patients with Diabetes Mellitus In Addition To Vac-Therapy witha Discrete-Time Markov Chain

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Abstract: The wound process in patients with diabetes mellitus in addition to VAC-therapy (Vacuum-assisted closure — VAC® therapy) is examined. The model of the biological system describing the wound process is built on three independently functioning subsystems; it is assumed to be ergodic and presented with a symmetric graph. The mathematical model of the wound process dynamics is constructed based on a discrete-time Markov chain and constitutes an eighth-order iterative matrix equation. A period of 24 hours is taken as the discrete time during which the probabilistic characteristics of the subsystems are assumed to be averaged. The phase course of the wound process in patients with diabetes mellitus in addition to VAC-therapy is viewed as a Markovian process of the biological system random walk among eight possible states depending on the preassigned baseline state and transition probabilities. It is tested for stability. The calculation algorithms modelling multidimensional Markovian processes are adapted to computer technology.

Keywords: VAC-therapy, diabetes, Markovian process, state graph, state probabilities.

INTRODUCTION

Studies [1, 2] are dedicated to the investigation of random processes in biological systems. They are dedicated to the development of the strategy and methods for intellectual support of diagnostics and treatment processes based on heuristically selected schemes, adequate mathematical models and corresponding calculation algorithms. Mathematical modelling of the wound process in patients with diabetes mellitus pertains to a scientific field allowing for the increase of the efficacy of comprehensive treatment [2]. Investigation of dynamics of the course of the wound process in patients with diabetes mellitus in addition to VAC-therapy constitutes an integral component of comprehensive treatment for purulent and necrotic complications in this population of patients.

It is appropriate to formulate and solve the examined topical problem using mathematical models in the form of Markov chains [3]. The description of the Markovian processes in a system with discrete states and discrete time comes down to building an iteration process linking the probabilities of states on the preceding and following steps divided with a determined period of time. The dynamics of the system random walk process among the possible states is determined with the property of a lack of after effect and stability. Investigations of Markovian process stability have determined the conditions for the existence of limit probabilities of states expressed through values of transition probabilities. The values of transition probabilities can be found analytically or using numerical methods in a computational experiment [4, 5].

Setting of the problem

Random processes in a biological system described with a uniform Markov chain with eight discrete states as well as discrete time assumed to be 24 hours are examined. The graph of states of this Markov chain is presented in symmetrical form in a figure (Fig. 1). Here $S_i \left(i = 1,\, 2,\, 3, ...8 \right)$ are the states of a biological system consisting of three independently functioning subsystems.

The first subsystem is characterised with the blood sugar level of the patient with diabetes mellitus. This subsystem reflects the achieving or deviating from the target blood sugar level. In case of carbohydrate metabolism compensation, that is achieving the target glycaemic level, at values ranging from 4 to 9 mmol/L, the normal phase course of the wound process is possible. This fasting glycaemic level should not exceed 6 mmol/L; in 1.5–2 hours after a meal it should not exceed 8 mmol/L. It should be noted that the target level is determined individually.

The second subsystem is characterised with the number of functioning capillaries per high power field in the biopsy material of the wound edge. This subsystem determines the microcirculation in the wound and, correspondingly, the reparation efficacy of VAC-therapy, that is, the terms of granulations occurrence and the wound readiness for closure.

The third subsystem reflects the degree of the wound microbial contamination and is characterised with the number of colony-forming units of microorganisms in the wound on the top of treatment, presented with the Lg of the total number of microorganisms in 1 g of tissue.

Each of the three subsystems is in one of two lumped states [6]:

— Functional, that is healthy, designated with the symbol $\oplus$;

— Non-functional, that is sick, designated with the symbol $\ominus$.

In the process of the function of the biological system, each of the three subsystems transits from the healthy state, characterised with reliability r_1, r_2, r_3, to the sick state with the probability of $\bar{r}_1$, $\bar{r}_2$, $\bar{r}_3$ (unreliability).

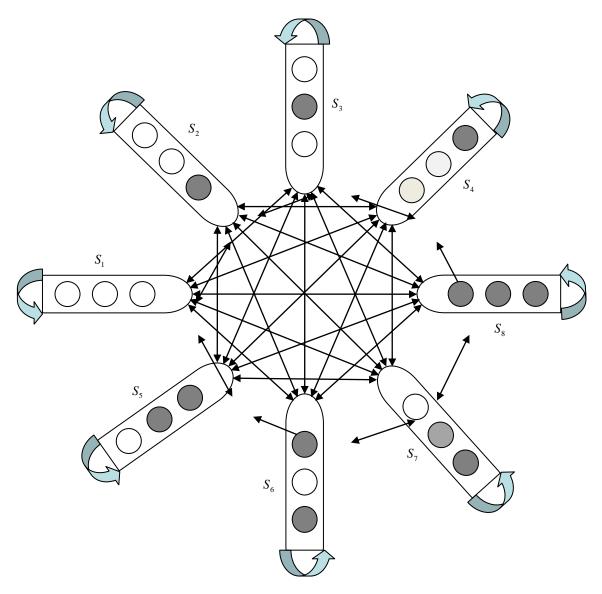**Fig. 1 Graph of biological system states.**

Each subsystem, being non-viable, restores and transits from the sick state to the healthy state with the probability of v_1, v_2, v_3 or remains in the sick state with the probability of $\bar{v}_1$, $\bar{v}_2$, $\bar{v}_3$ respectively. Here, subsystems' reliability and probabilities of their restoration are assumed to be found.

Random transitions of the biological system from one state to another occur in discrete moments of time

$$t_k = k \, \square t \quad (k = 0, 1, 2, 3, ...),$$

Divided with step $\square t$, assumed for the problem under consideration to be equal to 24 hours, It is also assumed that the probabilistic characteristics of the subsystems (reliability and restorability) preserve invariable values, independent of integral-valued argument k, that is, the discrete Markov chain is uniform. As a result of the diagnostic process the initial state of the biological system is known with certainty:

$$\text{at } k = 0 \quad P\left[S_j(0) \right] \quad (j = 1, 2, 3, ...8)$$

The task is to determine the probabilities of the eight state of the biological system at the next $(k+1)$-step: $P\left[S_j(k+1) \right]$ based on the probabilities of states at the preceding k-step: $P\left[S_j(k) \right]$. The sequence of random events related to the transition (random walk) of the biological system among the eight possible states in given discrete moments of time constitutes a random process in the discrete-time Markov chain. The current investigations of Markovian process stability at $k \to \infty$ seems important. It is appropriate to set limit probabilities of the biological system $P_j(\infty)$ (j=1,2,3,....8) at the ensured level of restorability v_i and reliability r_i of the three subsystems (i=1,2,3) for a stable process.

Mathematical model. Equations of states' probabilities:

In accordance with the drawn symmetrical graph of states of the examined biological system, the probabilities of its states are linked with the following matrix recurrence equation:

$$P(k+1) = P \cdot P(k) \quad (k = 0, 1, 2, 3, ...\infty).$$

Here $P(k+1)$, the column matrix of the system states' probabilities at any next $(k+1)$-step is determined through the matrix -(8×8) of transition probabilities

$$P = \begin{Vmatrix} p_{11} & p_{21} & p_{31} & \cdot & p_{81} \\ p_{12} & p_{22} & p_{32} & \cdot & p_{82} \\ p_{13} & p_{23} & p_{33} & \cdot & p_{83} \\ \cdot & \cdot & \cdot & \cdot & \cdot \\ p_{18} & p_{28} & p_{38} & \cdot & p_{88} \end{Vmatrix}$$

and the column market of the system states' probabilities at the preceding k-step, where the initial state of the system $(k=0)$ is assumed to be known:

$$p_j(0) \quad (j = 1, 2, 3, ...8)$$

For example, $p_1(0) = 0$, $p_2(0) = 0$, $p_3(0) = 0$, $p_4(0) = 0$, $p_5(0) = 0$, $p_6(0) = 0$, $p_7(0) = 0$, $p_8(0) = 1$, that is three subsystems are not viable in the biological system at the initial stage and state S_8 is true, and the other states S_1, S_2, S_3, S_4, S_5, S_6, S_7 are impossible.

Transition probabilities constitute respective conditional probabilities:

$$p_{11} = P_{S_1(k)}\left[S_1(k+1) \right], \ p_{21} = P_{S_2(k)}\left[S_1(k+1) \right], \ p_{31} = P_{S_3(k)}\left[S_1(k+1) \right], ... p_{81} = P_{S_8(k)}\left[S_1(k+1) \right],$$

$$p_{12} = P_{S_1(k)}\left[S_2(k+1) \right], \ p_{22} = P_{S_2(k)}\left[S_2(k+1) \right], \ p_{32} = P_{S_3(k)}\left[S_2(k+1) \right], ... p_{82} = P_{S_8(k)}\left[S_2(k+1) \right]$$

$$\vdots \qquad \vdots \qquad \vdots \qquad \vdots$$

$$p_{18} = P_{S_1(k)}\left[S_8\left(k+1\right)\right], p_{28} = P_{S_2(k)}\left[S_8\left(k+1\right)\right], \ p_{38} = P_{S_3(k)}\left[S_8\left(k+1\right)\right], \dots p_{88} = P_{S_8(k)}\left[S_8\left(k+1\right)\right].$$

In the expanded presentation, the transition probabilities are found through the subsystems' reliability and restorability as follows:

$$p_{11} = r_1 r_2 r_3, \quad p_{21} = r_1 r_2 v_3, \ p_{31} = r_1 v_2 r_3, \ \dots \ p_{81} = v_1 v_2 v_3,$$

$$p_{12} = r_1 r_2 \overline{r_3}, \quad p_{22} = r_1 r_2 \overline{v_3}, \quad p_{32} = r_1 v_2 \overline{r_3}, \quad \dots p_{82} = v_1 v_2 \overline{v_3},$$

$$p_{13} = r_1 \overline{r_2} r_3, \quad p_{23} = r_1 \overline{r_2} v_3, \quad p_{33} = r_1 \overline{v_2} r_3, \ \dots \ p_{83} = v_1 \overline{v_2} v_3,$$

$$\vdots \quad \vdots \quad \vdots \quad \quad \vdots$$

$$p_{18} = \overline{r_1} \overline{r_2} \overline{r_3}, \quad p_{28} = \overline{r_1} \overline{r_2} \overline{v_3}, \quad p_{38} = \overline{r_1} \overline{v_2} \overline{r_3}, \ \dots \ p_{88} = \overline{v_1} \overline{v_2} \overline{v_3}.$$

The probabilities of subsystems restoration v_i and non-restoration $\overline{v_i}$ $(i = 0, 1, 2, 3)$, their reliability r_i and unreliability $\overline{r_i}$ are linked with the obvious conditions:

$$r_i + \overline{r_i} = 1,$$

$$v_i + \overline{v_i} = 1. \ (\text{i=1, 2, 3})$$

Then, the transition probabilities have the following properties:

$$\sum_{j=1}^{8} p_{1j} = 1, \ \sum_{j=1}^{8} p_{2j} = 1, \sum_{j=1}^{8} p_{3j} = 1, \dots \sum_{j=1}^{8} p_{8j} = 1.$$

It should also be noted that the probabilities of the system states at each step satisfy the following condition:

$$\sum_{j=1}^{8} p_j(k) = 1, \quad \left(k = 0, 1, 2, \dots\infty\right).$$

CONCLUSION

The presented mathematical model of Markovian process in a biological system in the form of a matrix recurrence equation for states' probabilities at discrete moments of time demonstrates an iterative process, an important property of which is stability, convergence to a steady state that is to limit probabilities of the system states. The mathematical model of the course of wound process in patients with diabetes mellitus in addition to VAC-therapy allows for evaluating the significance of the subjective and objective wound characteristics and to determine the probability of the normal phase course of the wound process until the wound is ready to close.

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