

ON THE HUMAN'S VITAL FUNCTIONS DEGRADATION MODELLING

V. BAGDONAVIČIUS¹, A. BIKELIS¹, M. MEILŪNAS²,
D. STOŠKUVIENĖ³

¹ *Vilnius University*

Naugarduko 24, 2006 Vilnius

E-mail: vilijandas.bagdonavicius@maf.vu.lt

² *Vilnius Gediminas Technical University*

Saulėtekio 11, 2054 Vilnius

Vilnius University

Universiteto 3, 2734 Vilnius

E-mail: mecislovas.meilunas@fm.vtu.lt

³ *Vilnius University*

Čiurlionio 21, 2009 Vilnius

E-mail: danutes@ligo.mf.vu.lt

Received September 17, 2000; revised November 3, 2000

ABSTRACT

Human vital functions can degrade due to genetic aging, violent factors and diseases. Most (~90%) people are affected by diseases. Degradation of the body functions can slope when disease is cured and progress to death when it is incurable. We propose human organism degradation model caused by disease which is based on the course of the vital functions damage and stopping of the patients, dead in the hospitals.

All concepts of this model are described first of all for the contingent of the deaths. The thanatogenetic process for this contingent is divided to separate levels (stages) and then transition probabilities from one level to other are estimated according to observation data. These estimations enable us to establish reliable connections between different links of the thanatogenesis. They are important for the prevention of the development of the terminal thanatogenetic syndromes in the intensive care units in the hospitals.

1. INTRODUCTION

The degradation of the biological functions in the human organism is called *thanatogenesis*. Complications of diseases are called *thanatogenetic syndromes* (TGS).

At the beginning of thanatogenesis the function of the vital importance (respiration, blood circulation and nervous regulation) are impaired. They are most important in the development of the TGS. When organs are damaged irreversibly, all vital processes subside and terminal TGS develops. Finally, one of the three vital functions (sometimes two or even three) stops and organism dies through the mechanism of impaired respiration, blood circulation or nervous regulation [2].

Human's vital functions can degrade due to genetic aging, violent factors and diseases. Most ($\approx 90\%$) of people are affected by diseases. Degradation of the body functions can slope when disease is cured and progress to death when it is incurable.

The model of degradation of the human organism caused by a disease is based on the observation of the vital functions damage process and it's terminating among the patients, deceased in hospitals.

We study transitions from one stage of the thanatogenetic process to the other in order to evaluate probabilities of such transitions.

2. MATHEMATICAL MODEL

The thanatogenetic process of the general population is divided to following separate levels (stages):

- A – healthy people;
- Λ – patients with known disease or a group of diseases;
- P – patients undergone one main TGS;
- T – patients undergone the terminal TGS;
- M – patients undergone the death mechanism;
- W – deceased.

Let us consider a group of patients who underwent all above mentioned stages. Each of them could be described by a specific condition at any stage.

Suppose that there are:

I states at the stage Λ : $\Lambda_1, \Lambda_2, \dots, \Lambda_I$;

J states at the stage P : P_1, P_2, \dots, P_J ;

K states at the stage T : T_1, T_2, \dots, T_K ;

L states in the death mechanism: M_1, M_2, \dots, M_L .

The stages A and W are one-state.

Denote by $p_i^{(0)}$ the probability to have the i -th disease, $p_{j/i}$ the transition probability from Λ_i to P_j by $q_{k/j}$ – the transition probability from P_j to T_k by $r_{l/k}$ – the transition probability from T_k to M_l and by $R_l^{(0)}$ the probability to die by the l th death mechanism.

Transitions from A to L are described by the vector $P^{(0)} = (p_1^{(0)}, p_2^{(0)}, \dots,$

$p_I^{(0)T}$, transitions from M to W – by the vector $R^{(0)} = (r_1^{(0)}, r_2^{(0)}, \dots, r_I^{(0)})^T$

Let us also consider the matrices of transition probabilities:

$$P_1 = \begin{bmatrix} p_{1/1} & p_{1/2} & \cdots & p_{1/I} \\ p_{2/1} & p_{2/2} & \cdots & p_{2/I} \\ \cdots & \cdots & \cdots & \cdots \\ p_{J/1} & p_{J/2} & \cdots & p_{J/I} \end{bmatrix}, \quad Q = \begin{bmatrix} q_{1/1} & q_{1/2} & \cdots & q_{1/J} \\ q_{2/1} & q_{2/2} & \cdots & q_{2/J} \\ \cdots & \cdots & \cdots & \cdots \\ q_{K/1} & q_{K/2} & \cdots & q_{K/J} \end{bmatrix},$$

$$R = \begin{bmatrix} r_{1/1} & r_{1/2} & \cdots & r_{1/K} \\ r_{2/1} & r_{2/2} & \cdots & r_{2/K} \\ \cdots & \cdots & \cdots & \cdots \\ r_{L/1} & r_{L/2} & \cdots & r_{L/K} \end{bmatrix} \quad (2.1)$$

All possible transitions are shown by the following chain of representations

$$A \xrightarrow{P_0} \Lambda \xrightarrow{P_1} P \xrightarrow{Q} T \xrightarrow{R} M \xrightarrow{R_0} . \quad (2.2)$$

So, for example, element $p_{j/i}$ of the matrix P_1 represents the transition probability from the disease i to the main syndrome j .

The probabilities of transition between non-adjacent levels can be calculated by using the formula of the complete probability.

For example, the product $P_1 P_0$ gives the transition probabilities from the states of the level A to the states of the level P , the product $R Q P_1$ gives the transition probabilities from the states of the level Λ to the states of the level T , etc. The element c_{st} ($1 < s < K$, $1 < t < I$), of the product $Q P_1$, means the transition probability from disease t to terminal syndrome s .

3. ESTIMATION OF THE TRANSITION PROBABILITIES BETWEEN VARIOUS LEVELS OF THE THANATOGENETIC PROCESS

The exact values of the transition probabilities are not known. Therefore we use point and interval estimators, obtained from the available data.

Let be n – total number of the deceased patients. Suppose that for each patient the disease (or group of diseases), the main and the terminal syndromes and the death mechanism are known.

The point estimator $\hat{p}_{j/i}$ of the transition probability $p_{j/i}$ from the state i to the state j is defined as the relative frequency m_{ij}/m_i , where m_{ij} is the number of individuals going from the state i to the state j , and m_i is the total number of individuals at the i th state.

The confidence interval of a parameter of a probability distribution is the interval, to which the real value of the parameter belongs with a certain confidence level.

We consider the confidence interval for $p_{j/i}$, the probability of transition from the state i to the state j .

The confidence level we denote by $g = 1 - \alpha$. Usually $g = 0,95$.

At first adjacent levels are considered. Point and interval estimators for the probability to have the terminal syndrome k given the disease i and the main syndrome j are obtained. The minimal sample size which gives the confidence interval of specified length and confidence level, is given.

The probability to have the terminal syndrome k given the disease i and the main syndrome j is

$$p_{k/ij} = p_{ijk} / p_{ij},$$

where p_{ijk} is the probability for an individual to have the i th disease, the j th main syndrome and the k th terminal syndrome $1 \leq i \leq I$, $1 \leq j \leq J$, $1 \leq k \leq K$.

Then the corresponding point estimator of this probability is

$$\hat{p}_{k/ij} = \frac{m_{ijk}}{m_{ij}}, \quad m_{ij} = \sum_{l=1}^K m_{ijl};$$

here m_{ijk} is number of the individuals with disease i , main syndrome j and terminal syndrome k ; m_{ij} – number of the individuals with disease i and main syndrome j . These numbers are random. Consider random vector M

$$M = \{m_{ijk}, i = 1, \dots, I, j = 1, \dots, J, k = 1, \dots, K\}$$

which has multinomial distribution with parameters n, p_{ijk} :

$$M \sim M(n, p_{ijk}, i = 1, \dots, I; j = 1, \dots, J; k = 1, \dots, K), \quad \sum_{i,j,k} p_{ijk} = 1.$$

The mean of the component m_{ijk} of the vector M is

$$E m_{ijk} = n p_{ijk},$$

the variance is

$$Var \{m_{ijk}\} = n p_{ijk} (1 - p_{ijk}) = n \sigma_{ijk,ijk}$$

and the covariation between the components are

$$cov(m_{ijk}, m_{i'j'k'}) = -n p_{ijk} p_{i'j'k'} = n \sigma_{ijk,i'j'k'}, \quad (i', j', k') \neq (i, j, k).$$

Investigating the properties of the estimators we use the following limit theorem given in [5]: consider a sequence of random variable $\{T_n\}$ having the property

$$\sqrt{n}(T_n - \theta) \xrightarrow{L} N[0, \sigma^2(\theta)], \quad (3.1)$$

where L means the convergence in distribution. If the function $g(\theta)$ is such that $g'(\theta) \neq 0$, then

$$\begin{aligned} \sqrt{n} [g(T_n) - g(\theta)] &\xrightarrow{L} N\left(0, [g'(\theta)\sigma(\theta)]^2\right), \\ \frac{\sqrt{n} [g(T_n) - g(\theta)]}{g'(T_n)} &\xrightarrow{L} N[0, \sigma^2(\theta)]. \end{aligned}$$

If $\sigma(\theta) \neq 0$, then

$$\frac{\sqrt{n} [g(T_n) - g(\theta)]}{g'(T_n)\sigma(T_n)} \xrightarrow{L} N(0, 1). \quad (3.2)$$

Let us consider the multivariate generalization of the last result. Denote by $N_m(a, \Sigma)$ normal distribution with the mean a and covariance matrix Σ . Suppose that we have a sequence of random vectors $X^n = (X_1^n, \dots, X_m^n)$ such that

$$\sqrt{n}(X_1^n - a_1, \dots, X_m^n - a_m) \xrightarrow{L} N_m(0, \sum_{m \times m}), \quad \sum_{m \times m} = (\sigma_{ij})_{m \times m}. \quad (3.3)$$

If f sufficiently smooth function and

$$Y^n = f(X_1^n, \dots, X_m^n), \quad (3.4)$$

then

$$\begin{aligned} \sqrt{n}\{f(X_1^n, \dots, X_m^n) - f(a_1, \dots, a_m)\} &\xrightarrow{L} \\ N_m\left(0, \sum_{r=1}^m \sum_{s=1}^m \sigma_{rs} \frac{\partial f(a_1, \dots, a_m)}{\partial a_r} \frac{\partial f(a_1, \dots, a_m)}{\partial a_s}\right). &\quad (3.5) \end{aligned}$$

Let us consider the above mentioned point estimator of the transition probability $p_{k/ij}$, which is the function of corresponding frequencies:

$$\hat{p}_{k/ij} = \frac{m_{ijk}}{\sum_{l=1}^k m_{ijl}} = f\left(\frac{m_{ij1}}{n}, \dots, \frac{m_{ijK}}{n}\right). \quad (3.6)$$

Then by the -Laplace theorem (see [4]):

$$\sqrt{n}\left\{\frac{m_{ij1}}{n} - p_{ij1}, \dots, \frac{m_{ijK}}{n} - p_{ijK}\right\} \xrightarrow{L} N_K(0, \sum_{ij}), \quad (3.7)$$

where

$$\sum_{ij} = (\sigma_{ijk,ijl})_{K \times K}.$$

The formulas (3.7), and (3.6) are the particular cases of the formulas (3.3) and (3.4), respectively. Therefore the formula (3.5) implies:

$$\sqrt{n}(\hat{p}_{k/ij} - p_{k/ij}) = \sqrt{n} \left(\frac{\frac{m_{ijk}}{n}}{\frac{\sum_{l=1}^K m_{ijl}}{n}} - \frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) \xrightarrow{L} N(0, \sigma_{K/ij}^2), \quad (3.8)$$

where

$$\sigma_{k/ij}^2 = \sum_{r=1}^K \sum_{s=1}^K \frac{\partial}{\partial p_{ijr}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) \sigma_{ijr,ijs} \frac{\partial}{\partial p_{ijs}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) \quad (3.9)$$

$$\sum_{l=1}^K p_{ijl} = p_{ij}, \quad p_{k/ij} = \frac{p_{ijk}}{p_{ij}}.$$

Let us calculate the asymptotic variance (3.9):

$$\begin{aligned} \sigma_{k/ij}^2 &= \left[\frac{\partial}{\partial p_{ijr}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) \right]^2 p_{ijk} (1 - p_{ijk}) \\ &\quad - 2 \sum_{s \neq k} \frac{\partial}{\partial p_{ijs}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) \frac{\partial}{\partial p_{ijk}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) p_{ijk} p_{ijs} \\ &\quad - \sum_{r \neq k} \sum_{s \neq k} \frac{\partial}{\partial p_{ijr}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) \frac{\partial}{\partial p_{ijs}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) \sigma_{ijr,ijs}. \quad (3.10) \end{aligned}$$

The derivatives are:

$$\begin{aligned} \frac{\partial}{\partial p_{ijk}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) &= \frac{\sum_{l=1}^K p_{ijl} - p_{ijk}}{\left(\sum_{l=1}^K p_{ijl} \right)^2} = \frac{\sum_{l \neq k} p_{ijl}}{\left(\sum_{l=1}^K p_{ijl} \right)^2} = \frac{\sum_{l \neq k} p_{ijl}}{p_{ij}^2}, \\ \frac{\partial}{\partial p_{ijss}} \left(\frac{p_{ijk}}{\sum_{l=1}^K p_{ijl}} \right) &= -\frac{p_{ijk}}{p_{ij}^2} (s \neq k). \end{aligned}$$

Let return to (3.10):

$$\sigma_{k/ij}^2 = \frac{\left(\sum_{l \neq k} p_{ijl} \right)^2}{p_{ij}^4} p_{ijk} (1 - p_{ijk}) + 2 \sum_{s \neq k} \frac{p_{ijk}}{p_{ij}^2} \frac{\sum_{l \neq k} p_{ijl}}{p_{ij}^4} p_{ijk} p_{ijs}$$

$$\begin{aligned}
& -p_{ijk}^2 \sum_{r \neq s} \sum_{s \neq k} p_{ijr} p_{ijs} + p_{ijk}^2 \sum_{r \neq k} p_{ijr} (1 - p_{ijr}) \} \\
= & \frac{1}{p_{ij}^4} (p_{ijk} + p_{ijk}^2) \left(\sum_{l \neq k} p_{ijl} \right)^2 - p_{ijk}^2 \sum_{r \neq k} \sum_{s \neq k} p_{ijr} p_{ijs} \\
& + p_{ijk}^2 \sum_{r \neq k} p_{ijr} (1 - p_{ijr}) \\
= & \frac{1}{p_{ij}^4} \left\{ \left(\sum_{l \neq k} p_{ijl} \right)^2 (p_{ijk} + p_{ijk}^2) - p_{ijk}^2 \sum_{r \neq k} \sum_{s \neq k} p_{ijr} p_{ijs} + p_{ijk}^2 \sum_{r \neq k} p_{ijr} \right\} \\
= & \frac{\sum_{l \neq k} p_{ijl}}{p_{ij}^4} \left\{ (p_{ijk} + p_{ijk}^2 - p_{ijk}^2) \sum_{r \neq k} p_{ijr} + p_{ijk}^2 \right\} \\
= & \frac{\left(\sum_{l \neq k} p_{ijl} \right) p_{ijk}}{p_{ij}^4} = \frac{(p_{ij} - p_{ijk}) p_{ijk}}{p_{ij}^3}. \tag{3.11}
\end{aligned}$$

While performing calculation, we used the equality:

$$\sum_{r \neq k} p_{ijr} = p_{ij} - p_{ijk},$$

The formulas (3.8) and (3.11) imply:

$$\sqrt{n}(\hat{p}_{k/ij} - p_{k/ij}) \xrightarrow{L} N\left(0, \frac{(p_{ij} - p_{ijk}) p_{ijk}}{p_{ij}^3}\right).$$

Replacing the probabilities p_{ijk} and p_{ij} by their estimations, we get the following estimator of the variance $\sigma_{k/ij}^2$:

$$\hat{\sigma}_{k/ij}^2 = \frac{(\hat{p}_{ij} - \hat{p}_{ijk}) \hat{p}_{ijk}}{\hat{p}_{ij}^3}.$$

We get:

$$\frac{\sqrt{n}(\hat{p}_{k/ij} - p_{k/ij})}{\hat{\sigma}_{k/ij}} \approx N(0, 1).$$

Let us choose the confidence level:

$$g = 1 - \alpha = 0,95.$$

The former equality implies:

$$P\left\{-z_{1-\alpha/2} \leq \frac{\sqrt{n}(\hat{p}_{k/ij} - p_{k/ij})}{\hat{\sigma}_{k/ij}} \leq z_{1-\alpha/2}\right\} \approx 1 - \alpha$$

when n is large, and, consequently,

$$P\left\{\hat{p}_{k/ij} - \frac{\hat{\sigma}_{k/ij}}{\sqrt{n}} z_{1-\alpha/2} \leq p_{k/ij} \leq \hat{p}_{k/ij} + \frac{\hat{\sigma}_{k/ij}}{\sqrt{n}} z_{1-\alpha/2}\right\} \approx 0,95;$$

here $z_{1-\alpha/2}$ is $(1 - \alpha/2)$ quantile of the standard normal distribution. We have the approximated confidence interval

$$\left(\hat{p}_{k/ij} - \frac{\hat{\sigma}_{k/ij}}{\sqrt{n}} z_{1-\alpha/2}, \hat{p}_{k/ij} + \frac{\hat{\sigma}_{k/ij}}{\sqrt{n}} z_{1-\alpha/2}\right),$$

which length is

$$\Delta = \frac{2\hat{\sigma}_{k/ij}^2}{\sqrt{n}} z_{1-\alpha/2}.$$

For the given confidence interval of the length Δ and the level g , we can estimate the minimal sample size: From former formula we get

$$n \geq \frac{4\hat{\sigma}_{k/ij}^2 z_{1-\alpha/2}^2}{\Delta^2}.$$

When n is small, the approximation of the probabilities $p_{k/ij} \in (0, 1)$ by normal distribution may be not exact and we can get a confidence interval with the negative left end and the right end which is greater than > 1 . To avoid such situation we find at first the confidence interval for the function

$$\Psi_{k/ij} = \ln\left(\frac{p_{k/ij}}{1 - p_{k/ij}}\right).$$

It takes the values in the interval $(-\infty, +\infty)$ and its estimator is

$$\hat{\Psi}_{k/ij} = \ln\left(\frac{\hat{p}_{k/ij}}{1 - \hat{p}_{k/ij}}\right).$$

Applying formula (3.1) to this function, we get:

$$\sqrt{n}(\hat{\Psi}_{k/ij} - \Psi_{k/ij}) \xrightarrow{L} N\left(0, \sigma \frac{\sigma_{k/ij}^2}{p_{k/ij}^2 (1 - p_{k/ij})^2}\right), \quad (3.12)$$

because

$$\left(\ln \frac{x}{1-x}\right)' = \frac{1-x}{x} \cdot \frac{1-x+x}{(1-x)^2} = \frac{1}{x(1-x)}.$$

The convergence (3.12) implies:

$$P\left\{-z_{1-\alpha/2} \leq \frac{\sqrt{n}(\hat{\Psi}_{k/ij} - (\Psi_{k/ij}))}{\hat{\sigma}_{k/ij}} \hat{p}_{k/ij}(1 - \hat{p}_{k/ij}) \leq z_{1-\alpha/2}\right\} \approx 1 - \alpha.$$

If we solve the inequalities, we get

$$\begin{aligned} P\left\{\left(1 + \exp\left\{-\left(\hat{\Psi}_{k/ij} - \frac{\hat{\sigma}_{k/ij} z_{1-\alpha/2}}{\hat{p}_{k/ij}(1 - \hat{p}_{k/ij})}\right)\right\}\right)^{-1} \leq p_{k/ij}\right. \\ \left. \leq \left(1 + \exp\left\{-\left(\hat{\Psi}_{k/ij} + \frac{\hat{\sigma}_{k/ij} z_{1-\alpha/2}}{\hat{p}_{k/ij}(1 - \hat{p}_{k/ij})}\right)\right\}\right)^{-1}\right\}. \end{aligned}$$

We have the following confidence interval for $p_{k/ij}$: $(\underline{p}_{k/ij}, \bar{p}_{k/ij})$,

$$\begin{aligned} \underline{p}_{k/ij} &= \left(1 + \exp\left\{-\left(\hat{\Psi}_{k/ij} - \frac{\hat{\sigma}_{k/ij} z_{1-\alpha/2}}{\hat{p}_{k/ij}(1 - \hat{p}_{k/ij})}\right)\right\}\right)^{-1}, \\ \bar{p}_{k/ij} &= \left(1 + \exp\left\{-\left(\hat{\Psi}_{k/ij} + \frac{\hat{\sigma}_{k/ij} z_{1-\alpha/2}}{\hat{p}_{k/ij}(1 - \hat{p}_{k/ij})}\right)\right\}\right)^{-1} \end{aligned}$$

4. COMPARING OF THE PROBABILITIES OF TRANSITION FOR THE INDIVIDUALS DECEASED DURING DIFFERENT PERIODS

Let us consider the hypothesis:

$$H_0 : p_{k/ij}^{(1)} = p_{k/ij}^{(2)}$$

where $p_{k/ij}^{(1)}$ and $p_{k/ij}^{(2)}$ are the probabilities of the transition from the state (i, j) to the state k for two populations of individuals diseased during two different periods. As in Section 3 we have:

$$\frac{\sqrt{n_\gamma}(\hat{p}_{k/ij}^{(\gamma)} - p_{k/ij}^{(\gamma)})}{\hat{\sigma}_{k/ij}^{(\gamma)}} \approx N(0, 1), \quad (4.1)$$

where

$$\begin{aligned} \hat{\sigma}_{k/ij}^{(\gamma)} &= \frac{\sqrt{(\hat{p}_{ij}^{(\gamma)} - \hat{p}_{ijk}^{(\gamma)})\hat{p}_{ijk}^{(\gamma)}}}{\hat{p}_{ij}^{(\gamma)}\sqrt{\hat{p}_{ij}^{(\gamma)}}}, \\ \hat{p}_{ijk}^{(\gamma)} &= \frac{\hat{m}_{ijk}^{(\gamma)}}{n_\gamma}, \quad \hat{p}_{ij}^{(\gamma)} = \frac{m_{ijk}^{(\gamma)}}{n_\gamma}, \end{aligned}$$

and $n_\gamma, m_{ij}^{(\gamma)}, m_{ijk}^{(\gamma)}$ are the values corresponding to the γ th year ($\gamma = 1, 2$). We have

$$\hat{p}_{k/ij}^{(\gamma)} - p_{k/ij}^{(\gamma)} \approx \left(0, \frac{(\sigma_{k/ij}^{(\gamma)})^2}{n_\gamma}\right),$$

when n is large.

If the hypothesis H_0 is correct, then

$$\hat{p}_{k/ij}^{(2)} - \hat{p}_{k/ij}^{(1)} \approx N\left(0, \frac{(\sigma_{k/ij}^{(1)})^2}{n_1} + \frac{(\sigma_{k/ij}^{(2)})^2}{n_2}\right). \quad (4.2)$$

Therefore

$$U = \frac{\hat{p}_{k/ij}^{(2)} - \hat{p}_{k/ij}^{(1)}}{\sqrt{\frac{(\sigma_{k/ij}^{(1)})^2}{n_1} + \frac{(\sigma_{k/ij}^{(2)})^2}{n_2}}} \approx N(0, 1). \quad (4.3)$$

Hypothesis H_0 is rejected with significance level α , if $|U| \geq z_{1-\alpha/2}$.

5. CONCLUSIONS

Using mathematical modeling and analysis of frequencies certain diseases and their TGS (main and terminal) and death mechanisms, we established reliable connections between chains of the thanatogenesis. Autopsies data of 345 patients and their thanatogenetic analysis was performed in [3]. It revealed statistically important relations for six diseases, which were accompanied by the main TGS, and these complicated later by the terminal TGS and the death mechanisms. These diseases are: the chronic ischaemic heart disease, thrombosis of magistral vessels, gastric carcinoma, acute ischaemic heart disease, diabetes mellitus and thrombosis of intestine vessels. These complications of diseases are life threatening, so the prevention of them is an important condition of mortality decrease in hospitals.

The most prevalent TGS are cardiogenic dysvolaemia (disorder of the circulating blood volume) among the main TGS and pulmonary disaerosis among the terminal TGS. Most of the patients have deceased because of the circulatory insufficiency, least of deaths were caused by the insufficiency of the central nervous regulation. Complications of these diseases and related TGS are the most dangerous.

We estimated the probabilities of transition between various chains of the thanatogenesis. Knowledge of these probabilities is important for prevention of development of the main and the terminal TGS in the intensive care units and for the hospital mortality decrease.

The syndromic analysis could be applied in the following situations: analysis of contingents of diseased individuals in hospitals gives the possibility to get information about treatment efficiency in hospitals. If probabilities of transition between various levels are calculated from the data of several years, differences of its values may be detected, which could provide the additional information about treatment efficiency in hospitals. If one wants to compare the treatment efficiency of different hospitals, it is necessary to follow up specific contingent of patients from one city or country, who are being treated in

these hospitals. For this purpose new groups of healthy and cured patients (i.e. who passed from the lower level of the degradation to the higher) should be included. In such a case it is reasonable to compare corresponding probabilities of transition between different hospitals. To end, we wish to thank professor R. Ptašekas for their advice and participation in the discussions.

REFERENCES

- [1] Ch. Livingstone. *Pocket medical dictionary*. Ch. Livingstone (ed.) INC, 1978, 392.
- [2] R. Ptašekas. *Thanatogenetic syndromes of human's diseases*. Vilnius, 1998, 131. (In Lithuanian)
- [3] R. Ptašekas, M. Černiauskaitė, R. Keblas, H. Ulevičius, V. Paulauskienė, M. Meilūnas, D. Stoškuvienė. Application of the syndrome analysis for the investigation of mortality and the determination of its decreasing directions in hospitals. *Medicina*, **35** (2) 1999, 152 – 164. (In Lithuanian)
- [4] M. Nikulin, V. Voinov. *Unbiased estimation and their applications, v.1*. Univariate case. Kluwer academic publishers: Dordrecht, 1993.
- [5] C. R. Rao. *Linear statistical inference and its applications*. Wiley, 1973, 395 - 400.

APIE ŽMOGAUS GYVYBINIŲ FUNKCIJŲ DEGRADAVIMO MODELIAVIMĄ

V. BAGDONAVIČIUS, A. BIKELIS, M. MEILŪNAS, D. STOŠKUVIENĖ

Žmogaus gyvybinės funkcijos gali degraduoti dėl genetiškai sąlygoto senėjimo, nelaimingų atsitikimų ir ligų. Daugelį atvejų (~90%) nulemia ligos. Organizmo funkcijų degradacija lėtėja, jei liga gydoma ir progresuoja iki mirties, jeigu ji nėra pagydoma. Siūlomas ligų sąlygojamas žmogaus organizmo degradacijos modelis, paremtas mirusiųjų ligoninėje pacientų gyvybinių funkcijų pakenkimo ir nutrūkimo stebėjimais. Visos modelio sąvokos yra taikomos visų pirma mirusiųjų kontingentui. Tanatogeneziniai (mirtį sąlygojantys) procesai tam kontingentui yra skirstomi į atskirus lygmenis (stadijas), ir yra keliamas uždavinys įvertinti perėjimo iš vienos stadijos į kitą tikimybes. Tokie įverčiai įgalina nustatyti patikimus ryšius tarp atskirų tanatogenezės grandžių. Tai yra svarbu tanatogenezinių procesų prevencijai ligoninių intensyvios terapijos ir reanimacijos skyriuose.