VILNIUS UNIVERSITY

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CHANGES IN THE QUALITY OF LIFE IN PATIENTS WITH PROLONGED STAY IN THE INTENSIVE CARE UNIT AND RISK FACTORS RELATED TO THE CHANGES

Summary Doctoral Dissertation

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VILNIAUS UNIVERSITETAS

Andrius Klimašauskas

LIGONIŲ, ILGAI GYDYTŲ INTENSYVIOSIOS TERAPIJOS SKYRIUJE, GYVENIMO KOKYBĖS POKYČIAI IR JŲ RIZIKOS VEIKSNIAI

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CONTENT

ABBREVIATIONS

APACHE II	Acute Physiology and Chronic Health Evaluation II score
GH	General Health
GHd	General Health Difference
CNS	Central Nervous System
MV	Mechanical Ventilation
MH	Mental Health
MHd	Mental Health Difference
VT	Vitality
VTd	Vitality Difference
ENMG	Electroneuromyography
PF	Physical Functioning
PFd	Physical Functioning Difference
ICU	Intensive Care Unit
CINMA	Critical Illness Neuromuscular Abnormalities
r^2	Coefficient of Determination
BP	Bodily Pain
SAPS 3	Simplified Acute Physiology Score 3
SF-36	Medical Outcomes Study Short-Form 36
SD	Standard Deviation
SOFA	Sequential Organ Failure Assessment score
SF	Social Functioning
SFd	Social Functioning Difference

BPd	Bodily Pain Difference
HRQOL	Health Related Quality of Life
TISS-28	Therapeutic Interventions Scoring System-28
RE	Role-Emotional
REd	Role-Emotional Difference
RP	Role-Physical
RPd	Role-Physical Difference

1. INTRODUCTION

A primary goal of treatment in an intensive care unit (ICU) is to reduce mortality in critically ill patients. The mortality rate in ICUs has long been the sole criterion in assessing the treatment efficacy in intensive care units. Improving survival rates in critically ill patients encouraged us taking the next step, i.e., knowing the further fate and life of survivors after intensive care. As survivors often suffer from post-ICU consequences, they normally cannot be regarded as fully recovered. ICU after-effects are caused by an illness itself, organ dysfunction developed before ICU admission or acquired during a stay in the ICU and/or prolonged intensive care support of failed organs. Organ and system failures in intensive care may have impacts on the life of ICU survivors long after their discharge from the ICU. Frequent post-ICU effects include limitations in the ability to work and performing the activities of daily life, organ dysfunction and/or impaired mental function. However, to evaluate the quality of health and life in such patients as a whole, mere objective information on the patient's ability to work and mobility as well as clinical or laboratory analyses of organ functions are not enough. Impairment or even disability after discharge from intensive care may as well have no effects on the health and life satisfaction for ICU survivors. Subjective perception of the physical and mental quality of life by patients themselves becomes more and more important for the evaluation of post-ICU outcomes. A combination of patient's health status and multiple non-medical aspects reflecting well-being is defined as health-related quality of life (HRQOL). Data suggest that for intensive care patients whose HRQOL was poorer prior to ICU admission, as compared to that of the population, further reduction in HRQOL scores was also observed after their discharge from

the ICU. HRQOL improves 9-12 months after ICU discharge. Poorer HRQOL after intensive care is influenced by factors related and unrelated to illness, health state upon ICU admission and ICU-related factors. Such illness-related factors as sepsis, multiple organ dysfunction and respiratory distress syndromes have been also reported to have negative implications for HRQOL in ICU survivors. ICU-related factors have the strongest effects on long-term ICU patients. Some data also suggest that a long stay in the ICU affects some domains of HRQOL. Physical activity and viability are most commonly impaired domains of HRQOL in patients after cardiac surgery and in other post-operative patients staying in the ICU for longer periods than usual (5-7 days). Knowing the factors affecting HRQOL in patients staying in the ICU longer than usual would enable prognostication of patient health state after discharge from the ICU. In turn, the above-mentioned prognostications would help to reduce or even eliminate the effects of the factors on HRQOL in ICU survivors. In order to identify these factors and assess their implications for HRQOL, we conducted a study of changes in HRQOL for long-term ICU patients.

2. PROPOSITIONS DEFENDED. OBJECTIVE AND AIM OF THE STUDY

Propositions defended

- A long stay in intensive care units reduces HRQOL in ICU survivors.
- HRQOL is influenced not only by health state upon admission to the ICU, but also by the course of intensive care treatment and health state upon discharge from the ICU.
- There is a relationship between HRQOL and post-ICU mortality.

Aim of the study

Measuring of HRQOL and other outcomes in long-term ICU patients 6 months after intensive care; identification of pre-ICU and post-ICU differences in HRQOL; identification of factors influencing the differences.

Objectives of the study

1. To measure HRQOL in long-term ICU patients 6 months after intensive care and to identify changes compared to HRQOL prior to ICU admission.
2. To assess the influence of ICU-related factors, severity of illness and organ/system impairment in long-term ICU patients on changes in their HRQOL.
3. To identify factors with major effects on HRQOL in long-term ICU patients 6 months after intensive care.
4. To identify factors for post-ICU mortality rates and to evaluate the relationship between HRQOL and mortality.

Scientific novelty of the research work

We conducted a research involving a prospective analysis of pre-ICU and post-ICU quality of life in more than 100 patients and determined the effects of critical illness neuromuscular abnormalities on the quality of life. There are no publications or other research/studies of such a scope.

It is the first research in Lithuania investigating the quality of life in ICU survivors after their discharge.

It is the first research in Lithuania investigating neuromuscular abnormalities in ICU patients.

Practical significance of the work and recommendations

Basing on the findings of the research, we ascertain that a prolonged stay in ICU reduces the patients' quality of life. This information is useful for further stages of inpatient and outpatient care of ICU survivors.

Follow-up of outcomes in critical illness survivors should be the focus of intensive care physicians. This would help to collect more patient-related information and find ways to improve post-ICU outcomes. We are of the opinion that shortening of MV duration may reduce impairment of the quality of life in ICU patients. Early weaning from mechanical ventilation would contribute to reduction of impairment in physical domains of patients' quality of life. In cases when severity of illness, number of organ/system dysfunctions and/or complications occurring during the treatment do not allow shortening of sedation, MV and stay in the ICU which turns to be prolonged, critical illness neuromuscular abnormalities should be suspected in each and every patient. Once a neuromuscular abnormality is diagnosed, it is necessary to provide early rehabilitation therapy.

We have proved the relationship between poor quality of life prior to ICU admission and mortality of long-term ICU survivors. Identification of pre-ICU health-related quality of life would contribute to the better identification of patients at the highest risk. Early and simple prediction of post-ICU mortality would be helpful in choosing proper methods for the treatment and rehabilitation of high-risk patients during their stay in the ICU, hospitalisation and after discharge.

Monitoring of health-related quality of life would not only improve outcomes for patients. It would also strengthen relations among ICU staff, patients and their relatives. In addition, this would enhance trust in and prestige of intensive care.

3. MATHERIAL AND METHODS

The study was carried out at the Centre of Anaesthesiology, Intensive Therapy and Pain Treatment of the Clinic of Anaesthesiology and Intensive Care (Vilnius University, Faculty of Medicine) in 2008-2010. The protocol for a clinical trial was approved by the Lithuanian

Committee of Bioethics, Biomedical Research Authorisation No. 26 was granted on 23 April 2008.

3.1. Study population

The research subjects were selected from the patients staying at the First Intensive Care Unit of Vilnius University Hospital *Santariškių Klinikos* (ICU 1).

Patient inclusion criteria:

1. Long-term ICU patients of both genders admitted to the ICU at least once within the same hospital stay.
2. Patients above 18 years of age.
3. Patients having agreed to take part in the research and having signed Participant Information Sheet and Patient Informed Consent Form.

The length of a prolonged stay was identified on the basis of measured average stay in ICU 1 (mean + SD; 5 + 2 days, i.e. 7 days and longer). For patients readmitted to ICU 1 for a period exceeding 7 days, the first admission to ICU 1 was investigated.

Patient exclusion criteria:

1. Patients not meeting at least one criterion for inclusion.
2. Patients speaking no Lithuanian or Russian.
3. Patients with primary mental diseases.

We used retrospective and perspective approaches for data collection. We assessed patients' health-related quality of life prior to ICU admission and 6 months after their discharge from the ICU, clinical data and ICU treatment parameters. The patients were additionally examined for post-ICU neuromuscular abnormalities.

3.2. Retrospectively collected and assessed data

Demographic (age, gender).

Clinical.

Health-related quality of life prior to hospitalisation was measured using SF-36v2 Health Survey. Preadmission information was collected by interviewing patients' closest relatives. HRQOL was measured in the following domains: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH).

Organ dysfunction upon admission to ICU 1 was assessed by the SOFA (Sequential Organ Failure Assessment) score. Impairment in each organ system was assessed separately. The SOFA score higher than 0 point was considered to indicate organ dysfunction.

Severity of illness on ICU admission was assessed according to SAPS 3 and APACHE II.

3.3. Prospectively collected and assessed data

A length of stay at the ICU and length of hospitalisation.

A duration of mechanical ventilation, sedation and analgesia; quantity of sedation and analgesia

The number of therapeutic interventions upon ICU discharge was scored on the last day of stay in the ICU according to the Therapeutic Interventions Scoring System (TISS-28).

Organ dysfunction upon discharge from the ICU was assessed by the SOFA score. Impairment in each organ system was assessed separately.

Neuromuscular abnormality was assessed basing on neurological clinical examinations and electroneuromyographic investigations. We used a standard protocol to conduct the neurological examination. All neurologically examined patients underwent electroneuromyographic examination (ENMG) involving assessment of nerve responses and nerve conductivity as well as examination of muscle activity for any denervation and/or myopathic changes. Polyneuropathy was diagnosed based on the criteria of distal symmetric

polyneuropathy for research. It was associated with critical illness, and critical illness neuromuscular abnormality was diagnosed based on the criteria for the diagnosis of distal symmetric polyneuropathy and myopathy. Diagnosis of CINMA was followed by an additional examination of a cohort with severe neuromuscular abnormalities. This cohort included patients with the signs of denervation (spontaneous activity) recorded during the ENMG examination.

Health-related quality of life 6 months after ICU discharge was measured using the SF-36v2 Health Survey. Data were collected by interviewing the patients by phone or sending them a questionnaire for filling it in. Differences in each HRQOL domain (PFd, RPd, BPd, GHd, VTd, SFd, REd, MHd) before treatment in ICU and 6 months after ICU discharge were calculated.

3.4. Statistical analysis

A statistical data analysis was carried out using statistical analysis software SPSS15. Initial distribution of research data was assessed prior to application of parametric and non-parametric statistical methods. The Kolmogorov-Smirnov test was used (significance level = 0.05).

The same level of significance was applied for the interpretation of our findings; when the P value was between 0.5 and 0.1, the results were considered as indicative of a trend. The Mann-Whitney U test was used for comparison of abnormal distribution of independent samples. Chi-square and Fisher's exact tests were used to compare categorical (nominal) variables. Spearman's correlation coefficient was used to identify possible correlation among demographic, intensive care variables, organ dysfunction and any of the domains of HRQOL. For several correlations of independent variables with statistical significance found in one domain, multiple linear regression was applied to identify the relationship between the variables. The strength of relationship was measured using standardised coefficients of the regression equation and the respective P values. The relationship was deemed to be stronger the larger was the absolute value of the standardised coefficient and the smaller the P value. The Wilcoxon's test was used to compare two

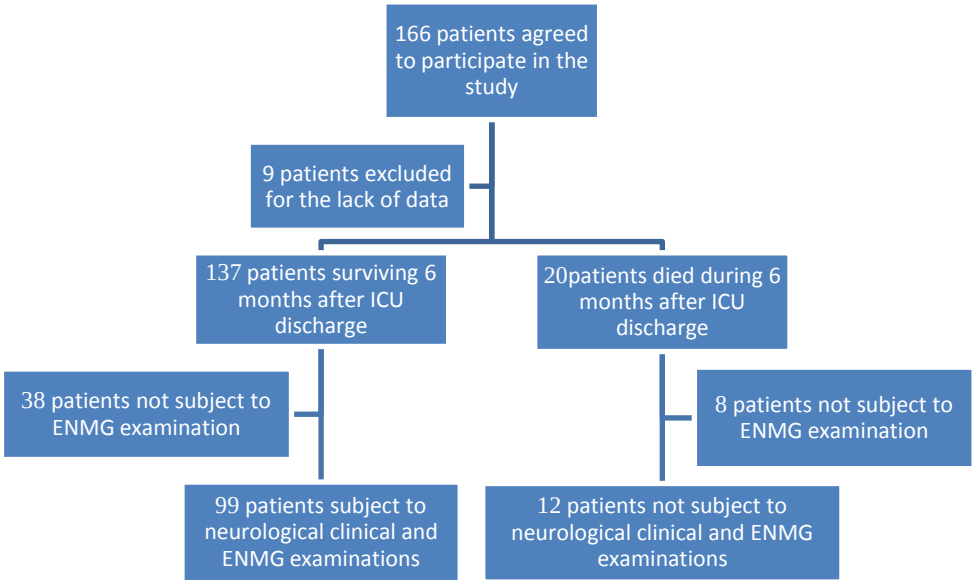
dependent domains of HRQOL. Differences between more than two groups were assessed using the Kruskal-Wallis H test. McNemar's test was used to evaluate the significance of changes. A one-factor disperse analysis was applied to identify the factor that had the strongest effect on changes in different HRQOL domains. The factor with the highest partial eta-squared coefficient was considered the most significant. To analyse prognostic value of variables, Receiver Operating Characteristics (ROC) curves and the area under the curves (AUC) were used for assessing mortality.

4. RESULTS

4.1. General patient characteristics

166 patients agreed to participate in the research. A detail diagram of the patients selected and examined for the research is presented in Chart 4.1.1.

Chart 4.1.1. **Patients selected and examined for the research**



Data of 9 patients (5.42%) were excluded from further analysis due to insufficient knowledge of their HRQOL prior to admission to the ICU. Demographic data, severity of illness upon admission to the ICU, organ dysfunction on the day of ICU admission, length

of stay at the ICU and duration of MV were the same as in the rest 157 patients. 20 patients (12.7%) died within 6 months after ICU discharge.

A total of 137 patients survived the first 6 months after ICU discharge. Characteristics of these patients are presented in Table 4.1.1.

***Table 4.1.1*. Characteristics of patients surviving 6 months after discharge from the intensive care unit**

	Patients surviving 6 months after ICU discharge (n=137)	
Gender (male/female)	80/57 (58.4%/41.6%)	
Age (years)	51.1±16.4 (19-86)°	52 (38-65)°°
APACHE II (points)	16.9±7.1 (4-50)°	16 (12-21)°°
SOFA (points) on the first day in the ICU	6.5±3.4 (1-15)°	6 (4-9)°°
SAPS 3 (points)	56.7±15.1 (19-109)°	53 (48-64)°°
Length of stay in the ICU (days)	16.8±11.6 (7-64)°	13 (9-19)°°
Duration of MV (hours)	206.8±270.7 (0-1242)°	120 (14-247)°°
Length of sedation (hours)	95.6±137.4 (0-864)°	45 (0-138)°°
SOFA (points) on the last day in the ICU	2.9±1.6 (0-11)°	2 (2-4)°°
TISS-28 (points) on the last day in the ICU	21.8±4.5 (13-31)°	21 (18-25)°°

Notes: ° Mean values with standard deviations as well as the lowest and highest values are presented; °° Medians and quartiles are presented; n –number of patients.

Neurological clinical and electroneuromyographic (ENMG) examinations were carried out in 111 patients (70.7%) out of a total of 157 patients with the assessed preadmission HRQOL. Critical illness neuromuscular abnormalities on ICU discharge were diagnosed for 50 patients (45.05%). Neuromuscular abnormalities unrelated to critical illness were diagnosed to 11 patients (9.91%).

4.2. Quality of life prior to admission to the intensive care unit and after the first 6 months

We scored HRQOL points in all domains prior to ICU admission and 6 months following ICU discharge. The scores were then compared and the difference in points in respective domains of pre-HRQOL and post-HRQOL was determined. The findings are displayed in Table 4.2.1.

***Table 4.2.1*. Comparison of survivors' preadmission HRQOL and HRQOL 6 months following ICU discharge**

	Pre-ICU	6 months following the ICU discharge	Difference in HRQOL domains prior to ICU admission and 6 months after ICU discharge	P value
	n=137			
PF°	73.5±25.9	58.8±30.5	14.7±34.4	**<0.001***
RP°	57.8±30.7	44.2±30.3	13.6±37.5	**<0.001***
BP°	38.1±27.5	34.1±26.8	4.0±33.8	0.17
GH°	60.7±13.3	60.3±15.5	0.4±19.2	0.8
VT°	41.8±11.0	44.3±10.3	-2.5±15.3	0.06
SF°	47.52±12.89	48.25±12.19	-0.73±17.53	0.63
RE°	63.66±29.79	59.19±31.20	4.47±41.65	0.21
MH°	48.09±11.11	49.78±10.90	-1.69±15.71	0.21

*Notes: ° Mean values with standard deviations are presented; Wilcoxon's test; * Statistically significant; n – number of patients.*

A statistically significant decrease in PF ($p<0.001$) and RP ($p<0.001$) was identified in our long-term ICU patients 6 months after discharge, as compared to pre-ICU performance.

4.2.1. Influence of demographic and ICU factors on health-related quality of life

We analysed the influence of demographic and ICU factors on HRQOL and the relationship between organ dysfunction during a stay in the ICU/health status upon ICU discharge and changes in HRQOL. We first tried to find out possible gender-related differences. Preadmission HRQOL and HRQOL 6 months after ICU discharge were compared in men and women.

A statistically significant difference in male and female HRQOL was identified only in the domain of mental health. Post-ICU mental health in women was worse than in men, as compared to pre-ICU mental health ($p=0.02$).

In order to assess the influence of patients' age and ICU factors on changes in HRQOL, we looked for any correlations between them and HRQOL differences in individual domains. Spearman's correlation coefficients revealed no correlation among HRQOL, SOFA points on the first and last days of stay in the ICU and APACHE II points. A statistically significant correlation was identified between poorer post-ICU physical

function/role-physical and the SAPS 3 score (r=0.25 *vs*. r=0.19; p=0.003 *vs*. p=0.02, respectively), the length of stay in the ICU (r=0.26 vs. r=0.23; p=0.002 vs. p=0.008, respectively), MV (r=0.40 vs. r=0.35; p<0.001 vs. p<0.001, respectively) and sedation (r=0.23 vs. r=0.19; p=0.006 vs. p=0.025, respectively) and the TISS-28 (r=0.20 vs. r=0.17; p=0.02 vs. p=0.045, respectively) score. A higher decrease in PF and RP was seen in patients with more severe illness according to the SAPS 3 score, a longer duration of MV, sedation and a stay in the ICU, and a bigger number of therapeutic interventions upon discharge from the ICU. No correlation was found between age and impaired PF/RP.

We further investigated which of the following factors – length of stay in the ICU, duration of sedation and MV, SAPS 3 and TISS-28 scores - has the greatest effect on PF impairment. As the length of stay in the ICU, duration of MV and sedation are interrelated, we constructed 3 multiple linear regression equations to find out the key variable. The regression equations also included the SAPS 3 and TISS-28 scores. Table 4.2.1.1 displays the results of the multiple linear regression model with the length of stay in the ICU being one of independent variables.

Table 4.2.1.1. **Multiple linear regression, where the length of stay in the ICU is one of independent variables and PFd is a dependent variable**

	Standardised coefficients (Beta)	**P value**
SAPS 3 (points)	0.18	0.02
Length of stay in the ICU (days)	**0.22***	<0.01
TISS-28 (points) on the last day in the ICU	0.21	0.01

*Notes: PFd – physical functioning difference; * PFd factor that has the strongest effect.*

A determination coefficient (r^2) was used to measure the effects of regression equation variables on PFd. In this equation, the value of R-squared is 0.14. Table 4.2.1.2 displays the results of the multiple linear regression model with duration of MV being one of independent variables.

Table 4.2.1.2. **Multiple linear regression, where duration of MV is one of independent variables and PFd is a dependent variable**

	Standardised coefficients (Beta)	**P value**
SAPS 3 (points)	0.16	0.05
Length of MV (hours)	**0.26***	0.001
TISS-28 (points) on the last day in the ICU	0.21	0.01

*Notes: PFd – physical functioning difference; * PFd factor that has the strongest effect.*

A determination coefficient (r^2) was used to measure the effects of regression equation variables on PFd. In this equation, the value of R-squared is 0.16. Table 4.2.1.3 displays the results of the multiple linear regression model with the length of sedation as one of independent variables.

Table 4.2.1.3. **Multiple linear regression, where the length of sedation is one of independent variables and PFd is a dependent variable**

	Standardised coefficients (Beta)	**P value**
SAPS 3 (points)	0.18	0.03
Length of sedation (hours)	0.18	0.03
TISS-28 (points) on the last day in the ICU	**0.24***	0.004

*Notes: PFd – physical functioning difference; * PFd factor that has the strongest effect.*

A determination coefficient (r^2) was used to measure the effects of regression equation variables on PFd. In this equation, the value of R-squared is 0.13.

Comparison of the values of the determination coefficients in different equations suggested that the determination coefficient had the highest value in multiple linear regression, where the length of MV is one of independent variables and PFd is a dependent variable. Accordingly, despite the identified correlation between the length of stay in the ICU, duration of sedation and MV, and PFd, the duration of MV was established to have had the strongest impact on PF impairment as compared to other aforementioned interdependent factors.

We further investigated which of the factors at issue affect patients' RP. We established a statistically significant correlation between RPd and the SAPS 3 score, length

of stay in the ICU, length of MV and sedation, and the TISS-28 score. Patients with higher SAPS 3 scores, longer MV, stays in the ICU and sedation, and a bigger number of therapeutic interventions upon discharge from the ICU had worse RP impairment. Therefore, RP correlated to the same variables as in case of PF impairment. These domains of HRQOL are interdependent, but not identical. We therefore tested the hypothesis of likeability of other factors to have more influence on RPd. As the length of stay in the ICU, length of MV and sedation are interrelated, we constructed 3 multiple linear regression equations to find out the factor that has the strongest effect on the impairment in RP. The regression equations also included the SAPS 3 and TISS-28 scores. Table 4.2.1.4 displays the results of the multiple linear regression model with the length of stay in the ICU being one of independent variables.

Table 4.2.1.4. **Multiple linear regression, where the length of stay in the ICU is one of independent variables and RPd is a dependent variable**

	Standardised coefficients (Beta)	**P value**
SAPS 3 (points)	0.16	0.05
Length of stay in the ICU (days)	**0.25***	0.003
TISS-28 (points) on the last day in the ICU	0.19	0.02

*Notes: RPd – role-physical difference; * RPd factor that has the strongest effect.*

A determination coefficient (r^2) was used to measure the effects of regression equation variables on RPd. In this equation, the value of R-squared is 0.13. Table 4.2.1.5 displays the results of the multiple linear regression model with duration of MV being one of independent variables.

Table 4.2.1.5. **Multiple linear regression, where the length of MV is one of independent variables and RPd is a dependent variable**

	Standardised coefficients (Beta)	**P value**
SAPS 3 (points)	0.14	0.09
Length of MV (hours)	**0.28***	0.001
TISS-28 (points) on the last day in the ICU	0.18	0.02

*Notes: RPd – role-physical difference; * RPd factor that has the strongest effect.*

A determination coefficient (r^2) was used to measure the effects of regression equation variables on RPd. In this equation, the value of R-squared is 0.15. Table 4.2.1.6 displays the results of the multiple linear regression model with the length of sedation as one of independent variables.

Table 4.2.1.6. **Multiple linear regression, where the length of sedation is one of independent variables and RPd is a dependent variable**

	Standardised coefficients (Beta)	**P value**
SAPS 3 (points)	0.16	0.06
Length of sedation (hours)	0.19	0.02
TISS-28 (points) on the last day in the ICU	**0.21***	0.01

*Notes: RPd – role-physical difference; * RPd factor that has the strongest effect.*

A determination coefficient (r^2) was used to measure the effects of regression equation variables on RPd. In this equation, the value of R-squared is 0.11.

Comparison of the values of the determination coefficients in different equations suggested that the determination coefficient had the highest value in multiple linear regression, where the length of MV is one of independent variables and RPd is a dependent variable. Accordingly, despite the identified correlation between several ICU factors (SAPS 3 score, length of stay in the ICU, length of sedation and MV, TISS-28 score on the last day in the ICU) and RPd, the length of MV was established to have had the strongest impact on role limitation due to physical problems (role-physical).

We further explored durations of MV and severity of illness according to SAPS 3 and TISS-28 scores with the greatest impact on PFd and RPd. For this purpose we tried to identify numeric values of the factors impairing HRQOL. As the length of MV is the factor that has the strongest effect on PF reduction and worsening RP, we first tried to identify the length of MV with the strongest effect on PF and RP. The patients were divided into cohorts by the length of MV: 100 hours, 120 hours (median), 200 hours, 206 hours (mean), 300 hours, 400 hours, 500 hours and 600 hours and then the cohorts with longer and shorter duration of MV were compared. The greatest differences were found in the comparison of

groups with a duration of MV being 120 hours (median) or shorter and exceeding 120 hours and groups with a duration of MV being 206 hours (mean) or shorter and exceeding 206 hours. Comparison of the groups divided by MV median, PFd and RPd is presented in Table 4.2.1.7.

Table 4.2.1.7. **Effects of MV exceeding 120 hours on PFd and RPd**

	Duration of MV ≤ median (n=69)	**Duration of MV > median (n=68)**	**P value**
PFd°	3.1±30.0	26.4±34.7	**<0.001***
RPd°	1.4±34.4	26.1±36.5	**<0.001***

*Notes: Mann-Whitney U test; Mean values with standard deviations are presented; * Statistically significant.*

In the cohort with a longer duration of MV (more than 120 hours) impairment of physical functioning in patients was even by 23 points higher compared to the cohort with a shorter duration of MV ($p<0.001$). A difference in RP impairment was 25 points on average ($p<0.001$) – more difficulties were mentioned by patients in the cohort with a longer duration of MV.

Comparison of the groups divided by the mean duration of MV, PFd and RPd is presented in Table 4.2.1.8.

Table 4.2.1.8. **Effects of MV exceeding 206 hours on PFd and RPd**

	Duration of MV ≤ mean (n=91)	**Duration of MV > mean (n=46)**	**P value**
PFd°	6.76±32,12	30.33±33.62	**<0.001***
RPd °	3.91±35,08	32.88±34.77	**<0.001***

*Notes: Mann-Whitney U test; Mean values with standard deviations are presented; * Statistically significant.*

In the cohort with a longer duration of MV (more than 206 hours) impairment of physical functioning in patients was also by 23 points on average higher compared to the cohort with a shorter duration of MV ($p<0.001$), while a difference in RP impairment was even higher - 29 points on average ($p<0.001$) .

This suggests that both MV exceeding the mean duration (206 hours) and MV exceeding the median (120 hours) similarly contribute to impairment in PF and RP.

Severity of illness according to the SAPS 3 score correlated to impaired PF and RP. We therefore continued with testing the effects of illness severity according to the SAPS 3 score on PFd and RPd. The patients were assigned to cohorts by the number of SAPS 3 points: 40; 45; 50; 53 (median); 55; 56.7; (mean), 60, 65, 70, 75, 80. The cohorts were then compared by higher and lower SAPS 3 points. The greatest difference was found in cohorts with SAPS 3 ≤ 56.7 points (mean) and > 56.7 points. Data of the group comparison are displayed in Table 4.2.1.9.

***Table 4.2.1.9*. Effects of the severity of illness on PFd and RPd**

	SAPS 3 ≤ mean (n=81)	**SAPS 3 > mean (n=56)**	**P value**
PFd°	7.7±33.9	24.7±32.7	**0.005***
RPd°	7.6±39.0	22.3±33.5	**0.024***

*Notes: Mann-Whitney U test; Mean values with standard deviations are presented; * Statistically significant; n – number of patients.*

It was found out that patients with illness severity upon admission to the ICU exceeding 56.7 points according to the SAPS 3 score had statistically significantly lower PF and more impaired RP after 6 months, as compared to patients with less severe illness upon ICU admission.

4.2.2. Effects of organ dysfunction on health-related quality of life

We measured an overall organ failure in points according to the SOFA score. Assessment of data on the first and last days revealed no correlation with worsening of HRQOL.

We further investigated a relationship between individual organ/system dysfunction, as measured in SOFA points, and changes in HRQOL. Spearman's correlation coefficients were determined. Analysis of the influence of organ dysfunction on the first day in the ICU on individual domains of HRQOL revealed a positive correlation between CNS dysfunction and RPd (r=0.23; p=0.006). We compared RPd in patients with diagnosed CNS dysfunction

upon admission to the ICU and those without diagnosed CNS dysfunction. The findings are presented in Table 4.2.2.1.

***Table 4.2.2.1*. Impact of central nervous system dysfunction upon ICU admission on RPd**

	No CNS dysfunction on the first day in the ICU (n=117)	CNS dysfunction present on the first day in the ICU (n=20)	P value
RPd °	10.3±36.9	33.1±35.3	**0.007***

*Notes: °Mean values with standard deviations are presented; Mann-Whitney U test; *Statistically significant; n – number of patients.*

We established that CNS dysfunction on the first day in the ICU statistically significantly worsened HRQOL in the RP domain.

We further tested a hypothesis of the presence of an organ or system which dysfunction upon ICU discharge affects the quality of life, particularly in respect of decreased physical functioning and role-physical We tried to identify an organ system which dysfunction had fundamental effects on the quality of life. As respiratory system dysfunction was still present and CNS dysfunction was absent nearly in all patients upon discharge from the ICU, we were not able to measure the impact of these organ dysfunctions on the quality of life.

We analysed effects of circulatory, hepatic and coagulation system dysfunction on PF and RP. Only coagulation system dysfunction upon ICU discharge had a negative impact on one of the above-mentioned HRQOL domains. Such patients showed poorer physical functioning (p=0.024) as compared to the patients without this system dysfunction.

4.2.3. Effects of neuromuscular abnormalities on health-related quality of life

Neuromuscular abnormalities upon ICU discharge were examined in 111 patients out of a total of 157. 99 patients survived the first 6 months. We compared their pre-admission HRQOL and HRQOL 6 months after ICU discharge. The findings are displayed in Table 4.2.3.1.

***Table 4.2.3.1*. Pre-admission HRQOL and HRQOL 6 months after ICU discharge in patients examined for neuromuscular abnormalities**

	Pre-admission HRQOL	HRQOL 6 months after ICU discharge	Difference in quality of life, points	P value
	n=99			
PF°	77.5±23.4	55.5±30.5	21.0±32.1	**<0.001***
RP°	61.0±29.3	42.7±30.0	18.3±36.3	**<0.001***
BP°	37.4±27.2	36.5±27.7	0.9±35.0	0.72
GH°	60.1±13.7	61.9±15.5	-1.8±19.7	0.43
VT°	41.4±11.0	45.2±9.6	-3.7±13.6	**0.008***
SF°	48.2±12.3	48.2±12.2	0.0±17.9	0.91
RE°	64.3±29.4	56.7±30.3	7.6±41.0	0.08
MH°	47.3±10.7	49.6±11.4	-2.2±16.0	0.15

*Notes: °Mean values with standard deviations are presented; Mann-Whitney U test *Statistically significant; n – number of patients.*

A statistically significant worsening in HRQOL was established in the same domains (PF and RP) as for the whole group of our patients (137 patients surviving the first 6 months).

We divided the patients into three cohorts: 1) patients with critical illness neuromuscular abnormalities; 2) patients with neuromuscular abnormalities unrelated to critical illness; 3) patients without neuromuscular abnormalities. Analysis of HRQOL changes among the groups revealed no differences in any domain but MH (p=0.07; indicative of a trend).

There were no statistically significant changes identified in PF and RP between patients with CINMA and those without CINMA. As we failed to identify worsening of the quality of life, physical functioning in particular, in all patients with neuromuscular abnormalities, we examined the cohort with severe neuromuscular abnormalities for further analysis. We compared changes in HRQOL between patients with severe CINMA and those without CINMA. The findings are presented in Table 4.2.3.2.

Table 4.2.3.2. **Comparison of differences in health-related quality of life between patients with severe CINMA and without CINMA**

	No neuromuscular abnormality (n=47)	Severe critical illness neuromuscular abnormality (n = 18)	P value
PFd°	18.2±30.9	40.0±24.6	**0.007***
RPd°	12.5±41.0	37.1±24.6	**0.019***
BPd°	2.5±37.1	0.6±31.1	0.96
GHd°	-1.4±20.0	-5.9±20.1	0.18
VTd°	-3.1±12.2	-2.2±14.1	0.87
SFd°	0.5±15.4	-3.7±20.1	0.26
REd	5.1±45.0	11.3±35.6	0.40
MHd°	2.2±15.7	-4.4±12.5	0.25

*Notes: °Mean values with standard deviations are presented; Mann-Whitney U test *Statistically significant; n – number of patients.*

Patients with severe neuromuscular abnormalities acquired during their stay in the ICU demonstrated reduced PF ($p = 0.007$) and RP ($p = 0.019$), as compared to the patients without diagnosed CINMA.

4.2.4. Relationship between the number of intervention upon ICU discharge and health-related quality of life

We compared changes in the quality of life prior to ICU admission and 6 months after ICU discharge between patients who were physiologically stable upon ICU discharge, i.e. requiring prophylactic follow-up only (TISS-28 score < 20) and patients requiring more intensive treatment and nursing (TISS-28 score ≥ 20). We failed to identify any differences in PF and RP between these two cohorts.

In order to find out the number of therapeutic interventions with the strongest impact on differences in HRQOL, we divided the patients to three cohorts by TISS-28 scores: 17; 18; 19; 20; 21 (median); 21.8 (mean); 22; 23; 24; 25; 26; 27; 28 and compared the cohorts with lower and higher TISS-28 scores upon discharge from the ICU. We found out that 26 points upon ICU discharge represent the TISS-28 score differentiating the groups with the greatest differences in PF, RP and RE. The findings are shown in Table 4.2.4.1.

***Table 4.2.4.1*. Data of patients representing the greatest differences in HRQOL domains**

	TISS-28 score <26 (n=105)	TISS-28 score ≥26 (n=32)	P value
PFd°	9.7±32.9	30.9±34.6	**0.004***
RPd°	8.5±36.7	30.5±35.2	**0.005***
BPd°	5.0±33.7	0.6±34.6	0.57
GHd°	0.1±19.0	1.4±20.0	0.79
VTd°	-2.1±14.5	-3.7±17.7	0.77
SFd°	-0.5±16.3	-1.6±21.2	0.60
REd°	0.6±40.0	17.2±44.9	**0.035***
MHd°	-2.4±15.9	0.6±15.0	0.115

*Notes: °Mean values with standard deviations are presented; Mann-Whitney U test *Statistically significant; n – number of patients.*

We found out a 20-point decrease on average in PF, a 22-point decrease on average in RP and a 17-point decrease in RE for patients with the number of therapeutic interventions on the last day in the ICU being above or equal to 26 points according to TISS-28.

We further looked for differences in demographic and ICU factors between the above-mentioned cohorts. Patients with the TISS-28 score ≥26 were found to have had a longer duration of MV, but other factors didn't show any differences.

4.3. Factors with the strongest effects on changes in health-related quality of life

Analysis of effects of demographic and ICU-related factors, severity of illness and organ/system dysfunction in long-term ICU patients on changes in HRQOL demonstrated that a decrease in PF correlates to illness severity upon ICU admission, as determined according to the SAPS 3 score, duration of MV, number of therapeutic interventions on the last day in the ICU, as determined according to the TISS-28 score, and severe CINMA and circulatory system dysfunction upon ICU discharge; a decrease in RP correlates to illness severity upon ICU admission, as determined according to the SAPS 3 score, duration of MV, number of therapeutic interventions on the last day in the ICU, as determined

according to the TISS-28 score, and severe CINMA and CNS dysfunction on the first day in the ICU.

The research aimed at identifying the factors that have the greatest impact on changes in different HRQOL domains. For this purpose, we conducted a one-factor disperse analysis with PFd or RPd as dependent variables Factors with effects on PFd and RPd proved during the research were chosen as independent variables. The results of the one-factor disperse analysis are presented in Tables 4.3.1 and 4.3.2.

Table 4.3.1. **Factors affecting a decrease in PF**

Factors affecting a decrease in PF	P value	**Partial eta-squared coefficient**
SAPS 3 score > 56.73	0.004*	0.06°
Duration of MV > 206 hours	<0.001*	0.106°
Duration of MV > 120 hours	**<0.001***	**0.116°**
TISS-28 score ≥ 26	0.002*	0.069°
Severe CINMA	0.005*	0.078°
Circulatory system dysfunction upon ICU discharge	0.037*	0.032°

*Notes: ° - determined in respect of each factor individually; * - statistically significant*

Table 4.3.2. **Factors affecting a decrease in RP**

Factors affecting a decrease in RP	P value	**Partial eta-squared coefficient**
SAPS 3 score > 56.73	0.024*	0.037°
Duration of MV > 206 hours	<0.001*	0.134°
Duration of MV > 120 hours	**<0.001***	**0.135°**
TISS-28 score ≥ 26	0.003*	0.062°
Severe CINMA	0.014*	0.06°
CNS system dysfunction on the first day in the ICU	0.011*	0.047°

*Notes: ° - determined in respect of each factor individually; * - statistically significant*

The one-factor disperse analysis suggested that a duration of MV exceeding 120 hours had the biggest partial eta-squared coefficient (0.116) in factors affecting a decrease in PF. Likewise, the duration of MV exceeding 120 hours had the biggest partial eta-squared coefficient (0.135) in factors affecting a decrease in RP. Accordingly, the duration of MV exceeding 120 hours is the factor with the strongest effect on a decrease in PF and RP. Severe CINMA is the second factor by effects on PF decrease. The number of therapeutic interventions upon discharge from the ICU, when the TISS-28 score is above or equal to 26 points, is the second factor by effects on RP decrease.

4.4. Effects of pre-ICU health-related quality of life on patient mortality after ICU discharge

In order to find out the relationship between pre-ICU HRQOL and post-ICU mortality of long-term ICU patients, we compared HRQOL in patients surviving the first 6 months after ICU discharge and in those who died during 6 months after discharge from the ICU. The findings are displayed in Table 4.4.1.

Table 4.4.1. **Comparison of pre-ICU HRQOL in patients who survived and those who died during the first 6 months after ICU discharge**

	Pre-ICU HRQOL of ICU surviving patients (n=137)	**Pre-ICU HRQOL of non-surviving patients (n=20)**	**P value**
PF°	73.5±25.9	50.2±35.2	**0.004***
RP°	57.8±30.7	42.5±33.6	**0.037***
BP°	38.1±27.5	44.0±28.4	0.35
GH°	60.7±13.3	64.7±11.2	0.29
VT°	41.8±11.0	44.7±8.2	0.18
SF°	47.5±12.9	43.7±16.5	0.60
RE°	63.7±29.8	53.7±31.7	0.15
MH°	48.1±11.1	45.5±10.1	0.16

*Notes: ° Mean values with standard deviations are presented; * Statistically significant; n – number of patients.*

In non-surviving patients, pre-ICU HRQOL was statistically significantly worse in PF and RP domains (p=0.004 and p=0.037, respectively). We compared demographic and

ICU factors in non-surviving and surviving patients. The findings are presented in Table 4.4.2.

***Table 4.4.2*. Comparison of demographic and ICU factors in patients who died after discharge from the ICU and those who survived the first 6 months after ICU discharge**

	Surviving patients (n=137)	**Non-surviving patients (n=20)**	**P value**
Gender, male/female°	8/12	80/57	0.15
Age (years) °°	51.1±16.4	57.2±17.3	0.1
APACHE II (points) °°	16.9±7.1	17.7±4.8	0.29
SAPS 3 (points) °°	56.7±15.1	64.3±17.2	0.063
SOFA (points) on the first day in the ICU °°	6.6±3.4	6.6±3.4	0.89
Length of stay in the ICU (days) °°	16.8±11.6	24.1±22.6	0.31
Duration of MV (hours) °°	206.8±270.7	384.9±521.8	0.08
Length of sedation (hours) °°	95.6±137.4	120.2±175.8	0.39
SOFA (points) on the last day in the ICU°°	2.9±1.6	3.3±2.0	0.78
TISS-28 (points) on the last day in the ICU°°	21.8±4.5	25.3±5.1	**0.007***

*Notes: Mean values with standard deviations are presented; °Fisher's exact test; °° Mann-Whitney U test; * - Statistically significant; n - number of patients.*

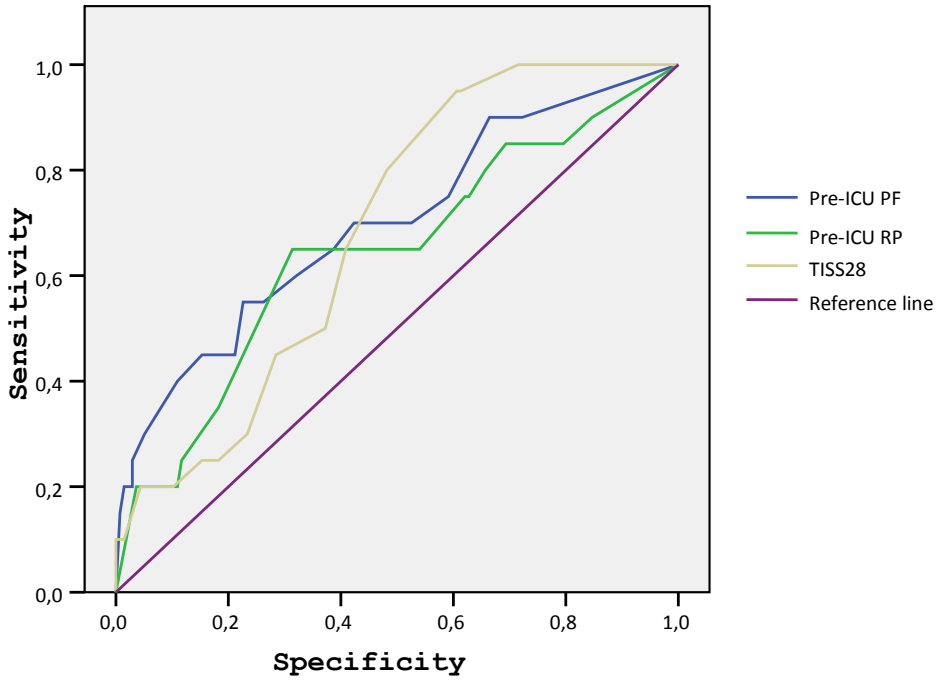
There were no statistically significant differences in the age, severity of illness according to APACHE II, organ dysfunction on the first and last days in the ICU and the length of stay in the ICU in patients who died after discharge from the ICU. The non-surviving patients demonstrated severity of illness according to SAPS 3 by more than 7 points higher, while duration of MV was by 7 days longer. Yet, these differences had no statistical significance (p=0.063 and p=0.084; indicative of a trend). A statistically significant difference was found only in the number of therapeutic interventions measured by the TISS-28 score; in post-ICU non-surviving patients this number was by more than 3 points higher (p=0.007).

Analysis of the above data suggests that neither the SAPS 3 score nor the APACHE II score upon admission to the ICU can serve for predicting post-ICU mortality in patients. Only lower physical functioning and higher levels of role limitations due to

physical problems (role-physical) prior to ICU admission and the TISS-28 score on the last day in the ICU might be useful factors for predicting post-ICU mortality.

In order to identify the factor (pre-ICU PF, pre-ICU RP or TISS-28 score upon ICU discharge) bearing the maximum prognostic value, we constructed ROC curves (chart 4.4.1) in which mortality is the variable of the status.

***Chart 4.4.1*. Determination of a factor with the maximum prognostic value for mortality after ICU discharge**



Calculations of the area under the curve (AUC) are presented in Table 4.4.3.

***Table 4.4.3*. Area under the curves, where post-ICU mortality is the variable of the status**

Factor	Area under the curve (AUC)	P value
Pre-ICU PF	0.70	0.004
Pre-ICU RP	0.64	0.038
TISS-28 score on the last day in the ICU	0.68	0.008

All three factors appear to be useful for predicting post-ICU mortality ($p < 0.05$). The most significant factor for predicting mortality is pre-ICU PF with the maximum AUC (0.7).

5. CONCLUSIONS

1. Prolonged treatment in the intensive carte unit has negative implications for patients' health-related quality of life. Physical functioning and role-physical 6 months after ICU discharge remain worse than prior to ICU admission.
2. A decrease in physical functioning and role physical in long-term ICU patients 6 months after their discharge from the ICU is associated with:
    - Severity of illness above 53 points according to the SAPS 3 score;
    - Duration of mechanical ventilation longer than 120 hours;
    - Number of therapeutic intervention on the last day of intensive care above 25 points by the TISS-28 score;
    - Severe critical illness neuromuscular abnormalities.
3. Mechanical ventilation with duration over 120 hours has the strongest effect on reduced physical functioning and role-physical in long-term intensive care patients 6 month after ICU discharge. The following factors by significance include critical illness neuromuscular abnormalities and the number of therapeutic interventions upon discharge from the intensive care unit.
4. Long-term ICU patients who died after discharge from the ICU had worse physical functioning and role physical prior to ICU admission as compared to patients surviving the first 6 months after ICU discharge.

6. LIST OF PUBLICATIONS AND PRESENTATIONS

Publications:

- Klimašauskas A., Ivaškevičius J. Quality of life in evaluation of long term ICU outcomes. Theory and Practice in Medicine, 2010; 16(2): 139-146
- Klimašauskas A., Sereikė I., Klimašauskienė A., Ivaškevičius J. Influence of neuromuscular disorder to the quality of life in case of long term ICU treatment. Seminars in neurology, 2011; 15(47): 31-37
- Klimašauskas A., Sereikė I., Klimašauskienė A., Kėkštas G., Ivaškevičius J. The impact of medical conditions upon discharge on the intensive care unit survivors' quality of life. Medicina (Kaunas); 2011; 47(5): 270-277.

Poster presentations:

- Klimašauskas A., Kėkštas G. Simple prediction of mortality in case of readmission to the intensive care unit. Abstract of 27th International symposium on Intensive Care and Emergency Medicine. Brussels, Belgium, March 27-30, 2007. Critical Care, 2007, 11 Suppl. 2: P469.
- Klimašauskas A., Sereikė I., Kėkštas G., Klimašauskienė A., Ivaškevičius J. Determinants of critical illness polyneuropathy in case of long term ICU treatment. Abstract of 29th International symposium on Intensive Care and Emergency Medicine. Brussels, Belgium, March 24-27, 2009. Critical Care, 2009, 13 Suppl. 1: P109.
- Sereikė I., Klimašauskienė A., Klimašauskas A. Clinical and electrophysiological signs of critical illness neuropathy. Abstract of 6th Baltic congress of neurology (Balcone). Vilnius, Lithuania, May 13-16, 2009. Seminars in Neurology, 2009, T.13, Suppl. 1: S63
- Sereikė I., Klimašauskienė A., Klimašauskas A. Peripheral nerve damage after treatment in intensive care unit. Abstract of 6th Baltic congress of neurology

(Balcone). Vilnius, Lithuania, May 13-16, 2009. Seminars in Neurology, 2009, T.13, Suppl. 1: S63

- Sereikė I, Budrys V, Klimašauskienė A, Klimašauskas A. Peripheral nerve damage after long-term treatment in intensive care. 14th congress of the European Federation of Neurological Societies. Geneva, Switzerland, September 25-28. European Journal of Neurology, 2010, 17, Suppl. 3: P1560.

Oral presentations:

- Quality of life – part of long term assessment of ICU patients. 4th International Baltic congress of anaesthesiology and intensive care (2008 12 11-13, Riga, Latvia).
- Quality of life after long term ICU treatment. 5th International Baltic congress of anaesthesiology and intensive care (2010 10 21-23 Tartu, Estonia).
- Denervation of intercostal muscles after critical illness. Conference of Lithuanian society of anesthesiology and intensive care. (2011 05 27 Klaipėda, Lithuania).

7. CURRICULUM VITAE

Andrius Klimašauskas was born in Vilnius, Lithuania, on April 11, 1967.
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Education

1985 graduated from Vilnius Secondary School No. 7

1985-1991 Vilnius University, Faculty of Medicine

1991-1994 Resident in anaesthesiology and intensive care at the Vilnius University, Faculty of Medicine

2007-2011 Doctoral (Ph. D.) studies at the Vilnius University, Faculty of Medicine.

Professional Experience:

1992 – 1997 –Vilnius University Hospital "Raudonasis Kryžius". Department of Anaesthesiology. Anaesthesiologist.

1993 – till present - Vilnius University Hospital "Santariskių Klinikos", Centre of Anaesthesiology, Intensive Therapy and Pain Treatment. First Intensive Care Unit. Intensive care doctor.

2009 – till present. Vilnius University, Faculty of Medicine, Clinic of Anaesthesiology and Intensive Care. Assistant.

Membership:

- Lithuanian Society of Anaesthesiology and Intensive Care (member)
- Lithuanian Society of Parenteral and Enteral Nutrition (board member).

Research interests:

Quality of life after treatment in the intensive care unit; readmission to the intensive care unit; clinical nutrition

8. REZIUMĖ

Įvadas

Ilgą laiką ligonių mirštamumas intensyviosios terapijos skyriuose (ITS) buvo vieninteliu kriterijumi vertinant gydymo juose efektyvumą. Pagerėjus sunkiai sergančių ligonių išgyvenamumui susidomėta tolesniu buvusio ITS ligonio likimu ir gyvenimu po gydymo ITS. Neretam išgyvenusiam po gydymo ITS pacientui lieka pasekmių, todėl

dažniausiai jo visiškai pasveikusiu pavadinti negalima. Padarinius po gydymo ITS sukelia pati liga, organų pažeidimas, išsivystęs iki gulėjimo ITS ar jau gydymo jame metu, ilgai trunkantis organų veiklą palaikantis ITS gydymas. Vertinant tokių ligonių sveikatos ir gyvenimo kokybės visumą, nepakanka tik objektyvios informacijos apie paciento darbingumą ir mobilumą surinkimo bei klinikinio ar laboratorinio organų funkcijos ištyrimo. Likęs po gydymo ITS pažeidimas ar net neįgalumas gali ir neturėti įtakos buvusio ITS ligonio savijautai bei pasitenkinimui gyvenimu. Subjektyvus paties ligonio fizinės bei emocinės būklės suvokimas tampa vis svarbesniu faktoriumi vertinant išeitis po gydymo ITS. Ligonio sveikatos būklės derinys su nemedicininiais gyvenimo gerovę atspindinčiais aspektais apibrėžiamas su sveikata susijusios gyvenimo kokybės (SSSGK) terminu. Yra duomenų, kad ligonių, kurie buvo gydyti ITS, SSSGK jau iki gydymo ITS buvo blogesnė nei populiacijos, taip pat pastebėtas ir tolesnis jos pablogėjimas po gydymo ITS. Įtakos prastesnei SSSGK po gydymo ITS turi nuo ligos nepriklausantys bei su liga susiję veiksniai, būklė gydymo ITS pradžioje, su gydymu ITS susiję faktoriai. Atliktuose tyrimuose nustatyta, kad ligonio būklės sunkumas ir organų sistemų pažeidimas turi įtakos SSSGK po gydymo ITS. Su gydymu ITS susiję veiksniai ypač veikia ilgai jame gydomus pacientus. Yra duomenų, kad ilga gydymo ITS trukmė susijusi su pokyčiais kai kuriose SSSGK srityse. Veiksnių, kurie turi įtakos ilgiau nei įprastai ITS gydytų ligonių SSSGK, žinojimas leistų prognozuoti tokių ligonių savijautą po iškėlimo iš ITS. Prognozuodami galėtume sumažinti arba galbūt net pašalinti šių veiksnių įtaką ITS ligonių SSSGK. Siekdami nustatyti šiuos veiksnius ir įvertinti jų įtaką SSSGK, atlikome ilgai ITS gydytų ligonių SSSGK pokyčių tyrimą.

Darbo tikslas

Įvertinti ilgai ITS gydytų ligonių SSSGK ir kitas išeitis praėjus šešiems mėnesiams po gydymo ITS, nustatyti SSSGK iki ir po gydymo ITS skirtumus bei veiksnius, kurie turi įtakos šiems skirtumams.

Darbo uždaviniai

1. Įvertinti ilgai ITS gydytų ligonių SSSGK praėjus šešiems mėnesiams po gydymo
   ITS ir nustatyti jos pokyčius lyginant su buvusia iki gydymo.
2. Įvertinti ilgai ITS gydytų ligonių su gydymu ITS susijusių veiksnių, būklės sunkumo ir organų bei jų sistemų pažeidimo įtaką SSSGK pokyčiams.
3. Nustatyti veiksnius, kurie turi didžiausią įtaką ilgai ITS gydytų ligonių SSSGK po
   šešių mėnesių.
4. Nustatyti veiksnius, kurie turi įtaką ilgai ITS gydytų ligonių mirštamumui po iškėlimo iš ITS bei įvertinti SSSGK ir mirštamumo ryšį.

Tyrimo metodika

Tyrimas atliktas Vilniaus universiteto Medicinos fakulteto Anesteziologijos ir reanimatologijos klinikos Anesteziologijos, intensyviosios terapijos ir skausmo gydymo centre 2008-2010 metais. Į tyrimą įtraukti ligoniai ilgai (7 ir daugiau parų) gydyti ITS.

Duomenis rinkti retrospektyviai ir perspektyviai. Įvertinti pacientų SSSGK iki gydymo ITS ir praėjus šešiems mėnesiams po gydymo, klinikiniai duomenys ir gydymo ITS parametrai. Pacientai papildomai tirti ieškant neuroraumeninio pažeidimo po gydymo ITS.

SSSGK prieš guldymą į ligoninę vertinta pagal SF-36 sistemą. Duomenys surinkti apklausiant artimiausius ligonio gimines. Nustatyta SSSGK šiose srityse: fizinio aktyvumo (FA), veiklos apribojimo dėl fizinės būklės (VADFB), skausmo, bendro

sveikatos vertinimo, energingumo ir gyvybingumo, socialinių ryšių, veiklos apribojimo dėl emocinės būklės, emocinės būklės (EB).

Organų sistemų pažeidimas nustatytas pagal SOFA sistemą ligonio guldymo į ITS ir iškėlimo iš ITS metu. Įvertintas kiekvienos organų sistemos pažeidimas atskirai.

Būklės sunkumas guldymo į ITS metu nustatytas pagal SAPS 3 ir APACHE II sistemas.

Įvertinta gulėjimo ITS ir ligoninėje trukmė, DPV, sedacijos ir analgezijos trukmė.

Terapinių intervencijų skaičius apskaičiuotas paskutinę gydymo ITS parą ligonio iškėlimo iš ITS metu. Naudota TISS-28 sistema.

Neuroraumeninis pažeidimas vertintas atlikus klinikinį neurologinį tyrimą ir elektroneuromiografinį (ENMG) tyrimą. Diagnozavę kritinių būklių neuroraumeninį pažeidimą (KBNRP), papildomai išskyrėme ligonių su sunkiu KBNRP grupę.

SSSGK ištirta praėjus šešiems mėnesiams po išvykimo iš ITS. Duomenys rinkti telefonu apklausiant tiriamąjį arba nusiuntus jam užpildyti anketą. Nustatyti SSSGK skirtumai iki ir po gydymo ITS kiekvienoje srityje (FAs; VADFBs ir t. t.).

Statistinė duomenų analizė atlikta panaudojant kompiuterinę statistinės analizės programą SPSS 15. Spearman‘o koreliacijos koeficientas naudotas vertinant koreliaciją tarp demografinių, intensyviosios terapijos rodiklių, organų sistemų pažeidimo bei atskirų SSSGK sričių. Vienoje srityje aptikus kelias statistiškai reikšmingas nepriklausomų rodiklių koreliacijas, taikyta daugialypė tiesinė regresija ryšiams tarp kintamųjų nustatyti. Priklausomybės stiprumas matuotas naudojant standartizuotus regresijos lygties koeficientus ir atitinkamas p reikšmes. Vienfaktorinė dispersinė analizė taikyta faktoriaus, turinčio didžiausią įtaką atskirų SSSGK sričių pokyčiams, nustatymui. Faktorius, kurio dalinis Eta-kvadrato koeficientas buvo didžiausias, laikytas reikšmingiausiu. Analizuojant prognostinę rodiklių vertę mirštamumo vertinimui naudotos ROC kreivės ir skaičiuoti plotai po jomis.

Rezultatai

Tyrime sutiko dalyvauti 166 ligoniai. Devynių (5,42%) ligonių duomenys neanalizuoti dėl trūkstamų SSSGK iki gydymo ITS duomenų. 20 (12,7%) ligonių mirė per šešis mėnesius nuo iškėlimo iš ITS.137 ligoniai išgyveno šešis mėnesius po iškėlimo iš ITS. Vidutinis išgyvenusių ligonių amžius buvo 51,1±16,4 metai; pirmos ITS dienos SOFA sistemos balų skaičius - 6,5±3,4; SAPS 3 sistemos balų skaičius - 56,7±15,1; gulėjimo ITS trukmė - 16,8±11,6; dirbtinės plaučių ventiliacijos (DPV) trukmė - 206,8±270,7 valandos; sedacijos trukmė - 95,6±137,4 valandos; paskutinės ITS dienos SOFA sistemos balų skaičius - 2,9±1,6; paskutinės ITS dienos TISS-28 sistemos balų skaičius - 21,8±4,5. KBNRP iškėlimo iš ITS metu diagnozuotas 45% pacientų.

Įvertinome ilgai ITS gydytų ligonių SSSGK pokyčius praėjus šešiems mėnesiams po gydymo ITS lyginant su buvusia iki patekimo į ITS. Nustatėme statistiškai patikimą FA sumažėjimą ($p<0,001$) ir VADFB padidėjimą ($p<0,001$) lyginant su buvusiais iki patekimo į ITS.

Koreliacijos tarp pirmos ir paskutinės ITS parų SOFA ,APACHE II balų skaičiaus ir SSSGK nenustatėme. FA sumažėjimas ir VADFB padidėjimas po gydymo ITS statistiškai patikimai siejosi (teigiama koreliacija) su SAPS 3 balų skaičiumi, gulėjimo ITS, DPV ir sedacijos trukmėmis ir TISS-28 balų skaičiumi. Nors suradome ryšį tarp gulėjimo ITS, sedacijos bei DPV trukmių ir FAs bei VADFBs, nustatėme, kad DPV trukmė labiausiai iš šių tarpusavyje priklausančių veiksnių turi įtakos FA blogėjimui ir VADFB didėjimui.

Nustėme skaitines veiksnių, bloginančių SSSGK, reikšmes. Pacientus suskirstėme į grupes pagal DPV trukmę. Didžiausius skirtumus nustatėme lygindami grupes, kurių DPV trukmė trumpesnė arba lygi 120 valandų (mediana) ir ilgesnė nei 120 valandų, bei grupes, kurių DPV trumpesnė arba lygi 206 valandoms (vidurkis) ir ilgesnė nei 206 valandos.

Ilgesnės DPV trukmės grupėse (daugiau kaip 120 ir daugiau kaip 206 valandos) ligonių FA pablogėjimas buvo didesnis lyginant su trumpesnės DPV trukmės grupėmis ($p<0,001$ ir $p<0,001$). VADFB padidėjimas taip pat statistiškai patikimai skyrėsi ($p<0,001$ ir $p<0,001$)).

Nustatėme būklės sunkumo pagal SAPS 3 sistemą įtaką FAs ir VADFBs. Sunkesnės nei 56,7 balo (vidurkis) pagal SAPS 3 sistemą būklės guldymo į ITS metu ligonių FA po šešių mėnesių buvo statistiškai patikimai mažesnis ($p=0,005$), o VADFB statistiškai patikimai didesnis ($p=0,024$), lyginant su ligoniais, kurių būklė guldymo į ITS buvo lengvesnė.

Nenustatėme neigiamos koreliacijos tarp SSSGK pablogėjimo ir pirmos, paskutinės paros SOFA sistemos balų skaičiaus bei inkstų, plaučių, kepenų ir krešumo sistemų pažeidimo.

Analizuodami pirmos ITS dienos organų sistemų pažeidimo įtaką atskiroms SSSGK sritims nustatėme, kad yra teigiama koreliacija tarp centrinės nervų sistemos (CNS) pažeidimo ir VADFBs ($r=0,23$; $p=0,006$) - CNS pažeidimas pirmą ITS parą statistiškai patikimai pablogina SSSGK gyvenimo kokybę VADFB srityje ($p=0,007$).

Kraujotakos sistemos pažeidimas iškėlimo iš ITS metu turėjo neigiamos įtakos ligonių FA. Tokių ligonių FA buvo blogesnis ($p=0,024$) nei ligonių, kuriems šis pažeidimas nenustatytas.

Pacientus, kuriems atlikta ENMG suskirstėme į tris grupes: 1) pacientus su KBNRP; 2) pacientus su neuroraumeniniu pažeidimu, nesusijusiu su kritine būkle; 3) pacientus be neuroraumeninio pažeidimo. Palyginę SSSGK pokyčius tarp grupių SSSGK skirtumų nenustatėme nė vienoje srityje išskyrus EB ($p=0,07$; tendencija).

Palyginome ligonių, kuriems nustatytas sunkus KBNRP ir ligonių, kuriems KBNRP nenustatytas SSSGK pokyčius. Ligonių, kuriems gydymo ITS metu išsivystė

sunkus KBNRP FA buvo mažesnis (p=0,007), o VADFB – didesnis (p=0,019) nei ligonių, kuriems KBNRP nebuvo nustatytas.

Nustatėme, kad FA sumažėja vidutiniškai 20-čia balų (p=0,004), VADFB padidėja vidutiniškai 22 balais (p=0,005) ligoniams, kurių terapinių intervencijų paskutinę ITS parą skaičius pagal TISS-28 sistemą buvo didesnis arba lygus 26.

Atlikę vienfaktorinę dispersinę analizę konstatavome, kad tarp veiksnių, turinčių įtakos FA mažėjimui didžiausią dalinį Eta-kvadrato koeficientą (0,116) turi ilgesnė nei 120 valandų DPV. Tarp veiksnių, turinčių įtakos VADFB didėjimui didžiausią dalinį Eta-kvadrato koeficientą (0,135) taip pat turi ilgesnė nei 120 valandų DPV. Taigi DPV, kurios trukmė ilgesnė nei 120 valandų – veiksnys, turintis didžiausią įtaką FA sumažėjimui ir VADFB padidėjimui. Sunkus KBNRP – antrasis veiksnys pagal įtaką FA blogėjimui (dalinis Eta-kvadrato koeficientas – 0,078). Terapinių intervencijų iškėlimo iš ITS metu skaičius, kai TISS-28 balų skaičius didesnis arba lygus 26 – antrasis veiksnys pagal įtaką VADFB (dalinis Eta-kvadrato koeficientas – 0,062).

Mirusių ligonių SSSGK iki gydymo ITS buvo statistiškai patikimai blogesnė FA (p=0,004) ir VADFB (p=0,037) srityse. Palyginome mirusių ir išgyvenusių ligonių grupių demografinius ir ITS rodiklius. Statistiškai patikimai skyrėsi tik TISS-28 sistemos balų skaičius iškėlimo iš ITS metu, jis tarp mirusiųjų iškėlimo iš ITS metu buvo daugiau nei trimis balais didesnis (p=0,007). Mažesnis FA ir didesnis VADFB iki gydymosi ITS ir paskutinės ITS dienos TISS-28 balų skaičius gali padėti prognozuoti mirštamumą po iškėlimo iš ITS.

Reikšmingiausias faktorius mirštamumo prognozei – FA iki gydymo ITS, kurio AUC – didžiausias (0,7).

Išvados

1. Ilgas gydymas intensyviosios terapijos skyriuje turi neigiamos įtakos ligonių su sveikata susijusiai gyvenimo kokybei. Praėjus šešiems mėnesiams po gydymo intensyviosios terapijos skyriuje ligonių fizinis aktyvumas ir veiklos

apribojimas dėl fizinės būklės lieka prastesni nei buvo iki gydymo intensyviosios terapijos skyriuje.

2. Ilgai intensyviosios terapijos skyriuje gydytų ligonių fizinio aktyvumo sumažėjimas ir veiklos apribojimo dėl fizinės būklės padidėjimas po šešių mėnesių nuo iškėlimo iš ITS susiję su:
    - sunkesne nei 53 balai būkle pagal SAPS 3 sistemą;
    - ilgesne nei 120 valandų dirbtinės plaučių ventiliacijos trukme;
    - didesniu nei 25 balai pagal TISS-28 sistemą terapinių intervencijų skaičiumi paskutinę gydymo intensyviosios terapijos skyriuje parą;
    - sunkiu kritinių būklių neuroraumeniniu pažeidimu.
3. Didžiausią įtaką ilgai intensyviosios terapijos skyriuje gydytų ligonių fizinio aktyvumo po šešių mėnesių nuo iškėlimo iš intensyviosios terapijos skyriaus sumažėjimui ir veiklos apribojimo dėl fizinės būklės padidėjimui turi ilgesnė nei 120 valandų dirbtinė plaučių ventiliacija, sekantys pagal reikšmingumą veiksniai - kritinių būklių neuroraumeninis pažeidimas ir terapinių intervencijų skaičius iškėlimo iš intensyviosios terapijos skyriaus metu.

4. Ilgai intensyviosios terapijos skyriuje gydytų ir po iškėlimo mirusių ligonių fizinis aktyvumas iki gydymo intensyviosios terapijos skyriuje buvo mažesnis, o veiklos apribojimas dėl fizinės būklės - didesnis nei išgyvenusių šešis mėnesius.