IDENTIFYING PSYCHOSOCIAL FACTORS INFLUENCING SHORT- AND LONG-TERM MORTALITY AND MORBIDITY AFTER ADULT CARDIAC SURGERY

PhD thesis

Zsuzsanna Cserép MD

Semmelweis University Doctoral School Cardiovascular Medicine and Research Division



Supervisor: Andrea Székely, MD, DSc

Official reviewers: János Varga, MD, PhD, Tamás Végh, MD, PhD

Head of the Complex Examination Committee: Alán Alpár, MD, DSc

Members of the Complex Examination Committee: László Cervenák, MD, PhD, Mihály Kovács, MD, DSc

Budapest 2024

1. Introduction

Cardiovascular disease (CVD) is the most common form of heart disease in the developed world, and one of the leading causes of mortality and morbidity in these countries. In recent decades, numerous studies focused on the link between CVD and various psychosocial factors. The prevalence of depression among patients with diagnosed CVD is between 20 and 45%. Elevated anxiety scores have been reported from 20 to 55%. The link between cardiovascular disease and anxiety/depression has long been known: both conditions are possible risk factors for CVD and/or CVD may lead to mood disorders. Affective disorders (major depression, anxiety disorders, hostility and anger) and chronic stressors (low social support and low socioeconomic status) contribute to the development of atherosclerosis and cardiac events. Similar prevalence rates were found in patients undergoing coronary artery bypass grafting surgery (CABG). Symptoms of anxiety and unipolar depression are common in patients undergoing CABG surgery. Numerous prospective cohort studies have focused on the short and long term outcome of CABG. As a result, they found that not only clinical factors e.g. cardiac status, comorbities and intraoperative factors have impact on the outcome. Comparison of morbidity and mortality rates associated with psychosocial factors to morbidity and mortality rates related to traditional risk factors (smoking, obesity, and physical inactivity) showed priority of psychosocial background.

2. Objectives

Three studies contributed to this thesis, with the following objectives:

2.1. Associations between cardio- and cerebrovascular events and psychosocial factors after cardiac surgery

Patients awaiting elective CABG or heart valve surgery were assessed for depression [Beck Depression Inventory (BDI)], anxiety [Spielberger State and Trait Anxiety Questionnaire (STAI-S and STAI-T)], social support, negative affectivity, social inhibition, illness intrusiveness, sleep disturbance, and sel-rated health (SRH) status. Our first aim was to investigate the association between all cause mortality and hospitalisation for major cardio- and cerebrovascular events (MACCE) (angina, congestive heart failure, myocardial infarction, percutaneous coronary angioplasty, successful resuscitation after cardiac arrest, cardiac-related mortality, stroke, re-CABG, and heart valve replacement) and test scores in addition to relevant clinical factors. Our second aim was to examine whether test scores change with improvement or even deterioration in patient health over the follow-up period.

2

2.2 Effects of preoperative anxiety and education level on long-term outcome of cardiac surgery

Patients awaiting elective CABG or heart valve surgery, were assessed for depression (BDI), anxiety (STAI-S and STAI-T), as well as education level was analysed. Our aim was to analyse the role of test scores and level of education, in addition to clinical factors, in the mortality and rehospitalisation rates. We investigated the association between depression and anxiety in the same patient and how scores altered with changes in health status over the follow-up period.

2.3 Associations of anxiety, depression, happiness, satisfaction and self-rated health with length of stay in intensive care unit (ICU) and hospital after cardiac surgery

Patients awaiting elective CABG, combined CABG/valve, or valve surgery were assessed for depression (BDI), anxiety (STAI-T), happiness, satisfaction and self-rated health. We first analysed the association between a 3-day ICU stay or a hospital stay of at least 10 days and test scores. Second, the relationship between depression, anxiety, happiness and satisfaction were examined in the same individual. We created a clinical multivariable risk model for ICU stay/hospital stay, and hypothesized that adding certain psychosocial factors to the model would improve the c index.

3. Methods

- 3.1. MACCE and survival analysis
- 3.1.1. Study population for

The study population consisted of 197 consecutive patients admitted for elective CABG or valve surgery at the Gottsegen Hungarian Institute of Cardiology, between July 2000 and May 2001. There were no eligibility restrictions by age, sex or cardiac condition and no classification by onand off-pump procedures. The participants were not managed differently than the other patients, e.g. there was no psychosocial preparation, it was an observational study. Baseline questionnaires were completed one to five days before surgery. Of the 197, 17 patients were excluded because of cancelled surgery (n=9) or inability to complete the psychological tests (n=8). Thus, a total of 180 patients were prospectively studied.

3.1.2. Clinical factors

The two studies examined, with minor differences, a number of medical and psychosocial factors as potential determinants of outcome. Preoperative medical factors included: previous myocardial infarction and cerebrovascular disease, history of arrhythmia, diabetes mellitus, hyperlipidaemia, peripheral arterial disease, chronic renal insufficiency, hypertension, previous psychiatric treatment,

use of anxiolytics/antidepressants. Perioperative factors were the following: reoperation for any reason, cardiopulmonary bypass time, myocardial infarction, acute heart failure, serious infection, number of grafted vessels, arrythmia, duration of ICU and hospital stay, additive EUROSCORE. The additive EUROSCORE was calculated based on preoperative risk factors to assess and predict the odds of recovery and fatal outcome in patients with coronary and heart valve operations. Intraoperative characteristics included number of grafted vessels, cardiopulmonary bypass time, and aortic cross-clamp time. Postoperative complications were the following: permanent stroke (new-onset cerebrovascular accident persisting for more than 72 hours), reoperation for any reason, serious infection (e.g., positive blood culture, deep sternal wound infection and catheter-related infection), prolonged mechanical ventilation (ventilation support for more than 48 hours), renal failure requiring dialysis and myocardial infarction. The diagnosis of acute heart failure required the use of an intra-aortic balloon pump, the use of continuous intravenous inotropic support for at least 48 hours, or autopsy evidence of heart failure. Among postdischarge factors presence of MACCE, arrythmia, malignancy and rehospitalisation were analysed.

3.1.3. Psychosocial factors

Demographic data on age, sex, living status (alone ot with someone else), and education (number of successfully completed years of schooling) were collected. Education was measured by school years and categorized into three groups: less than 8 years, more than 12 years and more than 8 but less than 12 years. Years of schooling were calculated on the basis of the number of years of schooling successfully completed (i.e., if somebody needed to retake the fifth grade, they were considered to have completed fifth grade despite 6 full years of schooling). Self-rated health was assessed by a single question "How do you rate your health in general?" There were five possible responses: very good, good, fair, poor, and very poor. Negative affectivity refers to the tendency to experience negative emotions across time/situations. Social Inhibition refers to the tendency to inhibit the expression of emotions/behaviours in social interactions to avoid the disapproval by others. Type D patients are defined as having both Negative affectivity and Social Inhibition scores of 10 points or higher. The STAI-S measures the transitional emotional status evoked by a stressful situation, such as surgery. The STAI-T score reflects relatively persistent individual differences in the proneness to anxietys. The BDI is a 21-item self-report instrument measuring clinical manifestations of depressive symptoms that correspond to the DSM-IV criteria. Scores 0-9 indicate that a person is not depressed, 10-18 indicate mild-moderate depression, 19-29 indicate moderatesevere depression and 30-63 indicate severe depression.

3.1.4. Follow-up surveillance

The BDI, STAI-S and T tests were sent to the patients, along with an additional questionnaire about their hospitalization and the primary reason for their hospital admission since the last contact. The patients were contacted by mail 6, 12, 24, 36, 48 60 and 82 months after discharge. The social support, negative affectivity, social inhibition, illness intrusiveness, and insomnia tests were sent with the second and fifth year questionnaires. At the end of the second and fifth year, we phoned patients who had not responded and asked for information about their medical history. At 82 months only BDI, STAI-S, and STAI-T tests were sent to the patients along with the additional questionnaire.

3.1.5. End-point assessment

We have chosen all-cause mortality and hospitalisation due to MACCE (angina, congestive heart failure, myocardial infarction, percutaneous coronary angioplasty, survived cardiac arrest, and death due to cardiac causes, stroke, re-CABG, and valve replacement) as clinical end-points after five years and all-cause mortality after nearly seven years. In 70% of cases, clinical data were obtained from the records of the hospital where the patients were treated, and in the remaining 30% from the records of general practitioners. Therefore, mortality and death dates were available for each patient in the study population.

3.1.6. Statistical analysis

All analyses were performed using the SPSS 13.0 statistical package (SPSS Inc, Chicago, IL). Data were described as mean and standard deviation (SD) or median and interquartile range (25th to 75th percentile) for continuous variables and as number and percent for categorical variables. The median (25th to 75th percentile) follow-up was computed according to the Kaplan-Meier method. The observation time extended from the date of discharge to the date of first MACCE event/death or censoring. The cumulative MACCE free survival/ survival probability and 95% confidence intervals (CIs) were computed and plotted separately for patients with and without MACCE/ survivals and deads according to the Kaplan-Meier method. Preoperative and operative patient characteristics were compared according to the occurrence of MACCE/ postoperative mortality by means of the Student t test or the Mann-Whitney U test and the Chi-square/ Fischer exact test for continuous and categorical variables, respectively. We used Cox proportional-hazards analysis to identify factors associated with MACCE/ mortality after cardiac surgery. Candidate variables were included in the initial Cox regression model if they were associated with mortality in a univariate analysis (P < 0.20). The final multivariable Cox proportional hazards regression model was then

derived according to the backward deletion of the least-significant predictors. This statistical model is a type of survival model in which predetermined covariates or risk factors, such as patient characteristics and co-morbidities, are assessed for their independent association with the hazard of mortality. Hazard ratios and the corresponding 95% Confidence intervals (C.I.s) are reported. Furthermore, we quantified the discriminatory power of the final multivariable model using the cindex, which corresponds to the area under the receiver operating characteristic curve, ranging from 0.5 (performance at chance) to 1.0 (perfect performance). All tests were 2 sided, and a value of P<0.05 was considered statistically significant. In the MACCE study we adjusted the Cox model for the propensity score of MACCE to account for the confounding effect of preoperative and operative characteristics, It was calculated by including variables linked to MACCE in a multivariate logistic model with MACCE being the dependent variable and the following variables being regressors: previous myocardial infarction, previous CABG, history of arrhythmia, congestive heart failure, diabetes mellitus, hypercholesterolemia, cerebrovascular disease, chronic renal insufficiency, hypertension, and previous psychiatric hospitalisation, additive EUROSCORE, number of grafted vessels, cardiopulmonary bypass and aortic cross clamp time, permanent stroke, reoperation for any reason, serious infection, prolonged mechanical ventilation, renal failure requiring dialysis, duration of ICU and hospital stay. The c-statistic for this model was computed to 0.78. We also evaluated the role of psychosocial factors investigated (measured at the 2nd and 5th year and the mean of the 2 measurements) during follow-up in the Cox model by adjusting for propensity score. In the survival study paired t-test and Pearson correlation were used for analyzing the pre- and post-discharge BDI and STAI-T points.

3.2. ICU and hospital stay after cardiac surgery

3.2.1. Study population

Six hundred forty-four consecutive patients awaiting elective CABG, combined CABG/valve, or valve surgery at Gottsegen Hungarian Institute of Cardiology were eligible to participate between November 1, 2006 and October 31, 2007. We considered all patients eligible to participate regardless of age, sex, cardiac condition or on- versus off-pump surgical procedures. The only exclusion criterion was severe psychological/psychiatric comorbidity, as these patients were unable to answer our questionnaires. The patients in the study were admitted to the surgical ward at least 2 days before surgery. After admission, we invited patients to participate in our study. Patients completed baseline questionnaires 1.56 days (SD = 0.7) before surgery. Tests were fulfilled by the patients. Two hundred sixty-seven (41.5%) patients agreed to participate and provided informed consent. Surgery was cancelled for 4 patients and 3 patients had non-CABG surgery (2 pericardectomy, 1 porcelain aorta). Nineteen patients were unable to complete the psychological

tests for various reasons (e.g., mental disabilities and dysgraphia). If patients refused or were unable to participate (n = 370; 57.5%), we used only their medical data from the institutional database. The participation of patients with neuropsychiatric disorders was very low, only 2 patients had treated depression, 1 patient had major depressive psychosis, 2 patients had preoperative stroke. In the postoperative period, 10 patients (3.7% of 267) had neurological complications and antidepressant treatment was started in 9 patients in the postoperative period.

3.2.2. Clinical factors

We evaluated medical, demographic and psychosocial factors as potential predictors of length of ICU and hospital stay. Medical factors were similar to those described in previous studies above, along with the following: history of chronic obstructive pulmonary disease (COPD), gastrointestinal disease, peripheral arterial disease, pulmonary hypertension, BMI, NYHA III/IV functional status. Smoking was also evaluated, we categorized patients into two groups: those who had stopped smoking before operation (previously smoking group) and those who had not (right before operation group). In addition, we examined specific aspects of the surgical procedure. We marked the responsible surgeon, whether an intraoperative intraaortic balloon pump and/or a heart-lung machine was used (i.e., an on/off pump procedure). Continuous variables from patient medical charts included the number of grafts, cardiopulmonary bypass time, aortic cross clamp time and total duration of surgery (in minutes). Postoperative complications were defined as above. These post-operative complications were summed and the number of post-operative complications was considered a continuous variable (postoperative complication score). We also measured the duration of ICU and total hospital stay. We investigated eight demographic variables (age, sex, marital status, current living/working arrangements, number of children and siblings, and years of education completed) as potential covariates. We used several validated psychosocial tests (SRH, STAI-T, STAI-S, BDI). The question "How happy are you in general?" assessed happiness. The answer was rated from unhappy (0) to happy (10). General satisfaction was measured by a single question "How satisfied are you?".

3.2.3. Outcome assessment

The clinical outcomes were length of ICU and hospital stay (i.e., the number of days from the date of surgery to the date of ICU discharge). A longer post-operative stay in the ICU was defined as a length of stay of at least 3 days, and prolonged hospital stay was defined as >10 days.

3.2.4. Statistical analyses

We used different variables from EUROSCORE and those showing p < 0.20 in the univariate analysis were entered into a multivariable logistic regression model (e.g. gender, COPD, diabetes, pulmonary hypertension). To create a base model, multivariate analysis used predictors from medical records, including age, sex, preoperative clinical variables and intraoperative surgical factors. To minimize collinearity, we used the length of the operation instead of cardiopulmonary bypass time and aorta cross-clamp time, because they were highly correlated. Next, we developed a patient survey model using predictors from the patient survey data (socioeconomic questions and psychosocial measures) to identify predictors that, after adjusting for the baseline variables, were associated with extended ICU stay and hospital stay. In the patient survey model, univariate analysis analysed the relationship between extended ICU stay and the psychosocial test scores. The multivariable model combined the base model with the patient survey model to identify psychosocial predictors that were independently associated with longer ICU stay after controlling for sociodemographic and medical predictors. Again, we entered all predictors (p < 0.2) into the model. We assessed the fit of the logistic models using the Hosmer-Lemeshow Goodness-of-Fit test. Bootstrapping method was used to examine the discriminating power of the logistic model using the area under the receiver operating characteristic (AUC-ROC) curve.

4. Results

4.1. Major adverse cardiac and cerebrovascular events after cardiac surgery

There was no difference in the urgency status (all of them were elective patients), length on the waiting list, number of delayed surgery and previous location before admission (home or other hospital) between MACCE positive and MACCE negative patients. The overall incidence of MACCE was 45.0 % (81 patients of the 180 patients). Median follow-up was 52 months (interquartile range: 36-64 months). At the end of the second year, 146 (81.0%) patients responded. Among the patients who completed the 2nd year questionnaires, 62 (34.4%) experienced MACCE. At the end of the 5th year, 118 (65.5%) patients completed the questionnaires. Among the patients who responded at the end of the 5th year, 40 patients (22.2%) experienced adverse events (MACCE positive) and 78 patients (43.3%) were event-free. The median of event free survival was 36 months (95 % C.I.: 30-42 months) in the MACCE positive patients. Twenty-eight patients (15.5 %) died during the study period with a mortality rate of 2.25 per 100 person-years (Figure 1).



Figure 1.

Kaplan-Meier analysis of the two groups. Time after discharge is plotted against the cumulative survival.**MACCE:** Major Adverse Cardiac and Cerebrovascular event

MACCE positive patients had higher preoperative BDI scores (P=0.006), STAI-S (P=0.012) and STAI-T (P<0.001) scores compared to the event free patients after five years. After propensity score adjustment, the distribution of observed baseline covariates was identical in the MACCE positive and event free group. Among the 2nd year questionnaires, scores of SRH, illness intrusiveness, sleeping problems, BDI, STAI-S and STAI-T scores had a positive hazard for MACCE after adjustment of medical factors. At the end of year 5, we found results similar to the year 2 follow-up without significant differences in sleeping problems. Additionally, social inhibition (P=0.02) and negative affectivity (P=0.003) and their sum (P=0.005) were also associated with increased hazard for MACCE after propensity score adjustment. Type D personality had an adjusted hazard of 2.14 (95 % C.I.: 1.08-4.23) at the end of year 5. A comparison of MACCE positive and negative patients' scores at the end of years 2 and 5 showed that in the MACCE positive group, scores of illness intrusiveness, social inhibition and sum of social inhibition and negative affectivity, and the rate of sleeping disorders increased significantly from years 2 and 5. In contrast, intra-patient depression and anxiety scores did not change over the study period. Both groups reported reduced family and broad social support over the three-year period (P< 0.001).

4.2. Long term survival after cardiac surgery

During a median follow-up of 7.6 years (25th to 75th percentile, 7.4 to 8.1 years), the mortality rate was 23.6% (95% C.I. 17.3-29.9; 42 deaths). Seven patients died in hospital. Despite the relatively long follow up period, 15 patients did not respond ("were lost to follow-up") to our questionnaires. Therefore, the analysis of postoperative anxiety and depression levels had a smaller sample size. The non-responder patients were more likely to spend more than two days in the ICU, and were more likely to have diabetes than those who responded to our postal questionnaires. Patients who died were generally older, had a higher risk score (EUROSCORE), and were more often diabetic, had hiperlipidaemia, received psychiatric treatment, used anxiolytics/antidepressants spent more time at the ICU and hospital than patients who were alive at the end of the follow-up period. Patients who died had also higher preoperative BDI, STAI-S, and STAI-T and higher postdischarge BDI and STAI-T scores and a history of lower education level than patients who were alive at the end of the follow-up. During the follow-up period, the incidence of MACCE, malignancy and rehospitalization was significantly higher in the non-survivor group. There were no significant changes in the mean pre- and postdischarge STAI-T (-0.48 vs. -1.49; p = 0.37) and BDI (-0.83 vs. -0.12; p = 0.58) between patients who died during follow-up and those who were alive at the end of the follow-up. Pre- and postoperatively measured BDI (r = 0.64; p < 0.001) and STAI-T (r = 0.67; p < 0.001) scores in the same patients showed a strong correlation (Figures 2 and 3). Patients who died had also higher preoperative BDI, STAI-S, and STAI-T and higher postdischarge BDI and STAI-T scores: during the follow up the high level of depression and anxiety did not change. No interaction was found between anxiolytics, psychiatric treatment, BDI and STAI-T values (data not shown).



Figure 2. Figure shows the correlation between the preoperative and the mean of postdischarge BDI points. The line shows correlation and 95% C.I.



Figure 3. Figure shows the correlation between the preoperative and the mean of postdischarge STAI-T points. The line shows correlation and 95% C.I.

At the end of follow-up, 64.7% (44 patients) in the low education group, 80.7% (63 patients) in the medium education group and 91.1% (31 patients) in the high education group were alive (Figure 4). Survival was influenced strongly by education. The mean survival time for patients with an academic degree was 8.01 years (95% C.I.: 7.37 to 8.65), the mean survival time for patients with a 9-12 year degree was 7.73 years (95% C.I.: 7.31-8.16), and the mean survival time for patients with a degree of 8 years or less was 7.03 years (95% C.I.: 6.41-7.64). There were significant differences in survival analysis between patients with 8 years of education or less and patients with 8-12 years of education (P = 0.032) and patients with an academic degree (P = 0.006). Patients with less education had a worse life expectancy. There was no significant difference between patients with 9 to 12 years of education and those with university education (P = 0.18).



Figure 4. Kaplan-Meier analysis by education level. Time after discharge is plotted against the percent survival.

In the perioperative and the postdischarge multivariable Cox models, the additive EUROSCORE, length of ICU stay, preoperative STAI-T points, school years and the occurrence of MACCE were independently associated with mortality. In the multivariable Cox regression model patients were categorized: anxious only, depression only, neither, or both. In the study population, 54 (29.8%) patients had no depression or anxiety, 48 (26.5%) patients had only anxiety, (defined as STAI-T \geq 40), 14 (7.7%) patients had depression (defined as BDI \geq 10) and 65 (35.9%) patients had both anxiety and depression. Comparing the number of survivors and deaths, anxious and anxious and depressed patients had a significantly higher risk for death. Patients with high EUROSCORE, low education and MACCE were also more likely to die.

4.3. Length of stay at the intensive care unit and hospital following cardiac surgery

Of the 644 eligible patients, 267 (41.5%) were analysed. The mean age was 60.3 years (SD: 8.9 years) and 73% of the patients were male. Most common preoperative conditions were hypertension, hyperlipidemia, previous myocardial infarction, diabetes and arrhythmia. Median length of ICU stay was 1 day (range = 0- 46 days). Those who spent 3 or more days in the ICU were treated for 839 days out of a total of 1,437 (58.4%). Mean hospital stay was 9.55 days (SD: 6.22) and 62 patients (23.3%) spent more than 10 days in the hospital. There was no significant difference in terms of age and BMI between the two groups; patients with long hospital stay had longer operation time, longer ICU stay and more complications in the ICU. These patients were

more likely to have preoperative arrhythmia, COPD, NYHA III/IV, and they had more postoperative complications, such as the need for IABP, respiratory failure, neurological disorder (any new neurological deficit after surgery), sepsis and the need for antidepressant use. There were more female patients among them. We also investigated the relationship among the psychosocial tests. BDI and STAI-T scores were correlated (r: 0.24, p < 0.001), BDI and happiness showed an inverse correlation (r:-0.21, p < 0.001). Satisfaction and happiness were strongly correlated (r: 0.72, p < 0.001) and satisfaction and STAI-T were inversely correlated (r: -0.47, p < 0.001). Similarly, there was an inverse correlation between happiness and STAI-T scores (r: -0.51, p < 0.001). SRH showed no correlation with either test. Patients with an ICU stay of 3 days or more had lower SRH and lower happiness scores, but higher BDI scores. Pre-operative smoking, education and living alone did not affect the length of stay in intensive care. After controlling for medical and sociodemographic factors, lower SRH, lower happiness, longer operation time, higher NYHA stages and the occurrence of severe COPD were independently associated with long ICU stay. We adjusted for medical factors including age, sex, NYHA class, diabetes, complex surgery, operation time. The c-index of the multivariate model was 0.72 and the Hosmer-Lemeshow chi-square test = 5.3, p = 0.72. Adding psychosocial factors (BDI, STAI-T, SRH and happiness) to the model improved the c-index to 0.77. Long hospital stay (10 days or more) was associated with NYHA severity, COPD, longer operation time and female gender. Of the psychosocial factors, SRH remained a predictor. Adding psychosocial factors (BDI, STAI-T, self rated health and happiness) to the final multivariate model improved the c-index from 0.74 to 0.76 and the Hosmer-Lemeshow chi-square test = 6.8, p = 0.55.

5. Conclusions

In conclusion, depression, anxiety, illness intrusiveness, sleeping disorders, social inhibition and worse SRH were associated with increased risk for MACCE five years after cardiac surgery, after adjustment of biomedical factors. By measuring psychosocial factors, the future 'candidates' for rehospitalisation could be detected earlier, and rehospitalisation could be prevented by addressing these risk factors. Severity of illness intrusiveness, sleeping problems and social inhibition increased in the MACCE positive patients during the three-year period; these tendencies were not observed in the event-free group. Anxiety and depression scores did not change in the MACCE positive group over the three-year period from year two to year five. Both groups reported less social support at the end of fifth year. The MACCE positive group had higher BDI, STAI-S and T test points at baseline than the negative group, and this difference persisted over the whole observation period. Depressed and anxious patients adapt poorly to stressful situations, such as

major heart surgery, and their altered mood contributes to prolonged or poor recovery. Sleeping problems and social inhibition as traditional symptoms of depression and anxiety were frequent in the MACCE positive group supporting this concept.

In our study, patients with Type D personality had a more than 2 times the adjusted hazard of adverse events at the end of the fifth year. Scores of illness intrusiveness and sleeping disorders, social inhibition increased only in MACCE positive patients. This suggests that the patient's personality may also contribute to the development of major adverse events, or even make recovery more difficult. Both groups reported less social support during the three year observation period. SRH and illness intrusiveness were independently associated with increased risk for MACCE after controlling of biomedical factors.

We found that STAI-T scores and low education level were associated with a higher risk of mortality after adjusting for medical factors and postdischarge major cardiac and cerebrovascular events during 7.5 years of follow up after cardiac surgery. In accordance, a higher level of education was associated with a longer survival time. Non survivors had higher BDI and STAI-T points preand postoperatively than survivors. Within groups the pre- and postoperatively measured BDI and STAI-t points were correlated (e.g. those with high preoperative BDI had high postoperative BDI points, etc.) and did not change during follow-up. We used the additive EUROSCORE for risk estimation for cardiac surgery. The addition of anxiety and education to the risk model might help to further refine the risk factors associated with increased 7.5-year mortality, and these results highlight the importance of preoperative screening for anxiety in routine clinical practice. In our study group, survivors were more frequently treated with anxiolytics and/or antidepressants than those who died during the follow-up. However, levels of anxiety and depression remained high in the studied population.

We found that long operation time, high NYHA levels and severe COPD were significantly associated with ICU stay of than three days or longer after cardiac surgery. After adjustment for medical factors lower SRH and low happiness level were also independently associated with length of ICU stay. Long hospital stay was associated with the same clinical factors and female sex, but among psychosocial factors only SRH was predicting after adjusting for depression and anxiety. The main finding of the study was that low SRH and low happiness significantly predicted prolonged ICU stay. Low SRH was also associated with longer hospital stay. Preoperative assessment of both variables is a quick and non-invasive, easy tool for clinicians as each consists of a single question and takes only a short time to answer. SRH was associated with mortality, even after controlling for a wide range of health measurements and mortality risk factors. In our study, SRH was an independent but not an exclusive predictor of longer ICU and hospital stay. We

therefore recommend that the SRH score should be an additional outcome measure in clinical trials and clinical practice. In addition to its important predictive value, SRH also provides an opportunity for intervention. We showed that a lower happiness scores significantly predicted longer ICU stay. Low levels of positive emotions do not necessarily indicate depression and vice versa, since we found only moderate correlation between depression and happiness; however, there was a stronger inverse correlation between anxiety and happiness. These tests are easy to perform and do not take long time. Measures of self-rated health, happiness, and depressed and anxious moods have not been studied simultaneously before; thus, this study may fill a gap in the field of emotional factors and chronic stressors of cardiac surgery. The reliability of our risk model for ICU stay with medical factors could be improved by adding psychosocial factors (BDI, STAI-T, somatic severity, SRH and happiness) and the reliability of our risk model for prolonged hospital stay could be improved by adding BDI, STAI-T, SRH and happiness.

6. BIBLIOGRAPHY OF PUBLICATIONS

Publications related to the thesis:

- Cserép Zs, Losoncz E, Malik A, Székely A, Balog P, Kopp M. Nyitott szívműtéten átesett betegek életkilátásait meghatározó pszichoszociális tényezők. Orvosi Hetilap, 2008;149(33):1549-54.
- Cserép Z, Balog P, Székely J, Treszl A, Kopp MS, Thayer JF, Székely A. Psychosocial factors and major adverse cardiac and cerebrovascular events after cardiac surgery. Interact Cardiovasc Thorac Surg. 2010;11(5):567-72. cited by 43
- Cserep Z, Losoncz E, Balog P, Szili-Török T, Husz A, Juhász B, Kertai MD, Gál J, Székely A. The impact of preoperative anxiety and education level on long-term mortality after cardiac surgery. J Cardiothorac Surg. 2012:14;7(1):86. cited by 132 IF: 0.9
- Cserép Z, Losoncz E, Tóth R, Tóth A, Juhász B, Balog P, Vargha P, Gál J, Contrada RJ, Falger PR, Székely A. Self-rated health is associated with the length of stay at the intensive care unit and hospital following cardiac surgery. BMC Cardiovasc Disord. 2014 Nov 29;14:171. cited by 16 IF: 1.878
- Cserép Z, Batiz Á, Székely A. A szív- és érrendszeri betegségek és a pszichoszociális tényezők kapcsolata, valamint a beavatkozás lehetőségei [Associations between cardiovascular diseases and psychosocial factors and options for intervention]. Orvosi Hetilap, 2023 Mar 19;164(11):411-419. IF: 0.6
- 6. Book chapter: Zsuzsanna Cserép, Andrea Székely and Bela Merkely (2013). Short and Long Term Effects of Psychosocial Factors on the Outcome of Coronary Artery Bypass

Surgery, Artery Bypass, Dr Wilbert S. Aronow (Ed.), ISBN: 978-953-51-1025-5, InTech cited by 10

Publications not related to the thesis:

- Lex DJ, Tóth R, Cserép Z, Breuer T, Sápi E, Szatmári A, Gál J, Székely A. J Postoperative differences between colonization and infection after pediatric cardiac surgery-a propensity matched analysis. Cardiothorac Surg. 2013;2;8:166. IF: 1.018
- Lex DJ, Tóth R, Cserép Z, Alexander SI, Breuer T, Sápi E, Szatmári A, Székely E, Gál J, Székely A. A comparison of the systems for the identification of postoperative acute kidney injury in pediatric cardiac patients. Ann Thorac Surg. 2014;97(1):202-10. IF: 3.664
- Nagy AC, Cserép Z, Tolnay E, Nagykálnai T, Forster T. Early Diagnosis of Chemotherapy-induced Cardiomyopathy: a Prospective Tissue Doppler Imaging Study. Pathol Oncol Res. 2008;14(1):69-77. IF: 1.260
- Szekely A, Cserep Z, Sapi E, Breuer T, Nagy AC, Vargha P, Hartyanszky I, Szatmári A, Treszl A. Risks and predictors of blood transfusion in pediatric patients undergoing open heart surgery. Ann Thor Surg. 2009;87(1):187-97. IF: 3.644
- T. Breuer, E. Sápi, I. L. Hartyánszky, Zs. Cserép, P. Vargha, A. Treszl, M. D. Kertai, J. Gál, M. Tóth, A. Szatmári, A. Székely. Impact of blood glucose values in patients with and without insulin treatment following paediatric cardiac surgery. Interventional Medicine & Applied Science. Vol. 2 (1), pp. 10–16 (2010) IF: 0.857
- Tóth R, Breuer T, Cserép Z, Lex D, Fazekas L, Sápi E, Szatmári A, Gál J, Székely A. Acute Kidney Injury Is Associated With Higher Morbidity and Resource Utilization in Pediatric Patients Undergoing Heart Surgery. Ann Thorac Surg. 2012;93(6):1984-90. IF: 3.454
- Vácz G, Cselenyák A, Cserép Z, Benkő R, Kovács E, Pankotai E, Lindenmair A, Wolbank S, Schwarz CM, Horváthy DB, Kiss L, Hornyák I, Lacza Z. Effects of amniotic epithelial cell transplantation in endothelial injury. Interv Med Appl Sci. 2016 Dec;8(4):164-171 IF: 1.056
- Cserép Zs, Székely A. Édes élet? a hiperglikémia különösen veszélyes diabétesz nélkül: áttekintő elemzés ér- és szívsebészeti, valamint szívinfarktust szenvedett betegekben. Aneszteziológia és Intenzív Terápia, 2007;37:29-34.
- Nagy A, Cserép Z. A cukorbetegség és a diasztolés szívelégtelenség kapcsolata valamint az echokardiográfia diagnosztikus szerepe [Link between diabetes and diastolic dysfunction and the diagnostic role of echocardiography.]. Orvosi Hetilap, 2009;150(45):2060-7.

- György A., Forgács S, Arató G, Borsi L, Keresztury Á, Cserép Zs, Galler Z, Egyed Zs. Generalizált mastocytosis esete. Osteológiai Közlemények, 2011;4:24-30.
- 11. Tóth Roland, Cserép Zsuzsanna, Székely Andrea. A szívsebészeti eredetű veseelégtelenség etiológiája és diagnosztizálása gyermekek esetében. Hypertonia és nephrologia, 2012;16(3-4).
- Szentgróti R, Khochanskiy D, Szécsi B, Németh F, Szabó A, Koritsánszky K, Vereb A, Cserép Z, Sax B, Merkely B, et al. The Impact of Frailty Components and Preoperative Mechanical Cardiac Support Changes with Time after Heart Transplantation. Biomedicines. 2024; 12(5):1114. IF: 4.7

∑IF: 21.303