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

PhD thesis

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List of abbreviations

CABG	Coronary artery bypass grafting
BDI	Beck Depression Inventory
BMI	Body mass index
C.I.	Confidence interval
CVD	Cardiovascular disease
EF	Ejection Fraction
HADS	Hospital Anxiety and Depression Scale
ICU	Intensive Care Unit
MACCE	Major Cardio- and Cerebrovascular Event
N	Number
NYHA	New York Heart Association
P	Probability
SD	Standard Deviation
SRH	Self-rated health
STAI-S and STAI-T	Spielberger State and Trait Anxiety Questionnaire

1. INTRODUCTION

Cardiovascular disease (CVD) is the most common form of heart disease in the developed world and a leading cause of mortality and morbidity in these countries. In the past twenty years, numerous studies have analysed the association between CVD and various psychosocial factors (1). It has been reported that the prevalence of depression is between 20-40% and anxiety between 10-23% in CVD patients (2, 3). The relationship between cardiovascular disease and anxiety/depression has long been recognised: both conditions are potential risk factors for CVD and/or CVD may lead to mood disorders. Atherosclerosis and cardiac events are influenced by chronic stressors such as low social support and low financial standing, as well as affective disorders such as significant depression, anxiety disorders, hostility, and anger (4). Comparable rates of occurrence have been discovered in patients undergoing coronary artery bypass grafting (CABG). Anxiety and unipolar depression symptoms are prevalent among individuals undergoing CABG surgery. A large number of prospective cohort studies have examined the immediate and long-term effects of CABG. Consequently, they discovered that the outcome is influenced by not just only clinical parameters like cardiac state, comorbities, and intraoperative factors (5). Priority of psychosocial background was demonstrated by comparing the rates of morbidity and mortality linked to psychosocial factors to those linked to established risk factors (tobacco use, obesity, and physical inactivity) (1).

The publications on which this thesis is based were published more than 10 years ago. Since then, the body of knowledge on the subject has grown and the results of research have become part of the revascularisation guideline. In each sub-chapter, I have expanded the body of knowledge available at the time of my own publications to include recent data and new contexts that have since been identified. The relationship between psychosocial factors and CABG has been integrated into new guidelines, particularly in the area of pre- and postoperative rehabilitation interventions. According to the 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization, preoperative rate of depression in patients undergoing CABG ranges from 14% to 43%. Depressed patients have longer hospital stays and higher mortality rates. About 20% of patients remain depressed after CABG. Cardiac events and coronary revascularization represent significant stressors in life, resulting in psychosocial morbidity. Anxiety, depression and stress lead to poorer treatment adherence, reduced quality of life, higher health care expenditure, more cardiac events and are independent risk factors for CVD morbidity and mortality (6). In order to improve the outcome of cardiac interventions (both surgery and transcatheter) the importance of prehabilitation program has grown recently, as stated in 2024 ESC guideline for „Preinterventional frailty assessment in patients scheduled for cardiac surgery". One domain of this program is the assessment of anxiety and depression before the intervention besides patient education and psychological support (7). Corresponding to these findings the 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization recommends treatment with psychological counseling, cognitive behavioral therapy, and/or pharmacological interventions for patients with depression, anxiety, or nervousness to improve quality of life and cardiac outcomes (level of recommendation: I). Following revascularization, screening for depression and referral or treatment for depression may be warranted to enhance quality of life and recovery (level 2b) (6).

1.1. Depression

1.1.1. Depression and Coronary Heart Disease

The emotional element that has been examined the most is depression. Depression and CVD are often co-morbidties: depression is two to three times more common in patients with CVD than in the general population. Epidemiological studies conducted in the early 2000s found that patients with CVD had a 15–30% prevalence of depression, with women experiencing depression at a rate about twice that of males (8). The association between the two has been observed in people initially free of CVD and in different populations of individuals with CVD, including patients with acute coronary syndromes, heart failure, stable CVD, and previous coronary bypass surgery. From mild (subclinical) depressed symptoms to traditional severe depression, there is a wide variety of depressive illnesses. Depression is defined by the Diagnostic and Statistical Manual of Mental Disorders as low mood and/or anhedonia (loss of interest in previously enjoyable activities) lasting for at least two weeks, along with somatic complaints (insomnia, excessive sleep, loss of energy, fatigue, pain, aches, or digestive problems resistant to treatment) and significant functional impairment (1). Depression has been described as a distinct risk factor for coronary artery atherosclerotic plaques.

Depression leads to hypercortisolaemia, resulting in sympathetic-vagal dysbalance. This manifests as impaired blood pressure control, reduced heart rate variability, hypothalamic-pituitary-adrenal axis dysfunction, insulin resistance, elevated levels of coagulopathic factors such as fibrinogen and plasminogen activator inhibitor-1, impaired endothelial function and increased proinflammatory cytokin levels (indicating an increased inflammatory response), as well as unfavourable lifestyle factors such as smoking, poor eating habits, physical inactivity, social isolation. Cardiovasular disease, however, leads to the development of depression as a chronic stress caused by the perceived loss (Figure 1) (1, 9). Depressive patients are often ignore medical treatment regimens; therefore they are less likely to successfully change additional cardiac risk factors and participate in cardiac rehabilitation and have markedly lower quality of life (9).

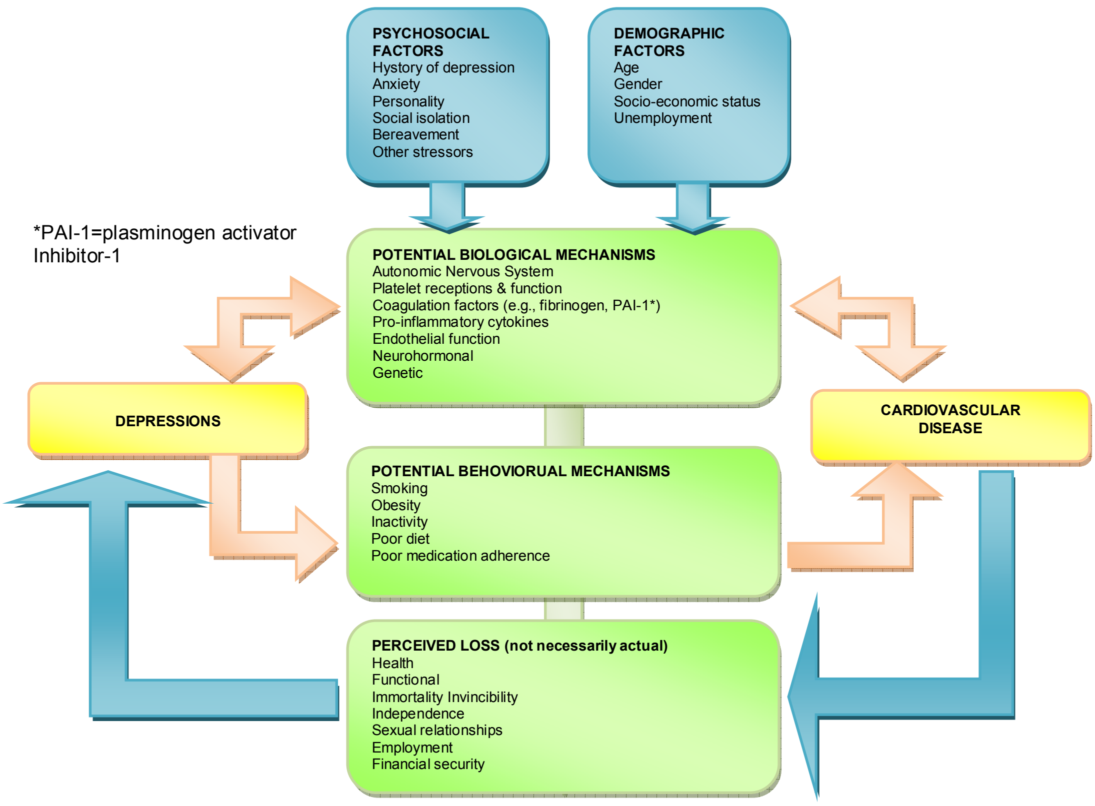

Figure.1. Potential factors that could explain the relationship between cardiovascular disease and depression (10) (by permission of Oxford University Press).

A large population based study was recently conducted on 30918 participants aged 20–85 years. Age, marital status, ethnicity, gender, educational, income, BMI, smoking status, comorbidities (e.g. arthritis, diabetes, hypertension, congestive heart failure, angina pectoris, and hyperlipidemia) were used to analyse the association between depression levels and the risk of CVD, stroke, and all-cause and cardiovascular mortality. The authors found a significant association between depression levels and increased risk of CVD. The risk of cardiovascular death and stroke increased with each level of depression (mild, moderate, moderately severe, and severe) by 38%, 120%, 84% and 275%, respectively (11). The 2021 ESC Guidelines on cardiovascular disease prevention recommends psychological stress screening for patients with CVD. The use of screening tools to assess depression, anxiety, and insomnia are recommended. CVD patients with stress should be referred to psychotherapeutic stress management. Patients with CVD and moderate-to-severe major depression should be given a selective serotinin reuptake inhibitor (12).

1.1.2. Depression and CABG

CABG surgery is a common surgical intervention in patiens with CVD, and the prevalence of depression in a meta-analysis ranged from 19% to 37% pre- and between 15% and 33% postoperatively. CABG combined with valve replacement has analogous rates, with the prevalence of depression ranging from 15% pre-CABG to 37.7% post-CABG. Preoperative depressive symptoms are associated with a higher risk of CVD, which may be manifested in dietary failure, physical inactivity, harmful behaviours or poor treatment adherence, or may manifest as postoperative complications, such as myocardial infarction, stroke or even kidney failure, leading to longer hospital stay, readmission and lower quality of life. Depression deteriorates quality of life and has a negative impact on the patient's social and family life. It increases the chance of new cardiac events and reduces functionality up to six months postoperatively, and increases the risk of hospital readmission for complications including arrhythmia, infection and volume overload in up to 20% of patients. It is important to measure levels of depression before and after CABG to assess clinically significant mood disorder for early intervention. The combination of structured coaching and counseling has the potential to alleviate symptoms of depression. As a part of cardiac rehabilitation programmes and cognitive-behavioural therapies it may lead to a shorter hospital stay (13). Curcio and colleagues assessed data from 306 patients before the operation, 30 days after and one year after surgery, using the Hospital Anxiety and Depression Scale (HADS) and Kansas City Cardiomyopathy Quality of Life measures. The HADS is a 14-question, standardized, self-administered questionnaire designed to assess general anxiety and depression in medical patients. The authors found that depressed patients use more and spend more on healthcare services after cardiac surgery and have lower Quality of Life than non-depressed patients after cardiac surgery. Individuals with anxiety disorders are more likely to seek outpatient care but do not show decreased Quality of Life (14). In a larger sample of 31309 CABG patients, 8.8% of whom were depressed, length of hospital stay and non-home discharge rates were analysed. After adjustment for multivariable analysis (comorbidities, age, income quartile, medical complexity), depressed patients had 70% increased odds of non-home discharge and 24% increased odds of prolonged length of stay (15). In a randomised clinical trial, preoperative cognitive and behavioural therapy had a positive effect on postoperative recovery after CABG. Patients who received adequate therapies had shorter hospital stays, less symptoms of depression and anxiety and better quality of life 4 weeks after discharge (16).

1.2. Anxiety

1.2.1. Anxiety and Coronary Heart Disease

Patients with CVD often present with anxiety symptomes: the prevalence of panic disorder can be as high as 50% and that of generalized anxiety disorder as high as 24% (17). Anxiety is a fearful, future-focused, negative affective state arising from a person feeling threatened and from not being able to predict, control, or accomplish desired results in impending circumstances. Tachycardia, hyperventilation, and sweating are its physical symptoms. Feelings of anxiety, restlessness, and apprehension are its psychological symptoms. It can also alter sleep patterns. Patients with anxiety have overactive sympathetic nervous system and produce an excessively high amount of catecholamines, leading to higher myocardial oxygen demand due increased heart rate, blood pressure, and the rate of ventricular contraction. In addition, impaired vagal control has been observed in patients with anxiety, manifested by an impaired baroreflex response and reduced heart rate variability. The latter are independent risk factors for ventricular arrhythmia and sudden cardiac death, as well as sensitive indicators of anomalies in autonomic cardiovascular function. For anxious individuals, the combined effects of harmful behavioral risk factors (such as excessive nicotine and probably coffee) should be taken into account along with to the biological hazards associated with anxiety (1). People with anxiety disorders are at higher risk of developing CVD than those without anxiety. Anxiety appears to be a substantial predictor of poor outcomes, including increased mortality, especially sudden cardiac death, and increased cardiovascular morbidity, according to recent studies of patients with coronary heart disease (18). Anxiety following a myocardial infarction is linked to long-term cardiac complications. Accordingly, in a cohort of 536 patients hospitalized with acute myocardial infarction, anxiety was associated with significantly higher levels of ventricular tachycardia, ventricular fibrillation, reinfarction and ischaemia, independent of clinical and sociodemografic risk factors. Cardiovascular changes were similar to depression, but anxiety was independently associated with a higher risk of cardiac complications and repeat revascularization (19).

1.2.2. Anxiety and CABG

In patients undergoing CABG, anxiety is particularly significant during the waiting period and until the surgery date is confirmed. Patients' anxiety levels are greatly influenced by their fear of dying before rather than during operation (1). In a study of 135 patients waiting for CABG, the HADS questionnaire was completed 1-2 days before surgery, 6 to 8 days after surgery (early) and 6 months after surgery (late). In 39.3% of patients, preoperative anxiety scores were elevated, compared to only 10.0% in the standard population. In the early postoperative period, anxiety scores decreased slightly to 34.4% (non-significant) and then further decreased to 28.9% 6 months after surgery ($p<0.01$). Thirty-five percent of patients who responded to surveys six months following surgery experienced complications such poor healing, chest pain, and needing further surgery. Anxiety levels were higher in patients with complications during or after surgery than in those without. There was no significant difference in the surgical technique e.g. on or off pump (20). Several years ago, a prospective cohort study involved participants after acute coronary syndrome or CABG who were offered a rehabilitation program. Using the HADS, anxiety and depression symptoms were evaluated at the completion of in-patient therapy as well as one, three, six, and eight years later. After 5 years, only about half of the participants had changed from moderate or severe symptoms at the beginning to no symptoms. Furthermore, patients with greater symptom severity and reduced physical activity had higher rates of cardiovascular events after 5 and 10 years. A greater BMI, less physical activity, and poorer education were associated with worsening depressive symptoms, while female sex and less physical activity were associated with worse anxiety symptoms (21).

1.3. Self-rated health

Self-rated health (SRH) is a subjective measure of an individual's health status that reflects an individual's mental, social, biological and functional aspects, in addition to their personal beliefs, cultural influences and health behaviours (22). It has been demonstrated that, even after adjusting for a number of sociodemographic and health variables, SRH remains a strong predictor of death and morbidity, functional decline, disability, and use of medical services. There are three possible explanations for the association: Compared to other psychosocial covariates in the analyses, SRH is a more sensitive and thorough measure of health status; (2) SRH assesses an individual's optimism or pessimism, which may be related to survival; or (3) SRH assesses traits unrelated to health status, such as social and psychological resources, family history, and health-related behaviors (1). The prognostic property of the SRH exceeds the conventional definition of health, which typically equates it with the lack of disease, suggesting that SRH is a comprehensive concept that includes various health dimensions relevant to survival. A fundamental idea of health theory is that experiences of health and illness can significantly modify an individual's perceptions of their own body. These impressions might be a reflection of significant physiological dysregulations, such as inflammatory reactions. Individual and subjective, SRH connects the social and psychological dimensions to the biological world and is associated with mortality. As a result, the response to the SRH question may cover the aspects of health that are most crucial and unique to each person. Since its creation in 1992, SRH has been regarded as one of the most significant health outcomes to date.

It is advised to be used as a primary care outcome indicator, a screening tool for illness risk, and a required component of studies (1, 23).

1.4. Psychological well-being

Recently, growing evidence shows that positive psychological well-being -which involves positive thinking and feelings, such as goal in life, an optimistic outlook and joy, is independently linked to a lower risk of CVD and may facilitate cardiovascular health. Positive emotions may influence cardiovascular health via 3 mechanisms 1) Direct effects on neurobiological functioning; 2) by influencing health-related attitudes indirectly; and 3) through psychosocial resources known about health promotion and stress management. Higher psychological wellbeing is related to lower blood pressure and lipid levels, but cross-sectional studies have not found associations between psychological well-being and blood glucose or glycosylated haemoglobin. Psychologically balanced persons often do not smoke, exercise regularly, reduce alcohol consumption and have better sleep quality. In the event of intolerable health problems, they are more likely to follow medical advice and take steps to prevent bad events. Optimistic people have a greater likelihood of seek help from society when faced with difficult situations and have a more extended network of helpful friends. High levels of emotional well-being may also help to resist the adverse effects of stress. For example, optimism can change the way you process and interpret everyday stressors, making them less threatening (24). Two previous studies have examined the link between optimism and rehospitalisation. Lower levels of optimism before CABG were a significant predictor of rehospitalisations for surgery and CVD, as well as rehospitalisations for all causes after surgery, after adjusting for cholesterol, sex, self-esteem, neuroticism and depression. In addition, lower degree of optimism was linked to higher all-cause rehospitalization 8 months after CABG, controlling for a number of sociodemographic, medical and psychological (depression and anxiety) variables (25). In a recent review, the authors found that optimism after CABG was significantly associated with reduced rehospitalisation rates, complications, pain, and improvement in quality of life, an increased rate fo returning to everyday activities, and better psychological status (26).

1.5. Illness intrusiveness

Engaging in psychologically enjoyable activities is one of the key factors that determines one's quality of life. Illnesses limit important activities, particularly chronic ones (1). Illness intrusiveness determines the extent to which a particular illness interferes with different aspects of the patient's life. These life domains encompass physical well-being, career, financial stability, personal relationships, leisure and social engagements (27). The Illness Intrusiveness Rating Scale is widely used in populations with chronic disease because it has strong psychometric properties and is sensitive to changes following therapeutic intervention (28). In the field of cardiac surgery, only one study is avaliable on the relationship between illness intrusiveness and heart transplantation. Compared to a liver or lung transplant, a heart transplant was associated with significantly more lifestyle disruptions due to the illness and its treatment (29). In a recent Hungarian study of patients with Marfan syndrome with cardiac complications, there was no difference in the extent to which their illness and/or its treatment interfered with their life compared to healthy individuals (30).

1.6. Social health

Initially, only social support has been analysed in behavioural cardiology. Social networks, which characterize the scope, composition, and regularity of interactions with the social support system around an individual, and functional support, which is further subdivided into received and perceived social support, are the two main kinds of social support. Received social support describes the kind and volume of resources offered by the social network, whereas perceived support relates to the people the individual perceives to be available to them when needed (1, 4, 31).

More recently, social health has synthesized social support, social isolation and loneliness. Social isolation is objectively characterised by a lack of or few social connections. In contrast, social support is a self-reported degree of effective or perceived access to peer resources. Loneliness is recognized as a negative emotional experience linked to feelings of being isolated (32). Social isolation and loneliness are common psychosocial conditions in adults and have been proven to be linked to poor CVD outcomes in the elderly population. There is a correlation between social isolation and loneliness with risk factors for CVD, particularly higher cholesterol, hypertension, smoking, obesity, physical inactivity or poor diet. Over time, risk factors stimulate neuroendocrine dysregulation and interfere with autonomic function. They can trigger activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, resulting in increased inflammation and oxidative stress. These changes can subsequently facilitate the progression of atherosclerosis and systolic hypertension (33). However, the connection between health and social health operates in both directions: deterioration in health (e.g. CVD event or decrease in cognitive function) can restrict or diminish social engagement. An analysis of 11486 persons aged 70 years and older showed that 12.32% of those with substantial social support suffered CVD event, compared to 24.56% of individuals with minimal social support (32). Limited social support and experiences of loneliness may predispose individuals to depression, and could indirectly lead to CVD. The incidence of rehospitalisation after myocardial infarction can be reduced by providing more support to patients. Community-based support networks have the potential to diminish stress in the population. There is a direct correlation between stress and hypertension. Social support may also have an effect on lifestyle, such as cigarette or tobacco use, diet, etc. Research indicates that social support is linked to improved compliance with treatment regimens and a reduced risk of mortality in individuals suffering from chronic illnesses (34). Two studies indicated a correlation between social support and survival rates. In a cohort of 337 patients who experienced myocardial infarction, diminished social support emerged as a significant predictor of both 5-year all-cause mortality and cardiac mortality in completely adjusted models. Increased social support was correlated with a reduction in rehospitalization rates and an improvement in 6-month survival among 29 men hospitalised for a first myocardial infarction (35).

1.7. Negative affectivity and Social inhibition

Negative affectivity is described as the proneness to experience negative emotions through time/situations. Social inhibition refers to the restraint of expressing emotions/behaviour in social interactions to avoid the disapproval of others. Patients with distressed (Type D) personality are defined as having both Negative affectivity and Social Inhibition scores of 10 points or higher. Type D personality is the existentialist. They like a slower, more relaxed approach to their work and life in general. They are hard-working, demand a sense of security and believe that risk-taking or change is dangerous and threatens the balance of life. Some early studies have found that Type D persons have a higher chance of experiencing a variety of unfavorable health outcomes, including death and morbidity in different cardiovascular populations. These outcomes include peripheral artery disease, ischemic heart disease, coronary intervention, and cardiac arrhythmias (1). In individuals with a decreased ejection fraction following myocardial infarction, Type D personality and global left ventricular dysfunction were distinct indicators of long-term cardiac events (36). Since then, a distressed personality profile has been identified as a predictive factor for emotional distress and adverse cardiovascular outcomes in patients with CVD. Nine psychosocial risk factors have been identified by the European Society of Cardiology as independent risk factors for cardiac disease incidence and prognosis, and Type D personality is one of them (37). A Type D patient feels inhibited, tense, and insecure around others (38). Individuals with a Type D personality have typically lower quality of life, have proneness to depressive reactions, reduced compliance with treatment and implementation of medical recommendation. 602 individuals undergoing CABG with stable coronary artery disease were split into two groups in a Russian study: those with a Type D personality and those without one. Between patients with and without Type D, there was no difference in overall mortality at five years. But five years following CABG, patients with Type D personalities were more likely to experience cardiac events than those without Type D personalities. The presence of diabetes, Type D personality and multifocal atherosclerosis were associated with worse outcome independent of sex, age, previous myocardial infarction and stroke in multivariate analysis (39). Objective biological evidence is available to explain the association between the unfavourable events and personality distress. In a population sample, the presence of Type D personality was assessed and coronary artery calcium was quantified by multispiral computed tomography. Patients with and without Type D personalities were separated into two groups. The coronary artery calcium score differed significantly between the two groups, with the greatest differences in the left coronary artery system. Type D personality resulted in high coronary artery calcium scores independently from sex, age, smoking, alcohol consumption, diabetes mellitus status, arterial hypertension status, cholesterol level, body mass index, history of stroke, coronary artery disease, myocardial infarction, depression and anxiety score (40).

1.8. Education

Education is an important determinant of health, with gender, ethnic and cultural differences. Those who have the opportunity to receive quality education in their lifetime tend to be healthier than those who do not. As the body of knowledge has grown, the details of their relationship have become clearer (41). The association between education and health falls into four groups: financial, health-behavioral, social-psychological and access to medical care. Education leads to secure, higher paying work with fewer safety risks and enables families to save assets that can be used to improve health. People with lower levels of education tend to earn less and have poorer health. Economic factors account for 30% of the link between education and health. Health behavior and lower adherence to medication and utilisation of preventive measures explain only a part of the impact of schooling on health: adults with lower education are more likely to smoke, eat unhealthily and not do exercise. People with high leves of education tend to have stable long lasting marriages and different sources of social support, which helps them cope with the challenges of stress and everyday life. Volunteering and participation in community groups help to build social relationships, maintain physical fitness and gives a sense of purpose. Access to health care plays a modest role in explaining health inequalities by education, despite its overall importance for individual and population health (42). In a Chinese study, education was classified as illiterate, primary school, secondary school and college. Mortality rates, stroke-specific mortality, recurrent stroke, and cardiovascular events were analysed 2 years after ischemic stroke. The incidence rates of cardiovascular events, stroke-specific death, and all cause mortality were highest among patients with the lowest educational attainment. After adjusting for covariates, the researchers found that illiteracy was responsible for a nearly twofold increase in all-cause mortality and recurrent stroke, and a nearly threefold increase in stroke-specific mortality and cardiovascular events, compared to college education (43). In a multi-national, prospective cohort study, mortality and major CVD were analysed for 14 potentially modifiable risk factors from 21 high-, middle- or low-income countries followed for a median of 9.5 years. In the study, prevalence, hazard ratios for CVD and mortality were linked to a set of behavioural factors (e.g. alcohol, smoking, physical activity, diet and sodium intake), metabolic factors (e.g. obesity, lipid levels, diabetes, blood pressure), psychosocial and socioeconomic factors (e.g. education, depressive symptoms). The predominant risk factors for CVD were metabolic factors, of which hypertension was the largest. Overall, behavioural risk factors contributed most to mortality, with low education being the single most important factor (44).

1.9. Sleeping disorders

Sleep deprivation has deleterious effects on many systems, with apparent alteration in the metabolic, endocrine and immune pathways. Not enough or too much sleep has adverse affect on health outcomes, e.g. all-cause mortality, type 2 diabetes, hypertension and respiratory disease, obesity in both children and adults and poor SRH (45). The recent American College of Cardiology/American Heart Association (2022) guidelines for cardiovascular prevention have identified the Life's Essential 8™, making healthy sleep essential for optimal cardiovascular health. The new sleep metrics recommends 7-9 hours of sleep per day for optimal cardiovascular health in adults, and more hours for children, depending on age (46). Sleep is essential for a healthy life and healthy functioning of the human body as a whole and of individual organs and systems. Insomnia, sleep fragmentation, sleep-disordered breathing and sleep deprivation are associated with increased cardiovascular risk. One possible explanation for this elevated risk is hypertension, which is associated with several pathophysiological mechanisms. In experimental conditions, sleep deprivation has led to overeating, which in the long term may lead to obesity, precipitating obesity-related hypertension. Six to eight hours of sleep a night is linked to a higher risk of impaired fasting glucose, central obesity and hypertension. Sleep restriction also leads to sympathetic activity, which raises the blood pressure. Epidemiological data have shown that absence of sleep of one hour is linked to an 8.1% rise in C-reactive protein and a 4.5% increase in interleukin-6 levels. Inflammatory cytokines elevate blood pressure through endothelial dysfunction. Decreased endothelium-dependent nitric oxide production plays a key role in the aetiology of hypertension, since nitric oxide acts as a vasodilatator: the decrease leads to increased levels of reactive oxygen species, which bind to nitric oxide before it diffuses into smooth muscle, ending in peroxynitrite through a process termed “nitric oxide scavenging”. Peroxynitrite in turn facilitates protein nitration and contributes to endothelial cell dysfunction and death. Insomnia sufferers often report trouble getting to sleep or sleeping, and have a 23% higher chance of cardiovascular death, largely due to a 50% increased risk of developing hypertension. In healthy individuals of college age, increasing sleep duration each night by fifteen minutes for 1 week reduced systolic blood pressure by 7 mmHg. However, long sleep duration has also been linked to poor outcomes in some epidemiological studies: who sleep more than 9 hours per night have a 30% higher risk of hypertension compared to those who sleep 7-8 hours (47). Zhu and colleagues investigated the relationship between patients' risk of unfavorable cardiovascular events and the quality and length of their sleep after percutaneous coronary intervention. They performed percutaneous coronary intervention with drug-eluting stents on 314 participants with first coronary artery disease and then followed them for nearly a year to assess the risk of serious adverse cardiovascular events. Subjects who slept less than 5 hours per day had sooner major adverse cardiovascular events than subjects who slept 6-8 hours. After adjusting for demographic and clinical confounders, subjects with less than 5 hours of sleep per day had a significantly increased risk of major adverse cardiovascular events. No association was found between long sleep duration (≥ 9 hours), sleep quality, or their combined effect and major adverse cardiovascular events (48).

2. OBJECTIVES

At the beginning of our research, little information was available on the impact of different psychological and social factors on the outcome of heart surgery. Separated studies in a small number of patients were conducted using different tests and different methods to assess the impact of each factor. To our knowledge, no similar study and analysis has been performed in the cardiac surgery population in Hungary, making our group a pioneer in this field at that time. Since then, numerous studies have been published on the subject, and the increasing reliability and standardisation of psychological tests and the interpretation of results with the help of extensive meta-analyses have led to the recommendation to consider social and psychological elements in addition to biological factors before revascularisation. We performed our studies by building and analysing databases containing detailed demographic, pre-, peri- and postoperative characteristics of cardiac surgery (elective CABG or heart valve surgery) patients. In addition to clinically relevant factors, we investigated various psychosocial variables using validated tests and aimed to explore the influential role of the latters in specific aspects and contexts on postoperative events. Our results have been published in three different studies:

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

- First, we hypothesised that all cause mortality and hospitalisation for major cardio- and cerebrovascular events (MACCE) would be influenced by psychosocial test scores besides relevant clinical factors.
- Second, we assumed that psychosocial test results would change as the patient's health improved or even deteriorated over the follow-up period.

2.2. Effects of anxiety, depression and education level on long-term outcome of cardiac surgery

- We hypothesized that, in addition to clinical factors, mortality and rehospitalisation rates would be influenced by psychosocial test scores and education level.
- Our second hypothesis was that depression and anxiety are associated in the same patient.
- Third, we hypothesized that depression and anxiety would change over the follow-up period in parallel with changes in the patient's health status.

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

- We hypothesized that psychosocial test scores would influence a 3-day ICU stay or a hospital stay of at least 10 days.
- Secondly, we hypothesised that depression, anxiety, happiness and satisfaction would be correlated in the same individual.
- Third, we hypothesized that adding certain psychosocial factors to the clinical multivariate risk model of ICU stay/hospitalisation would improve the c index.

3. METHODS

3.1. MACCE and survival analysis

3.1.1. Study population

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 on- and off-pump procedures. All patients signed the informed consent. The participants were not treated differently from other patients, e.g. there was no psychosocial coaching, it was an observational study. Baseline questionnaires were completed one to five days before surgery. Of the 197, 17 patients were excluded because they had cancelled surgery (n=9) or were unable to complete the psychological tests (n=8), giving a total of 180 patients prospectively studied. The study was approved by the Institutional Medical Ethics Committee on human research. The authors assumed the responsibility for the data's integrity and had complete access to it.

3.1.2. Clinical factors

The MACCE and survival study examined partly similar clinical factors as possible determinants of outcome, with minor differences being shown in the corresponding tables in the results section. Preoperative medical factors included: previous myocardial infarction and cerebrovascular disease, history of arrhythmia, diabetes, hyperlipidaemia, peripheral arterial disease, chronic renal insufficiency, hypertension, previous psychiatric treatment, anxiolytic/antidepressant use, additive EUROSCORE. Detailed definitions are available on the website of the Society of Thoracic Surgeons (STS National Database, data collection STS Adult Cardiac Database v2.52.1. Available at: http://www.sts.org/sections/stsnationaldatabase/datamanagers/adultcardiacdb/datacollection/index.html), accessed March 22, 2009. The additive EUROSCORE was calculated based on preoperative risk factors to assess and predict the odds of recovery and mortality in patients with coronary and heart valve operations (17 questions and corresponding response scores: age, sex, long-term use of bronchodilators or steroids for lung disease, extracardiac arteriopathy, neurological dysfunction severely affecting gait or activities of daily living, previous cardiac surgery requiring opening of the pericardium, serum creatinine >200 µmol/L (>2.26 mg/dL) preoperatively, patient still on antibiotics for endocarditis at the time of surgery, critical preoperative condition, angina pectoris at rest requiring intravenous nitrate until arrival in the anaesthetic room, left ventricular function, myocardial infarction within 90 days, systolic pulmonary artery pressure >60 mmHg, emergency: operation carried out on referral before the beginning of the next working day, any major cardiac procedure other than or in addition to CABG, surgery on the thoracic aorta due to ascending arch or descending aortic anomaly, postinfarction septal rupture.) (49). Perioperative factors were the following: reoperation for any reason, cardiopulmonary bypass time and aortic cross clamp time, myocardial infarction, acute heart failure, severe infection, number of grafted vessels, arrythmia, duration of ICU and hospital stay. The Society of Thoracic Surgeons Database (50) defines the key outcomes of postoperative complications, such as permanent stroke (new-onset cerebrovascular accident persisting more than 72 hours), reoperation for any reason, severe infection (e.g., positive blood culture, deep sternal wound infection and catheter-related infection), prolonged mechanical ventilation (ventilatory 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, continuous intravenous inotropic support for at least 48 hours or autopsy evidence of heart failure. Post-discharge factors were analysed: presence of MACCE, arrythmia, malignancy and rehospitalisation.

3.1.3. Psychosocial factors

Demographic data were collected on age, sex, living status (alone or with someone) and education (number of successfully finished school years). The applied psychosocial tests in the three study are described in Table 1. One popular reliability coefficient used to assess the internal consistency or reliability of a psychometric test result is the Cronbach's alpha. The reliability of variables taken from dichotomous and/or multi-point format surveys or scales (e.g., rating scale: 1 = poor, 5 = excellent) can be described using the alpha coefficient, which has a range of 0 to 1. The scale developed is more reliable the higher the score (51). The validity and reliability of the tests below are well documented in the Hungarian population. Cronbach’s alpha was calculated for the study population.

Table 1. Applied psychosocial tests and Cronbach's alphas for study population

Psychosocial test	Cronbach's alpha	Description, psychometric properties and references
Self-rated health (one question)		Question: "How do you rate your health in general?" There were five response options: very good, good, fair, poor and very poor (52). Cronbach's alphas for the study population are not available as there was only one question.
The Athens Insomnia Scale	0.74	Assess sleep complaints and identify possible cases of insomnia. The scale consists of 8 items. The first 5 items refer to nocturnal symptoms and 3 items ask about the daytime consequences of sleep disturbance (53).
Negative affectivity and Social Inhibition	Negative affectivity 0.89, Social Inhibition 0.78.	Negative affectivity is described as the proneness to experience negative emotions through time/situations. Social inhibition refers to the restraint of expressing emotions/behaviour in social interactions to avoid the disapproval of others. Type D patients (defined as having both Negative affectivity and Social Inhibition scores equal to or higher than 10) are at increased risk for a wide range of adverse health outcomes (e.g. cardiac death, risk of early ischemic CVD in men etc.) (54).
Spielberger State-Trait Anxiety Inventory	0.94	The short-term emotional state brought on by a stressful event, such surgery, is measured by the STAI-S. The STAI-T score captures comparatively long-lasting individual variances in anxiety susceptibility. In the US population, patients with a score higher than 40 are considered anxious (55).
Beck Depression Inventory	0.88	The BDI is a 21-item self-report instrument that measures clinical manifestations of depressive symptoms that meet the DSM-IV criteria. A score of 0-9 indicates that the person is not depressed, scores of 10-18 indicate mild to moderate depression, scores of 19-29 indicate moderate to severe depression, and scores of 30-63 indicate major depression (56).
Social Support Inventory	Board: 0.78, Family: 0.66	A five-item assessment evaluates cardiac patients' emotional and social support. The scale was 0 for no social support and 22 for the highest level of social support (57).
Illness Intrusiveness Rating Scale	0.91	A self-report tool that evaluates how much a person's illness and/or treatment interfere with thirteen different areas of their life. Ratings range from 1 (not very much) to 7 (very much) for each item. Higher scores reflect greater illness intrusion (58).

Education level was measured by years of schooling and classified into three groups: less than 8 years, more than 12 years, and more than 8 years but less than 12 years. In Hungary, compulsory education ends at the end of the eighth grade and secondary education at the end of the twelfth grade. The number of years of schooling was calculated on the basis of the number of years of schooling successfully completed (i.e. if someone had to repeat the fifth grade, they were considered to have completed the fifth grade despite having completed 6 years of schooling).

3.1.4. Follow-up surveillance

The BDI, STAI-S and T tests were sent to patients, along with a supplementary questionnaire about their hospitalisation and the primary reason for their hospital admission since last contact. Patients were contacted by post at 6, 12, 24, 36, 48, 60 and 82 months after discharge. Tests of social support, negative affectivity, social inhibition, illness intrusiveness, and insomnia were sent along with questionnaires at years 2 and 5. At the end of the second and fifth years, we called patients who had not responded and asked for information about their medical history. At month 82, only the BDI, STAI-S and STAI-T tests were sent to patients with the supplementary questionnaire. The psychological questionnaires were not completed by telephone to avoid bias due to different methodologies. For patients who did not respond and whose proxy could not be reached, we searched the Hungarian registry for mortality data at the end of the fifth and seventh years.

3.1.5. End-point assessment

We chose all-cause mortality and hospitalisation for MACCE (angina pectoris, congestive heart failure, myocardial infarction, percutaneous coronary angioplasty, survived cardiac arrest and death from heart disease, stroke, re-CABG and valve replacement) as the clinical endpoint after five years, and all-cause mortality after seven years. In 70% of the 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 the general practitioners. Therefore, the date and time of death were available for each patient in the study population.

3.1.6. Statistical analysis-general methods

The statistical program SPSS 13.0 (SPSS Inc., Chicago, IL) was used for all analyses. For continuous variables, the data were reported as mean and standard deviation (SD) or as median and interquartile range (25th to 75th percentile); for categorical variables, the data were reported as number and percent. The Kaplan-Meier method was used to calculate the follow-up's median (25th to 75th percentile). The observation period ran from the discharge date to the first MACCE event, death, or censoring date. The cumulative MACCE free survival/ survival probability and 95% confidence intervals (C.I.s) 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 test for continuous and categorical variables, respectively. Utilizing Cox proportional hazards analysis, we were able to determine the variables linked to mortality following heart surgery and MACCE. If a candidate variable showed a correlation ($P < 0.20$) with mortality in a univariate study, it was added to the original Cox regression model. The least-significant factors were then backward deleted to get at the final multivariable Cox proportional hazards regression model. Predetermined covariates or risk factors, such as patient features and co-morbidities, are evaluated for their independent association with the hazard of mortality in this statistical model, which is a form of survival model.. Hazard ratios and the corresponding 95% Confidence intervals are reported. Additionally, we used the c-index, or area under the receiver operating characteristic curve (ROC), which ranges from 0.5 (performance at by chance) to 1.0 (perfect performance), to quantify the discriminatory strength of the final multivariable model. Plotting the genuine positive rate (sensitivity) against the false positive rate (100-specificity) for various threshold levels results in the ROC curve. Any given point on the ROC curve represents a pair of sensitivity and specificity. The accuracy of the test (i.e. the ability of the test to correctly classify cases with and without a given condition) is measured by the area under the ROC curve. More areas under the curve means identifying more true positives while minimising the number/percentage of false positives. The different AUC values (0.90-1.00: excellent accuracy, 0.80-0.90: good accuracy, 0.70-0.80: fair accuracy,0.60-0.70:

poor accuracy,0.50: no discriminating ability) allow comparison of the accuracy of different diagnostic tests. All tests were 2 sided, and a value of $P<0.05$ was considered statistically significant.

3.1.7. Special analyses-MACCE study

Mortality rates (95% C.I.) per 100 person years were reported. The prognostic value of perioperative and psychosocial factors was evaluated by means of Cox regression. The MACCE propensity score was used to modify the Cox model in order to take into accounts the confounding effect of pre- and post-operative characteristics. Based on the pre-treatment features of each patient, the propensity score represents the conditional probability that a patient has MACCE. In order to account for variations in patient selection that are not explained by the other variables in the study, the propensity score modifies the apparent influence of the comparison variables of interest. The following variables served as regressors in a multivariate logistic model with MACCE as the dependent variable and the other variables as factors related to MACCE: 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 of the model was 0.78. In the Cox model, we also assessed the role of the psychosocial factors examined (scores at years 2 and 5 and the average of the two measures) during follow-up, adjusted for propensity score.

3.1.8. Special analyses-survival study

The pre- and post-discharge BDI and STAI-T points were analyzed using the Paired T-test and Pearson correlation. Using Cox regression, the predictive value of psychological and perioperative factors was assessed. The resulting multivariable model's discriminatory power was evaluated by determining the degree of over-optimism using the bootstrap method. When statistical modeling techniques are applied and the models provide outcomes for subsequent datasets that are not precisely predicted, this is known as over-optimism. One technique to attempt to account for this over-optimism is a bootstrapping process (59). For every bootstrap sample, the covariates in the final model were fitted. The original dataset was fitted using the coefficients of the bootstrap sample model, and thus, a c-index statistic was generated from this fit on the original dataset. The difference between the c-index from the bootstrap sample and from the bootstrap model fit on the original sample was then used to measure optimism. Only patients who were released from the hospital and had a minimum of one BDI and STAI-T score at the follow-up (n = 158) were analyzed in the post-discharge model.

3.2. ICU and hospital stay

3.2.1. Study population

Six hundred forty-four consecutive patients undergoing elective CABG, combined CABG/valve or valve surgery were enrolled at Gottsegen Hungarian Institute of Cardiology between November 1, 2006 and October 31, 2007. All patients were considered eligible to participate, regardless of age, sex, cardiac status, or on- versus off-pump surgical procedures. The only exclusion criterion was severe psychological/psychiatric comorbidity, as these patients were unable to respond to our questionnaires. Patients in the study were admitted to the surgical ward at least 2 days before surgery. After admission, patients were invited to participate in our study. Patients completed the baseline questionnaire 1.56 days (SD = 0.7) before surgery. The tests were completed by the patients. Two hundred sixty-seven (41.5%) patients agreed to participate and gave informed consent. Surgery was cancelled in 4 patients and non-CABG surgery was performed in 3 patients (2 pericardectomies, 1 porcelain aortic). Nineteen patients were unable to complete psychological tests for various reasons (e.g. intellectual disability and dysgraphia). Where patients refused or were unable to participate in the study (n = 370; 57.5%), only their medical records from the institutional database were used. The participation of patients with neuropsychiatric disorders was very low, with only 2 patients with treated depression, 1 patient with major depressive psychosis and 2 patients with preoperative stroke. In the postoperative period, 10 patients (3.7% of 267 patients) had neurological complications and 9 patients started antidepressant treatment in the postoperative period. This study was approved by the Institutional Medical Ethics Committee, registration number ECB 625-1/2006.

3.2.2. Potential covariates

We assessed 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 including: chronic obstructive pulmonary disease (COPD), gastrointestinal disease, peripheral arterial disease, pulmonary hypertension, BMI, NYHA III/IV functional status. Additionally, smoking was evaluated, and patients separated into two groups: those who had quit smoking prior to surgery (referred to as the "previously smoking group") and those who had not (referred to as the "just before operation group"). Furthermore, we looked at particular facets of the surgery. Whether a heart-lung machine or an intraoperative intraaortic balloon pump used (i.e., an on/off pump technique), we noted the responsible surgeon. The number of grafts, cardiopulmonary bypass time, aortic cross clamp time, and total surgical length (in minutes) were continuous variables obtained from patient medical documents. Postoperative complications were defined as above (50). These postoperative complications were summed and the number of postoperative 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 with Cronbach's alpha in parentheses for study population: SRH, STAI (0.81), BDI (0.80). The question "How happy are you in general?" assessed happiness. The answer was rated from unhappy (0) to happy (10). The same question was used in Hungarostudy (60). General satisfaction was measured by a single question "How satisfied are you?".

3.2.3. Outcome assessment

Clinical outcome was defined as the time spent in the ICU and in hospital (i.e. the number of days from the date of surgery to the date of discharge from the ICU and hospital). The length of the extended postoperative stay in the ICU was defined as at least 3 days for patients who were alive at the time of discharge. The mean ICU stay was 5.7 days (median = 1 day, 95% CI: 1-6 days), with a skew of 4.6 days. In previous literature, data on skewed length of stay have been modified or dichotomised (61). There is disagreement over the definition of a prolonged ICU stay; authors have defined it in terms ranging from 1 to 10 days. We decided to dichotomize this variable at 3 days, in accordance with Bucerius et al. (62), who defined prolonged ICU stay as ≥3 days, believing that this included almost all patients with postoperative complications. This definition listed a clinically meaningful group of patients (14.3%) with a higher incidence of postoperative events. Patients who have undergone uncomplicated surgery are usually discharged from hospital after 7 days, so prolonged hospital stay was considered to be longer than 10 days.

3.2.4. Statistical analyses-special methods

We used different variables from EUROSCORE, and those that confirmed $p < 0.20$ in the univariate analysis-such as sex, COPD, diabetes, and pulmonary hypertension-were added to a multivariable logistic regression model. Medical record predictors such as age, sex, preoperative clinical characteristics, and intraoperative surgical factors were included in a multivariate analysis to build a base model 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. After controlling for the base variables, we created a patient survey model and used predictors from the patient survey data (psychosocial measures and socioeconomic questions) to identify the factors linked to prolonged hospital stays and ICU stays. The association between a longer ICU stay and the results of the psychosocial tests was examined using univariate analysis in the patient survey model. After adjusting for sociodemographic and medical variables, the multivariable model integrated the base model with the patient survey model to identify the psychosocial predictors that were independently associated with prolonged ICU stay. Again, we entered the model with all predictors ($p<0.2$). We used the Hosmer-Lemeshow Goodness-of-Fit test to evaluate the logistic models' fit. By using the area under the receiver operating characteristic (AUC-ROC) curve, the bootstrapping approach was utilized to investigate the logistic model's discriminating power.

4. RESULTS

4.1. Major adverse cardiac and cerebrovascular events after cardiac surgery

There was no difference in urgency status (all were elective patients), time spent on the waiting list, number of delayed operations and previous place of stay before admission (home or other hospital) between MACCE positive and MACCE negative patients. The overall incidence of MACCE was 45.0 % (81 patients out of 180 patients). Median follow-up was 52 months (interquartile range: 36-64 months). At the end of the second year, 146 (81.0%) patients had responded. Of the patients, who completed the questionnaires in year 2, 62 (34.4%) had MACCE. At the end of year 5, 118 (65.5%) patients completed the questionnaires. Of the patients who responded at the end of 5 year, 40 patients (22.2%) had an adverse event (MACCE positive) and 78 patients (43.3%) were event free. The study profile and follow-up are shown in Figure 2.

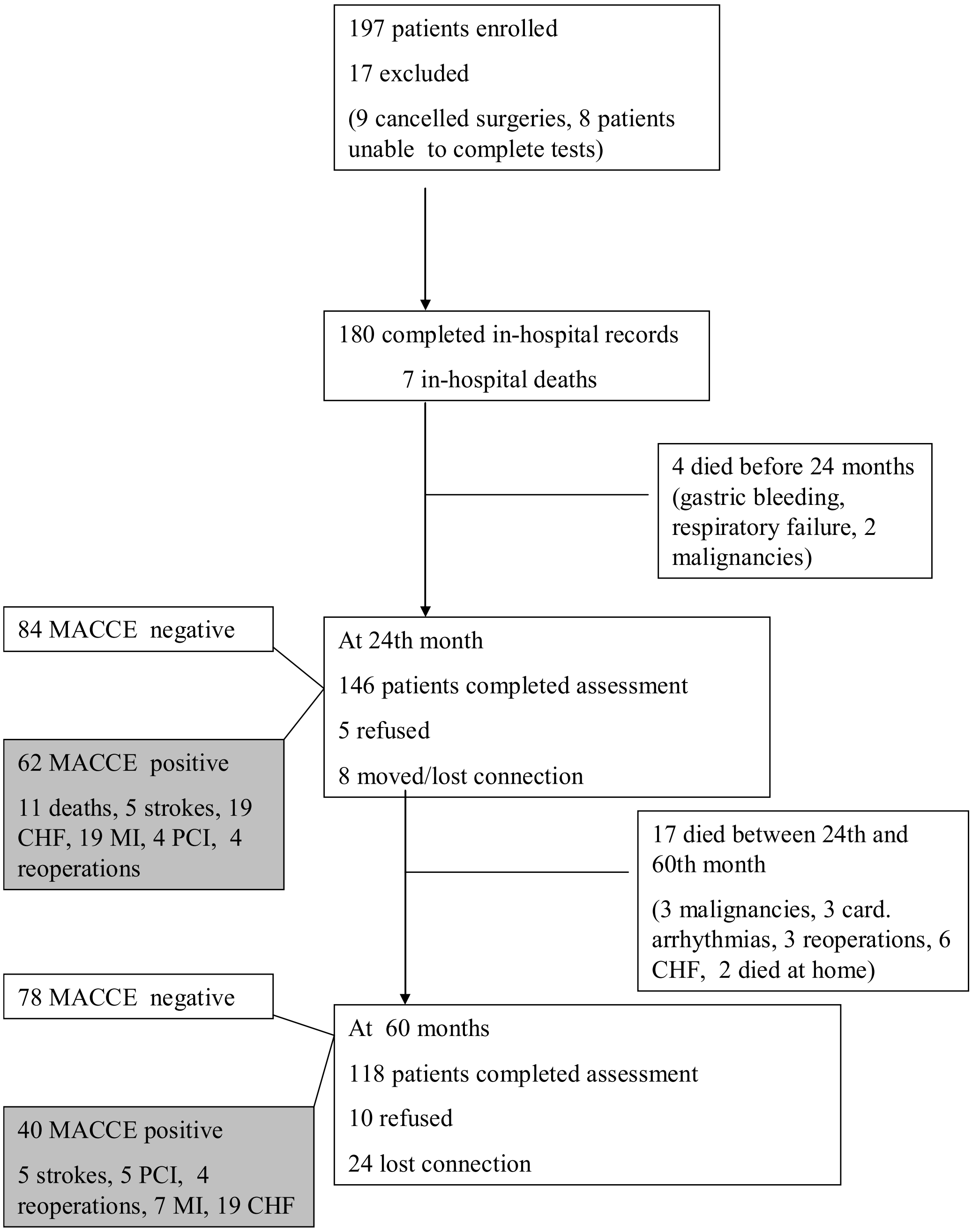

Figure 2. Study profile

The figure shows the main steps of the study, including patients who died and those who experienced major adverse outcome during the five-year follow up. ***CHF****: congestive heart failure,* ***MACCE:*** *Major Adverse Cardiac and Cerebrovascular event,* ***MI:*** *myocardial infarction,* ***PCI:*** *Percutaneous Coronary Intervention*

The median event-free survival in MACCE positive patients was 36 months (95 % C.I.: 30-42 months). Twenty-eight patients (15.5 %) died during the study period, with a mortality rate of 2.25/100 person-years (Figure 3).

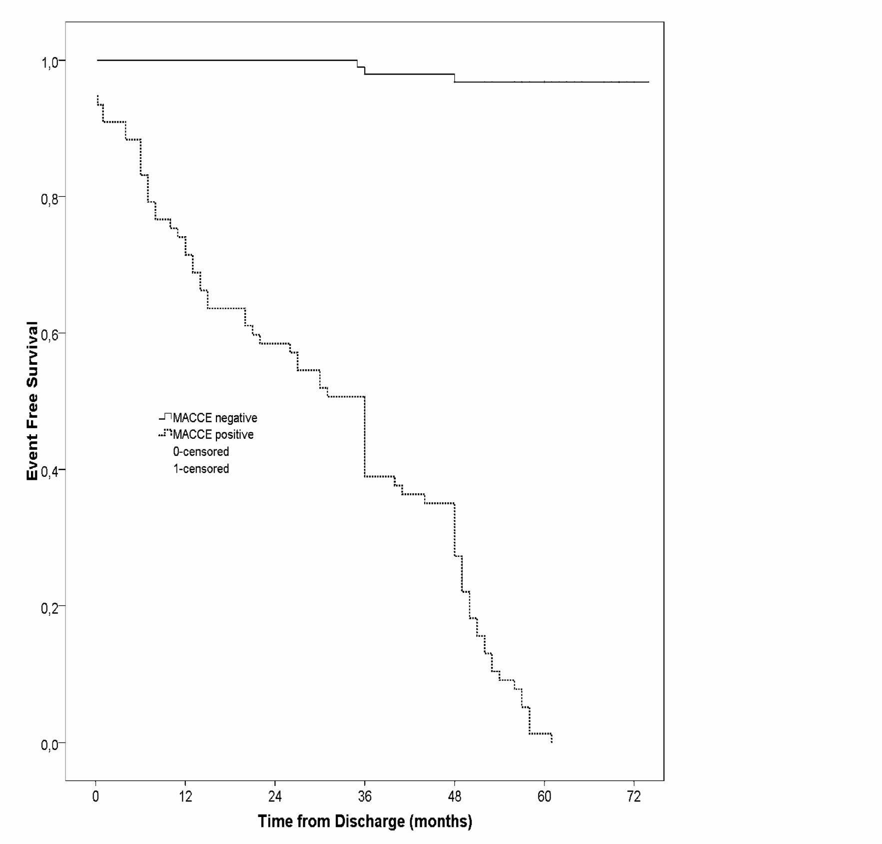

Figure 3. Kaplan-Meier analysis of the two groups.

Time after discharge is plotted against cumulative survival. ***MACCE:*** *Major Adverse Cardiac and Cerebrovascular event*

The pre- and perioperative characteristics of MACCE positive and MACCE negative patients at five years are shown in Table 2. After propensity score adjustment, the distribution of observed baseline covariates was the same in MACCE positive and event free group. 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 event-free patients.

Table 2. Preoperative, perioperative and psychosocial factors in MACCE positive and negative groups five years after cardiac surgery

BDI*: Beck Depression Inventory,* ***CABG:*** *Coronary artery bypass grafting,* ***CPB time:*** *cardiopulmonary bypass time,* ***MACCE:*** *Major Adverse Cardiac and Cerebrovascular event,* ***STAI-S:*** *state anxiety* *subscale in Spielberger State-Trait Anxiety Inventory, **STAI-T:** trait anxiety subscale in Spielberger State-Trait Anxiety Inventory. P values* are calculated after adjustment for propensity score*

	MACCE negative (N=99)		**MACCE positive (N=81)**		**p value**	**p value***
Preoperative factors						
Age (years)	56.8	11.2	59.1	8.2	0.11	0.63
Sex: female	32	32.3%	29	35.8%	0.63	0.75
Previous myocardial infarction	37	37.4%	29	35.8%	0.87	0.79
Diabetes	21	21.2%	26	32.1%	0.12	0.71
Kidney failure	8	8.1%	7	8.6%	1	0.99
Hypertension	40	40.4%	33	40.7%	0.54	0.68
Hyperlipemia	38	38.4%	26	32.1%	0.23	0.72
Cerebrovascular disease	11	11.1%	14	17.2%	0.28	0.76
Psychiatric disease	9	9.1%	17	20.9%	**0.03**	0.83
Euroscore (scores)	3.2	2.4	3.8	2.5	0.97	0.59
Perioperative factors						
CABG surgery	72	72.7%	61	75.3%	0.73	0.31
Valvular surgery	21	21.2%	27	33.3%	0.09	0.95
Reoperation	2	2.0%	9	11.1%	**0.01**	0.48
CPB time (min)	72	51	79	42	0.32	0.77
Number of bypasses	2.2	1.5	1.9	1.5	0.29	0.91
Myocardial infarction	13	13.1%	12	14.8%	0.82	0.93
Acute heart failure	9	9.1%	19	23.5%	**0.007**	0.89
Infection	9	9.1%	11	13.6%	0.35	0.96
Arrhythmias	19	19.2%	19	23.5%	0.47	0.82
Intensive care unit days	1.3	1.3	3.5	8.5	**0.024**	0.89
Hospital days	9.3	4.3	9.6	9.7	0.79	0.54
Psychosocial factors						
Education (years)	11.5	2.9	10.3	3.1	0.29	0.69
Single living	16	16.2%	11	13.6%	0.68	0.92
Preop. BDI (point)	8.2	5.1	11.8	8.7	**0.006**	
Preop. STAI-S (point)	42.9	11.3	47.2	11.1	**0.012**	
Preop. STAI-T (point)	41.8	9.2	48.1	9.9	**<0.001**	

Table 3 shows the propensity score-adjusted results of psychosocial tests at the end of the years 2 and 5 for MACCE positive and MACCE negative patients. Among the questionnaires at year 2, scores of SRH, illness intrusiveness, sleep problems, BDI, STAI-S and STAI-T scores were associated with a hazard for MACCE after adjustment for medical factors. At the end of year 5, we found similar results to those of year 2 follow-up, without significant differences in sleep problems. In addition, 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. The adjusted hazard of Type D personality was 2.14 (95 % C.I.: 1.08-4.23) at the end of year 5.

Table 3. Cox-models for assessing the role of psychosocial variables after stratification by biomedical variables

Psychosocial tests were entered separately into the Cox-model after adjustment for propensity scores including medical and perioperative variables. Adjusted hazard ratios were calculated for point increases in reported psychosocial test scores. For example, one point increase in the BDI score was associated with a 12 % increase in the risk of MACCE. ***BDI****: Beck Depression Inventory,* ***C.I.****: confidence interval,* ***NA****: Negative affectivity,* ***SI****: Social inhibition,* ***STAI-S****: state anxiety subscale in Spielberger State-Trait Anxiety Inventory,* ***STAI-T****: trait anxiety subscale in Spielberger State-Trait Anxiety Inventory*

	Year 2 (*N*=154)			**Year 5 (*N*=118)**		
	Adjusted Hazard Ratio	**95 %C.I.**	**p value**	**Adjusted Hazard Ratio**	**95 %C.I.**	**p value**
Self-rated health	0.67	(0.51-0.89)	**0.006**	0.72	(0.52-1.00)	**0.048**
Illness Intrusiveness	1.03	(1.00-1.05)	**0.018**	1.04	(1.02-1.05)	**<0.001**
Social support (family)	0.98	(0.92-1.04)	0.417	0.99	(0.91-1.08)	0.801
Social support (broad)	0.94	(0.87-1.03)	0.186	1.03	(0.92-1.17)	0.580
Sleeping disorders	1.14	(1.05-1.24)	**0.001**	1.06	(0.96-1.18)	0.258
Social inhibition (SI)	1.03	(0.97-1.08)	0.310	1.08	(1.01-1.14)	**0.020**
Negative affectivity (NA)	1.05	(1.00-1.11)	0.068	1.08	(1.03-1.14)	**0.003**
Sum SI+NA	1.02	(0.92-1.05)	0.108	1.04	(1.01-1.08)	**0.005**
BDI	1.12	(1.07-1.18)	**0.001**	1.05	(1.02-1.08)	**0.001**
STAI-S	1.09	(1.05-1.13)	**<0.001**	1.05	(1.03-1.08)	**0.001**
STAI-T	1.08	(1.05-1.11)	**<0.001**	1.04	(1.01-1.06)	**0.002**

Table 4 shows the differences between the scores at the end of years 2 and 5 for MACCE positive and negative patients. In the MACCE positive group, scores of illness intrusiveness, social inhibition and sum of social inhibition and negative affectivity, as well as sleeping disorders rate, increased significantly between years 2 and 5. In contrast, patient depression and anxiety scores did not change over the study period. Both groups reported decreased family and broad social support over the 3-year period (P< 0.001).

Table 4. Paired differences between MACCE positive and negative patients at the end of year 2 and 5

Individual differences in psychosocial variables in MACCE negative and MACCE positive study populations were examined using paired t-tests. Differences are presented as mean and standard deviation. Values in bold indicate significant differences between groups when P<0.05. ***BDI****: Beck Depression Inventory,* ***MACCE:*** *Major Adverse Cardiac and Cerebrovascular event,* ***NA:*** *Negative affectivity,* ***SD****: standard deviation,* ***SI:*** *Social inhibition,* ***STAI-S:*** *state anxiety subscale in Spielberger State-Trait Anxiety Inventory,* ***STAI-T:*** *trait anxiety subscale in Spielberger State-Trait Anxiety Inventory*

	MACCE negative		**MACCE positive**	
	Difference (SD)	**p value**	**Difference (SD)**	**p value**
Self-rated health	0.08 (0.81)	0.400	0.05 (0.85)	0.701
Illness Intrusiveness Scale	2.08 (17.80)	0.198	6.90 (14.71)	**0.014**
Social support (family)	-6.51 (5.80)	**<0.001**	-6.51 (6.22)	**<0.001**
Social support (broad)	-9.77 (4.10)	**<0.001**	-6.52 (6.23)	**<0.001**
Sleeping disorders	0.48 (2.40)	0.097	1.71 (3.40)	**0.009**
Social Inhibition (SI)	-0.30 (4.60)	0.590	1.66 (4.26)	**0.036**
Negative Affectivity (NA)	0.76 (4.98)	0.202	1.52 (4.51)	0.062
Sum SI+NA	1.05 (8.26)	0.280	3.15 (0.76)	**0.027**
BDI	-1.45 (5.88)	0.084	-0.66 (7.13)	0.589
STAI-S	0.02 (10.68)	0.990	-0.70 (12.88)	0.779
STAI-T	3.00 (10.12)	**0.015**	2.97 (10.61)	0.107

4.2. Long-term survival after cardiac surgery

During a median follow-up of 7.6 years (25^{th} to 75^{th} percentile, 7.4 to 8.1 years), the mortality rate was 23.6% (95% C.I. 17.3-29.9; 42 deaths). Despite a relatively long follow-up period, 15 patients did not respond to our questionnaires ("lost to follow-up"). Therefore, the analysis of postoperative anxiety and depression levels was performed with a smaller sample size. Non-responders were more likely to spend more than two days in the ICU and to have a history of diabetes than those who responded to our follow-up postal questionnaires. Patients who died were older, had a higher risk score (EUROSCORE), were more often diabetic, hiperlipidaemic, received psychiatric treatment, anxiolytic/antidepressant use and spent more time in ICU and hospital than patients who were alive at the end of the follow-up period. Patients who died had higher preoperative BDI, STAI-S and STAI-T, higher post-discharge BDI and STAI-T scores, and lower education level than patients who were alive at the end of the follow-up period. Postdischarge STAI-S did not affect long-term survival, test results are not shown. During the follow-up period, the prevalence of MACCE, malignancy and rehospitalisation was significantly higher in the non-survivor group (Table 5).

Table 5. Perioperative characteristics of the study population

N: *number,* ***SD:*** *standard deviation,* ***CPB time:*** *cardiopulmonary bypass time,* ***ICU:*** *intensive care unit,* ***BDI****: Beck Depression Inventory,* ***STAI-S:*** *state anxiety subscale in the Spielberger State-Trait Anxiety Inventory,* ***STAI-T:*** *trait anxiety subscale in the Spielberger State-Trait Anxiety Inventory,* ***MACCE****: major adverse cardiac and cerebral event*

	Survivors (N = 138)		**Death (N = 42)**		
	Mean/N	**(SD)/%**	**Mean/N**	**(SD)/%**	**p value**
Preoperative factors					
Age (years)	56.9	(10.5)	60.9	(7.9)	**0.02**
Diabetes	28	20.3%	11	26.2%	**0.04**
Hypertension	57	41.3%	18	42.9%	0.76
Hyperlipidaemia	54	39.1%	12	28.6%	**0.03**
Peripheral vascular disease	16	11.6%	9	21.4%	0.09
Arrhythmia	29	21.0%	9	21.4%	0.89
Reoperation	5	3.6%	6	14.3%	0.21
Psychiatric treatment	14	10.1%	12	28.6%	**0.003**

	Survivors (N = 138)		Death (N = 42)		
	Mean/N	**(SD)/%**	**Mean/N**	**(SD)/%**	**p value**
Anxiolytics/ antidepressants	61	44.2%	12	28.6%	**0.02**
Perioperative factors					
CPB time (min)	72.1	(47.7)	88.2	(46.1)	0.05
EUROSCORE (additive)	3.1	(2.3)	4.5	(2.6)	**0.002**
ICU stay (days)	1.4	(1.1)	5.4	(11.6)	**0.001**
Hospital stay (days)	8.9	(3.4)	11.6	(13.8)	**0.04**
Preoperative psychosocial factors					
BDI	8.7	(5.7)	13.6	(9.8)	**<0.001**
STAI-S	43.7	(10.8)	48.5	(12.5)	**0.02**
STAI-T	42.7	(9.2)	51.1	(9.8)	**<0.001**
School years	11.4	(3.1)	9.5	(2.6)	**<0.001**
Postdischarge factors					
MACCE	42	30.4%	36	85.7%	**<0.001**
Arrhythmia	29	21.0%	9	22.0%	0.90
Malignancy	0	0.0%	4	9.5%	**<0.001**
Rehospitalisation	50	39.7%	22	88.0%	**<0.001**
BDI (mean)	7.8	(5.5)	14.2	(10.1)	**0.004**
STAI-T (mean)	40.7	(9.2)	48.5	(12.7)	**0.004**

The BDI ($r = 0.64$; $p < 0.001$) and STAI-T ($r = 0.67$; $p < 0.001$) scores measured before and after surgery in the same patients showed a strong correlation (Figures 4 and 5). There was no significant difference between the pre- and the mean post-discharge STAI-T (-0.48 vs. -1.49; $p = 0.37$) and BDI (-0.83 vs. -0.12; $p = 0.58$) points in survivals and non survivals. This means that anxiety and depression measured before and after surgery did not change during follow-up. We found no interaction between anxiolytics, psychiatric treatment, BDI and STAI-T scores (data not shown).

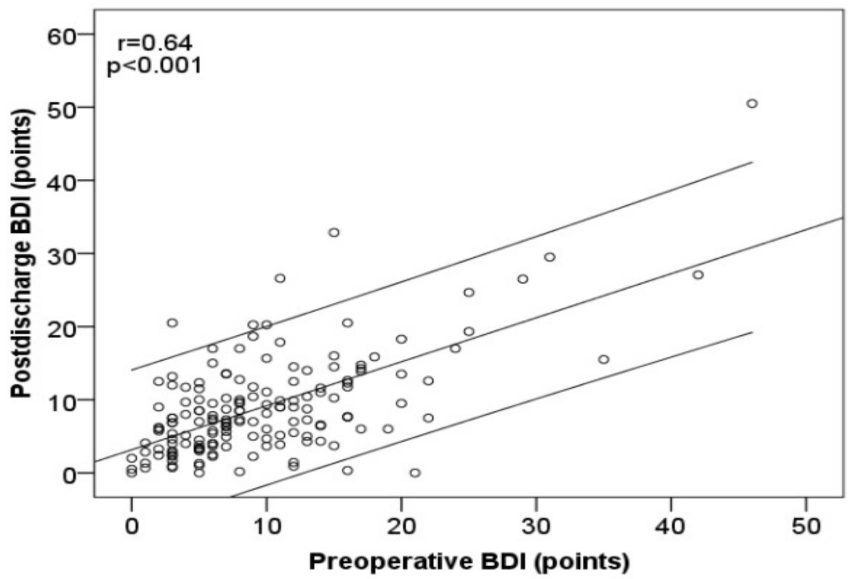

Figure 4. **The figure shows the correlation between the preoperative and mean of post-discharge BDI points. The line shows correlation and the 95% C.I.**

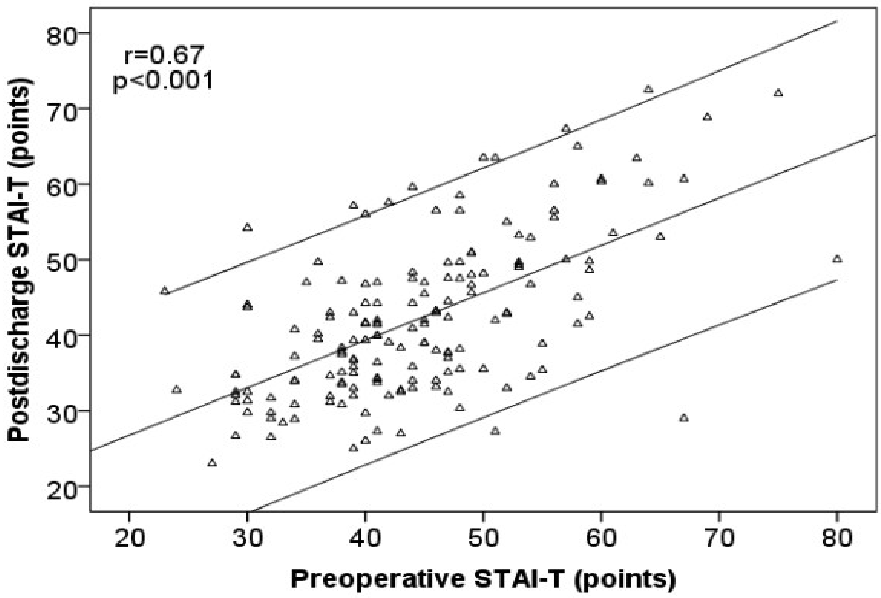

Figure 5. **The figure shows the correlation between the preoperative and mean of post-discharge STAI-T points. The line shows correlation and the 95% C.I.**

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 6). Survival was strongly influenced by education. The mean survival time for patients with academic degree was 8.01 years (95% C.I.: 7.37-8.65), the mean survival time for patients with 9-12 years of education was 7.73 years (95% C.I.: 7.31-8.16) and the mean survival time for the group with 8 years of education or less was 7.03 years (95% C.I.: 6.41-7.64). In the survival analysis, there were significant differences between patients with 8 years or less of education and patients with 8-12 years of education (P = 0.032) and patients with academic degree (P = 0.006). Patients with lower levels of education had worse life expectancy. There was no significant difference between patients with 9-12 years of education and those with academic degree (P = 0.18).

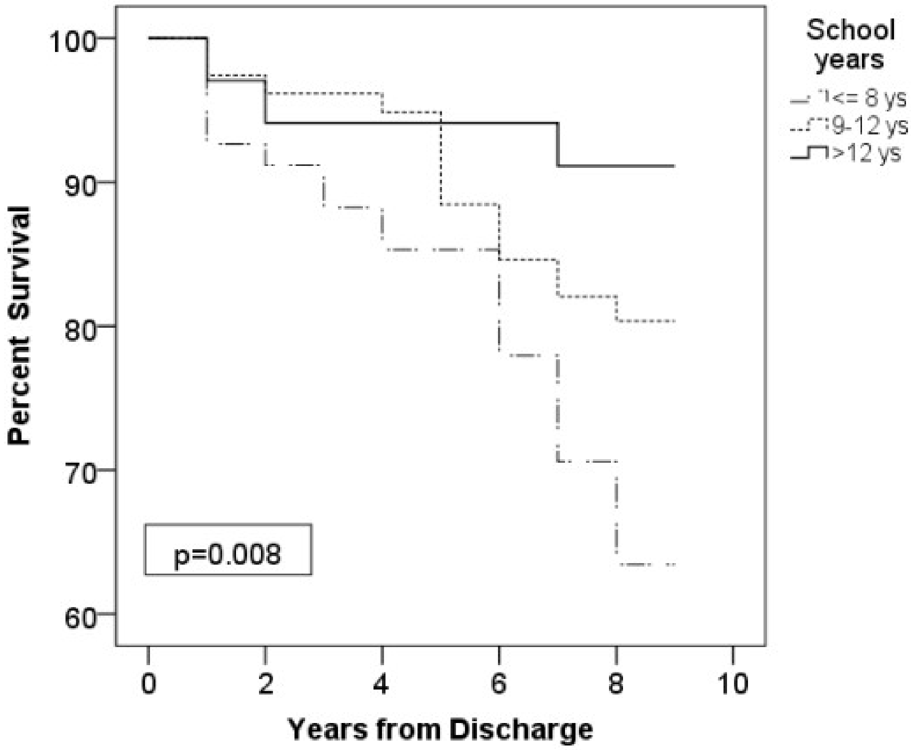

Figure 6. Kaplan-Meier analysis by education level. *Time after discharge is plotted against percent survival.*

In the perioperative and post-discharge multivariable Cox models, the additive EUROSCORE, preoperative STAI-T score, school years and MACCE prevalence were independently associated with mortality (Table 6). In the multivariable Cox regression model, patients were categorized as 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, (STAI-T ≥40), 14 (7.7%) patients had depression (BDI ≥10) and 65 (35.9%) patients had both anxiety and depression. When survivors and deaths were compared, patients with anxiety and patients with anxiety and depression combined had a significantly higher risk of death (Table 7). Patients with a high EUROSCORE, low education and MACCE were also more likely to die.

Table 6. Cox model adjusted for medical and psychosocial factors-perioperative and post-discharge model

Perioperative variables with $p < 0.20$ in univariate analysis were used in the Cox regression model. The first model is the perioperative model and the second is the postdischarge model. The c-index of the perioperative model was 0.697 before and 0.685 after bootstrapping. The c-index of the postdischarge model was 0.691 before and 0.681 after bootstrapping. ***B:*** *regression coefficient,* ***C.I.****: confidence interval,* ***STAI-T:*** *trait anxiety subscale in the Spielberger State-Trait Anxiety Inventory,* ***MACCE****: major adverse cardiac and cerebral event*

	B	Adjusted hazard ratio	(95.0% C.I.)	p value
Perioperative model				
Euroscore (Additive, points)	0.222	1.25	(1.10-1.41)	**0.001**
Preoperative STAI-T (points)	0.054	1.06	(1.02-1.09)	**0.001**
School years	−0.181	0.83	(0.73-0.95)	**0.008**
MACCE	1.946	6.99	(2.99-16.89)	**0.001**
Post-discharge model				
Euroscore (Additive, points)	0.264	1.30	(1.07-1.58)	**0.009**
Preoperative STAI-T (points)	0.055	1.06	(1.02-1.09)	**0.002**
School years	−0.156	0.86	(0.74-0.98)	**0.038**
MACCE	1.980	7.24	(2.65-19.66)	**<0.001**

Table 7. Multivariable Cox regression model for medical factors, anxiety and depression

Perioperative variables with $p < 0.20$ in univariate analysis were used in the Cox regression model. The c-index of the model was 0.697 before and 0.685 after bootstrapping. ***B:*** *regression coefficient,* ***C.I.****: confidence interval,* ***MACCE****: major adverse cardiac and cerebral event*

	B	Adjusted hazard ratio	(95.0% C.I.)	p value
Euroscore	0.166	1.18	(1.05-1.33)	**0.007**
School years	−0.191	0.83	(0.72-0.95)	**0.008**
MACCE	2.057	7.82	(3.02-20.27)	**<0.001**
Anxiety	1.401	4.06	(1.16-14.20)	**0.028**
Depression	−11.281	0.82	(0.42-1.63)	0.98
Anxiety + Depression	1.588	4.93	(1.45-16.68)	**0.01**

4.3. Length of stay in intensive care and hospital following cardiac surgery

Data from 267 (41.5%) of the 644 eligible patients were analysed. The mean age was 60.3 years (SD: 8.9 years) and 73% of the patients were male. The most common preoperative conditions were hypertension, hyperlipidemia, previous myocardial infarction, diabetes and arrhythmia. There were more CABG surgeries than valve, the majority of the surgeries were off-pump. Four patients (1.5%) died after surgery and the most common complication was bleeding (Table 8).

Table 8. Pre- and perioperative characteristic of participants

N: *number,* ***IQR****: Interquartile range;* ***SD****: standard deviation;* ***BMI****: body mass index;* ***COPD****: Chronic obstructive pulmonary disease;* ***NYHA****: New York Heart Association heart failure severity class;* ***CABG****: Coronary artery bypass grafting.*

	N=267	
	N/median/mean	**%/(IQR)/SD**
Preoperative factors		
Age (years)	60.3	8.9
Male	194	73.0%
Female	73	27.0%
Body weight (kg)	81.9	14.5
BMI (kg/m^2)	27.9	4.3
Medical history		

	N=267	
	N/median/mean	**%/(IQR)/SD**
Hypertension	204	76.4%
Diabetes	66	24.7%
Myocardial infarction	84	31.5%
Arrhythmia	62	23.2%
Hyperlipidemia	156	58.4%
Kidney failure	25	9.3%
COPD	37	13.8%
Gastrointestinal disease	57	21.3%
NYHA III/IV	30	11.2%
Atrial fibrillation	39	14.6%
Stroke	8	3.0%
Peripheral arterial disease	23	8.6%
Pulmonary hypertension	17	6.4%
Perioperative factors		
Valvular disease	101	37.8%
CABG	174	61.4%
Complex procedure	21	7.9%
Operation time	133	(110-160)
Cardiopulmonary bypass time	37	(0-71)
Off-pump procedure	147	55.1%
Surgeon A/B/C/D/E/F/G/H/ ,J,K	24/13/39/13/87/37/13/33/ 9	9.8/5.9/15.1/4.8/26.1/17.3/6.8/11.1/ 2.6
Postoperative complication		
Death	4	1.5%
Dialysis	6	2.2%
Intra-aortic balloon pump	11	4.1%
Mechanical ventilation for more than 48 hours	12	4.5%
Bleeding	20	7.5%
Acute myocardial infarction	7	2.6%
Sepsis	9	3.4%
Liver failure	9	3.4%
Multiple organ failure	5	1.9%
Neurological disorder	10	3.7%
Hospital days	9.5	6.2

The median length of stay in the ICU was 1 day (range = 0-46 days). Those who spent 3 or more days in the ICU were treated for 839 days out of total of 1,437 days (58.4%). The mean hospital stay was 9.55 days (SD: 6.22) and 62 patients (23.3%) spent more than 10 days in the hospital. There were no significant differences between the two groups in age and BMI; patients with longer hospital stays had longer operation time, longer ICU stays and more complications in the ICU. These patients were more likely to have preoperative arrhythmia, COPD, NYHA III/IV, and had more postoperative complications like need for IABP, respiratory failure, neurological disorder (any new neurological deficit after surgery), sepsis and need for antidepressant use. More of them were female patients (Table 9).

Table 9. Hospital stay

__N:__ number, __SD__: standard deviation; __BMI__: body mass index; __COPD__: Chronic obstructive pulmonary disease; __NYHA__: New York Heart Association heart failure severity class; __CABG__: Coronary artery bypass grafting; __IABP__: intraaortic balloon pump, __ICU__: Intensive Care Unit.

	Hospital stay < 10days N/mean (%/SD)	Hospital stay ≥10 days N/mean (%/SD)	p value
Age	59.8 (9.3)	62.1 (7.2)	0.39
Female	49 (23.9%)	24 (38.7%)	**0.02**
BMI	28.0 (4.2)	27.5 (4.5)	0.43
Hypertension	160 (78.4%)	44 (71.0%)	0.22
Diabetes mellitus	52 (25.4%)	14 (22.6%)	0.66
Arrhythmia	41 (20.0%)	21 (33.9%)	**0.02**
Hyperlipidemia	122 (59.5%)	34 (54.8%)	0.51
Renal failure	18 (8.8%)	7 (11.3%)	0.55
COPD	19 (9.3%)	18 (29.0%)	**<0.001**
NYHA III/IV	14 (6.8%)	16 (25.8%)	**<0.001**
Stroke	6 (2.9%)	2 (3.2%)	0.90
Perioperative factors			
Operation time	134.0 (40.2)	166.9 (74.6)	**0.001**
Off pump	118 (80.0%)	29 (19.7%)	0.14
CABG	137 (78.7%)	37 (21.3%)	0.30
Valve surgery	72 (71.3%)	29 (28.7%)	0.10
Postoperative factors			
ICU days	1.46 (3.0)	5.54 (9.2)	**0.001**
IABP	5 (2.4%)	6 (9.7%)	**0.012**

	Hospital stay < 10days N/mean (%/SD)	Hospital stay ≥10 days N/mean (%/SD)	p value
Respiratory failure	4 (2.0%)	8 (12.9%)	**<0.001**
Bleeding	12 (5.9%)	8 (12.9%)	0.07
Neurological disorder	3 (1.5%)	7 (11.3%)	**<0.001**
Sepsis	2 (1.0%)	5 (8.1%)	**0.002**
Antidepressant therapy	3 (1.5%)	6 (9.7%)	**0.002**

We also investigated the relationship between 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, $p < 0.001$). Similar inverse correlations were found between happiness and STAI-T scores (r: −0.51, $p < 0.001$). SRH showed no correlation with either test. Patients with an ICU stay equal to or longer than 3 days had lower SRH and lower happiness scores but higher BDI scores. Preoperative smoking, education level and living alone did not influence the length of ICU stay. After controlling for medical and sociodemographic factors, lower SRH, lower happiness, longer operation time, higher NYHA classes and the occurrence of severe COPD were independently associated with longer ICU stay (Table 10). We adjusted for medical factors, including age, sex, NYHA class, diabetes, complex surgery, operation time. The c-index for the multivariate model was 0.72, 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.

Table 10. Multivariable model for ICU stay

***C.I.**: confidence interval; **COPD**: chronic obstructive pulmonary disease; **NYHA**: New York Heart Association heart failure severity class, **SRH**: Self-rated health. P<0.05 indicates significance and is highlighted in bold.*

	Adjusted odds ratio	95 %C.I.	p value
COPD	3.34	1.30-8.56	**0.012**
NYHA III/IV	2.99	1.06-8.42	**0.038**
Operation time (30 min)	1.41	1.14-1.75	**0.001**
SRH (points)	0.60	0.36-0.99	**0.045**
Happiness (points)	0.84	0.71-0.98	**0.032**

Long hospital stays (10 days or more) were associated with NYHA severity, COPD, longer operation time and female sex. Among psychosocial factors, SRH remained a predictor (Table 11). The addition of 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, Hosmer-Lemeshow chi-square test = 6.8, p = 0.55.

Table 11. Multivariable model for hospital stay longer than 10 days

***C.I.**: confidence interval; **COPD:** chronic obstructive pulmonary disease; **NYHA:** New York Heart Association heart failure severity class; **SRH**: Self-rated health. P<0.05 indicates significance and is highlighted in bold*

	Adjusted odds ratio	95 %C.I.	p value
COPD	4.56	1.95-10.67	**<0.001**
NYHA III/IV	6.76	2.57-17.79	**<0.001**
Operation time (30 min)	1.45	1.19-1.76	**<0.001**
Female gender	2.16	1.06-4.40	**0.03**
SRH	0.63	0.41-0.99	**0.04**

5. DISCUSSION

5.1. Major adverse cardiac and cerebrovascular events after cardiac surgery

After adjusting for biomedical factors and perioperative variables after heart surgery, we found that psychosocial factors, such as SRH, illness intrusiveness, depression, anxiety, sleeping disorders, social inhibition, and negative affectivity, assessed by standardized questionnaires, had an independent correlation with the occurrence of MACCE. This finding supported our first hypothesis.

Secondly, our assumption regarding test variability over time was proved correct: in MACCE positive patients, the severity of illness intrusiveness, sleeping problems and social inhibition increased during the three-year period; these trends 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 2 to year 5. Both groups reported less social support at the end of year 5. The MACCE positive group had higher BDI, STAI-S and T test scores at baseline than the negative group, and this difference was retained over the entire observation period (63).

According to epidemiological research, psychological variables including anxiety and depressive symptoms are crucial to the onset and progression of CVD and have an impact on the long-term results following cardiac surgery, whether it is performed on or off pump. (64). However, time spent on the waiting list has been linked to anxiety and depression (65). Studies have shown that preoperative depression is a significant risk factor for mortality and rehospitalisation after CABG. This link between depression and poor prognosis indicates that depression may precede surgery and persist after major cardiac surgery (66). A large US study revealed that depression increased mortality risk following cardiac surgery by two to threefold, after adjusting for tobacco use, age, sex, diabetes, previous myocardial infarction, number of grafts and left ventricular ejection fraction (5). In other research, depression has also been identified as a separate risk factor for death after CABG (67, 68). The authors of an international investigation conducted in Australia on 158 patients having CABG with or without concomitant valve surgery demonstrated that preoperative generalized anxiety was a significant predictor of postoperative cardio- and cerebrovascular complications (69).

In accordance with these findings, we found that the MACCE positive group had higher levels of depression and anxiety in the preoperative period. These psychological factors not only contribute to a poor or extended recovery but can also be used as indicators of failure to adapt to stressful conditions such as major cardiac surgery. These ideas of psychosocial susceptibility could help to explain our observation that there was no significant change in BDI and STAI-T scores over the period of the three years. Sleeping problems and social inhibition as traditional symptoms of depression and anxiety were frequent in the MACCE positive group, which provides support for this concept (63).

Socially inhibited patients are difficult to treat because they are not aware that they need help. And if they do not feel they need it, they have little motivation to change. On the other hand, negative affectivity and social inhibition are two different components of the Type D personality construct, and both are linked to a higher risk of affective distress in individuals with cardiovascular disease (38). In our study, patients with Type D personality had a two fold adjusted risk of an adverse event at the end of the fifth year. Scores of illness intrusiveness, sleeping disorders and social inhibition were increased solely in MACCE positive patients. This indicates that the patient's personality might interfere with their ability to recover completely and perhaps lead to the development of serious adverse events. (63). Numerous studies have demonstrated the clinical significance of type D personality as a predictor of the intensity and persistence of anxiety in individuals with cardiac disease. There is a strong correlation between the two components of Type D and the various forms of anxiety. Comparing individuals with type D personality to those with merely high negative affectivity or high social inhibition, type D personality can also result in significantly higher depression and negative mood ratings as well as lower positive mood scores (38).

Both groups reported less social support during the three-year observation period (63). As the date of the heart surgery recedes, the difficult, stressful period ends. During this time, patients learn to cope and become less dependent on the help of others. CABG patients who have the suppor of their family, especially their spouse, recover faster than those who do not (70).

Simple question on self-rated health was a powerful predictor for mortality and stroke (71). Similarly, it has been suggested that illness intrusiveness can be utilized to assess the effectiveness of treatments and important, life-altering aspects of disease. (72). Accordingly, after adjusting for biological variables, we showed that SRH and illness intrusiveness were relevant to our study population and that both tests were independently linked to a higher risk of MACCE (63).

The current study contains a set of limitations. For example, to more accurately evaluate the impact of various psychological factors on long-term mortality and morbidity, a larger and more homogeneous patient sample is required. Furthermore, this statistical approach could not be used to analyze the frequency of rehospitalization. Since multiplicity was not taken into account in some comparisons, the likelihood of type I error is higher than the stated 5%. One more limitation is that most surveys were sent at the end of the second and fifth year, and not all questions were completed at all times. Unfortunately, we only measured the BDI, STAI-S and STAI-T at baseline. Another concern was that no information was collected on lifestyle variables or postoperative rehabilitation, despite the fact that rehabilitation may theoretically lower the prevalence of MACCE shown in this study. On a voluntary basis, patients were offered six weeks of cardiac rehabilitation immediately after discharge. Approximately 5% of the over-aged post-cardiac population participated in rehabilitation, which focused on stepwise physical load and dietary education (63).

Based on our results, several articles were published, some of which are highlighted below. Dennolet and colleagues investigated whether cardiac events in CVD are associated with a combination of negative affectivity and social inhibition, or whether they are the main effect of one of these components alone. A specific combination of emotional distress and inhibition was associated with an increased risk of adverse events, not the separate effect of either trait (73). Tully and his colleagues screened patients for depression after cardiac surgery using the Patient Health Questionnaire. Patients were divided into three groups; depressed (current antidepressant use or history of depression), depression screen-positive and depression screen-negative. The incidence with major adverse cardiac events, hospital readmissions, quality of life, symptomatic depression, and the use of psychotherapy, anxiolytics, and antidepressants were evaluated for each of the three groups after a 6-month follow-up. At six months, the depression-screening-positive group had a six-fold higher risk of depressive symptoms than the depression-control group, which had a three-fold higher risk. They were about five times more likely to have been prescribed psychotropic drugs (74). The primary psychological and social factors influencing postoperative outcomes in patients undergoing vascular surgery were the focus of Szabó's and his coauthors' investigation. Postoperative mortality was found to be independently correlated with cognitive impairment as assessed by Mini Mental State Examination scores. The study team could not show a relationship between the 4-year all-cause mortality and the observed BDI or STAI scores (75).

5.2. Long term survival after cardiac surgery

During 7.5 years of follow-up following heart surgery, we showed that STAI-T scores and poor education level were related to a greater risk of mortality after controlling for medical variables and post-discharge major cardiac events, and consequently our first hypothesis was proven. Non survivors had higher BDI and STAI-T points pre- and postoperatively than survivors. Our second hypothesis was confirmed: within groups, BDI and STAI-T scores before and after surgery were correlated (e.g. those with high preoperative BDI had high postoperative BDI scores, etc.) and did not change during follow-up (76), so the third hypothesis was rejected .

The role of preoperative anxiety and depression in the mortality following heart surgery has been highlighted by numerous research (5, 77, 78). It has long been known that anxiety and depression are related. Studies investigating the pathophysiological relationships between negative emotions and ischemic heart disease have demonstrated that anxiety and depression share several similarities in their effects on coronary events, such as elevated levels of catecholamines, markers of autonomic dysfunction, elevated platelet activity, and subacute chronic inflammation (79). Even though there are several risk factors and a high co-morbidity between anxiety and depression, anxiety is a distinct emotional experience. Symptoms of anxiety may increase the risk of CVD (80), and anxiety is associated with a higher incidence of myocardial infarction and fatal ischemic heart disease after CABG (78). In a recent study of 180 patients investigating the effect of elective cardiac surgery on health-related quality of life, the STAI-T and S were found to be high both preoperatively and 6 months postoperatively. The authors found no significant reduction in trait anxiety levels after surgery. The authors suggest that assessing anxiety using the STAI may help in risk stratification and prediciton of health-related quality of life after surgery (81).

Depression is a common comorbidity in patients with CVD (5). After heart surgery, the prevalence of preoperative depression varies from 20 to 47%, while postoperative depression varies from 23 to 61%. The methods used to detect depression (questionnaires, psychiatric interviews), the criteria used to diagnose depression, and the follow-up after surgery differ, which accounts for the difference in the prevalence of depression before and after surgery. Patients may often complain of sleeplessness and exhaustion, which can make it difficult to differentiate between depression and these symptoms. The same pathophysiological mechanisms underlie preoperative and postoperative depression and may be associated with poor clinical outcomes. It's important to keep checking on the patient's mental state following surgery. Following surgery, a decrease in depressive symptoms is expected, which is linked to an enhanced quality of life. On the other hand, an increased risk of complications or major adverse cardiovascular events is linked to a rise in postoperative depression (82).

In our study group, survivors were more frequently treated with anxiolytics and/or antidepressants than those who died during follow-up. However, levels of anxiety and depression remained high in the study population. Further research is needed to identify the factors responsible for consistently high STAI-T and BDI scores (76).

Current risk prediction models classify individuals according to their predicted risk and match treatment to the classes most likely to benefit from it. Nonetheless, even though they may have very diverse combinations of risk variables, individuals who share the same estimated mortality risk probably shouldn't be treated similarly. It has long been believed that biological factors, which risk evaluation objectively quantifies, are the source of the risk of poor outcomes in heart surgery, ignoring other relevant aspects (e.g. emotional and social components) (83).

We used the additive EUROSCORE to estimate the risk of cardiac surgery (49). The risk model may be improved by including anxiety and education in order to identify additional risk factors linked to higher mortality. Preoperative screening for anxiety is crucial in everyday clinical practice, as evidenced by our finding that preoperative STAI-T scores were linked to an increase in 7.5-year mortality (76).

For patients with history of a myocardial infarction, low income and education levels are significant predictors of cardiovascular and all-cause death (84). A greater risk profile and subpar care are associated with low income and low education (85). This is supported by the finding that longer survival was linked to better education in our study (76). Patients with greater education levels typically earn more money, allowing them to engage in more costly sports and "healthy" diets (84). In a similar study of cardiac surgery patients, social and emotional factors associated with poor outcome were tested as prognostic factors. Low educational level and income were predictors of prolonged hospitalisation along with living alone. Following cardiac surgery prolonged ICU stay and readmission were also associated with living alone (83). These findings suggest that surgically successful heart surgery is not always associated with improved individual life outcomes (5).

Our study's limited sample size and thus low statistical power are its main limitations. However, the study's findings have been supported by the statistical approach that was applied. The results, however, might not apply to patient populations that are comparable because the study was limited to a single center. Additionally, we did not include patients who were unable complete the surveys and those who underwent emergency surgery or concomitant interventions, suggesting that our results may not be generalisable to patients with higher risk. There was no documentation of smoking history, actual blood pressure, or post-discharge medication during the follow-up period. We also cannot rule out the possibility that information from nonresponders changed the outcome. The study's strength is that it evaluated educational attainment in addition to anxiety. Furthermore, data is collected prospectively, and this study offers long-term follow-up. The model created and validated in this study may have important clinical implications, as it provides an estimate of the risk of mortality for each patient before surgery. We included patients having CABG and/or valve surgery, which could potentially have an impact on our findings (76) altough, a prior study found no appreciable differences in hospital-specific mortality and morbidity (86). However, in octogenarians, CABG+valve surgery was associated with an increased risk of in-hospital mortality (87). The risk-increasing role of psychosocial factors in the CVD population has been significantly more often proven in the literature than in the surgical population.

Our results have led to a number of publications, some of which with clinical relevance are presented here in a non-exhaustive list. A multicentre prospective study investigated HADS before and one year after elective CABG. All-cause mortality was assessed at 11 years after surgery. In both men and women, depression symptoms one year following surgery were linked to mortality. In general, anxiety symptoms prior to surgery did not correspond with death; however, among women, anxiety symptoms following surgery were predictive of death at 11 years (88).

An Italian study, based on American Heart Association guidelines, assessed inpatients in a CVD prevention and treatment unit for depression and anxiety. All patients who scored above the cut-off point for depression, anxiety or both were given the opportunity to undergo additional psychological testing by a licensed clinical psychologist and offered personalised support if needed. This study has demonstrated the need to apply a short screening procedure in the hospitals, where psychologists, in team work with doctors, give real bio-mental-social support to patients. Extensive therapeutic interventions could improve patients' adherence to treatment, quality of life and reduce hospital length of stay and associated costs (89).

In Pakistan, researchers screened 136 patients awaiting CABG for anxiety; of these, 80 patients had anxiety. Patients with anxiety received preoperative nursing education, which significantly reduced anxiety levels (90). In a similar study of open-heart surgery patients in Iran, patients in the control group received routine care, while patients in the study group received training based on needs assessment besides routine care. Patients received comprehensive information about the need for surgery, when and how it would be performed, how it would affect their health and quality of life, pre- and post-operative care (including diet, wound healing, and observation), potential complications from the procedure, and the medications used and their side effects. Consequently, the intervention group had a significant decrease in both state and trait anxiety (91).

5.3. Length of stay in intensive care and hospital after heart surgery

We demonstrated that an ICU stay of three days or more following heart surgery was significantly correlated with a prolonged operation, high NYHA levels, and severe COPD. After adjusting for medical factors, our first hypothesis was confirmed: the length of an ICU stay was also independently correlated with reduced SRH and poorer happiness scores. Prolonged hospital stays were linked to the same clinical characteristics and female gender, but among psychosocial factors, only SRH was predictive after adjusting for depression and anxiety. Our second hypothesis on correlation resulted in the following: depression and anxiety scores were correlated, depression and happiness showed an inverse correlation. Satisfaction and happiness were strongly correlated, and satisfaction and STAI-T were inversely correlated. In a similar way, the STAI-T scores and happiness showed an inverse relationship. The c-index for ICU stay in the multivariate model was 0.72. The c-index increased to 0.77 when the psychosocial components (BDI, STAI-T, SRH, and happiness) were included in the model. Adding psychosocial factors (BDI, STAI-T, SRH and happiness) to the final multivariate model for prolonged hospital stay improved the c-index from 0.74 to 0.76, confirming our third assumption (92).

Given that the in-hospital mortality rate following heart surgery is typically low (ranging from 2.6% to 6.6% in various studies) (93, 94), a number of research have examined the impact of medical and psychosocial factors on the length of hospital or intensive care unit stays as well as on postoperative complications. Intensive care is a limited and high-cost resource, accounting for the third of total hospital costs. Models exist to predict length of stay, but they are often based on different variables from small cohorts of a particular hospital, and there are little evidence of utility or even clinical practice. Modelling ICU lenght of stay as an outcome variable is difficult. Length of stay is subject to outliers, and neither a conventional definition nor any selection criteria exist for extended lengths of stay (95). Different approaches have been used to predict length of stay in ICU. Scoring tools have been used that indicate the complexity and type of disease, for example APACHE (Acute Physiology and Chronic Health Evaluation). These predictions are dependent on physiological characteristics at the time of ICU admission, therefore they are not always relevant for specific patients. They also frequently need the use of difficult statistics or a model for estimation (96).

In our research, severe COPD, heart failure and long operation time were linked to longer ICU stay. COPD is a major contributor to mortality and morbidity in cardiac surgery patients (92). Need for re-intubation or mechanical ventilation for a longer period after surgery increased mortality risk by 50%. COPD patients who were undergone CABG surgery with cardiopulmonary bypass are at greater risk for respiratory failure requiring reintubation or prolonged mechanical ventilation and postoperative complications: respiratory failure, pneumonia, wound infection, stroke, renal failure and require longer ICU and hospital stays after surgery (97). In patients of advanced age, the ventilatory reaction to hypoxia and hypercapnia is reduced and may be increased when respiratory depressants (opioids and inhaled drugs) are given. Furthermore, closing capacity increases with age, reaching functional residual capacity in the lying position at age 45 and in the standing position at age 65. This exaggerates the ventilation–perfusion mismatch, resulting in a decrease in arterial PaO_2. The above facts make the elderly more prone to postoperative hypoxemia. Regarding cardiac dysfunction, a lower left ventricular ejection fraction may cause elevated filling pressures and low cardiac output, which may result in higher hemodynamic instability and postoperative complications (98). In addition, long-term overloading of the respiratory muscles can lead to postoperative respiratory failure (99). In a prospective study, patients undergoing on-pump CABG surgery were analysed regarding for factors influencing the rate of low cardiac output syndrome. The incidence of low cardiac output syndrome was 21.5% after CABG. A significant rate of postoperative low cardiac output syndrome was linked to preoperative left ventricular dysfunction. Compared to patients without low cardiac output syndrome, postoperative patients with this condition experienced significantly longer hospitalizations in the intensive care unit and hospital as well as increased incidence of stroke, death, acute renal injury, and respiratory failure (100). In a large, multicentre international study, six-year data from 2016 to 2022 were analysed by 3 ejection fraction (EF) subgroups. The mortality of the EF ≤20%, EF 21%-35% and EF >35% cohorts was 6.9%, 3.7% and 1.6%, respectively. Patients with EF ≤20% required mechanical support, blood products, and cardiopulmonary bypass more frequently, and a higher rate of complications. In addition, the subgroup with EF ≤20% had significantly higher length of stay, number of hours spent in the ICU, number of readmissions to the ICU and hospital and the lowest discharge rate (101). In traditional on-pump CABG, global cold ischaemia duration >91 minutes with cardiopulmonary bypass time is known to be a risk factor for prolonged ventilation and thus longer ICU stay (98). In a small study, 274 patients with three vessel disease were assigned to on- and off-pump groups. Among several outcome variables, the prevalence of MACCE, lenght of ICU and hospital stay were investigated, and the results were comparable, with no difference between the two groups (102). In our study, female gender was found to be an independent risk factor for prolonged hospital stay (92). Women are more likely than males to experience short-term mortality and postoperative stroke following CABG and valve surgery combined with CABG, according to a meta-analysis. Regarding the replacement of the isolated aortic valve, there was no difference. In both sexes, long-term mortality is equal (103). It has been proposed that the higher death rate in women may be due to more severe illness, higher morbidity at presentation, smaller body surface area, and smaller coronary arteries, albeit the rationale is debatable (104, 105, 106). To reduce length of ICU/hospital stay, complications, readmission rates and costs, Enhanced Recovery After Cardiac Surgery guidelines have been invented. The pre-, intra and postoperative applied interventions have led to benefitial results and need to be spread among cardiac centers (107).

The main finding of the study is that low SRH and lower happiness significantly predicted prolonged ICU stay. Low SRH was also associated with longer hospital stay. Because each assessment just requires one question and a brief response time, it is a rapid, non-invasive tool for clinicians to use prior to surgery (92). Consistent with previous findings, SRH was associated with mortality after controlling for a wide range of health measures and mortality risk factors (22). In our study, SRH was an independent but not exclusive predictor of longer ICU and hospital stay (92).

It is still challenging to predict whether a critically ill patient would require a long ICU and hospital stay (and thus higher risk of morbidity and mortality). However, there are clear benefits to identifying patients who do not require ICU therapy. Individuals' subjective, broad perception of their health is known as SRH (108). SRH is associated with disease burden, mental health and social context. It goes beyond the disease-free model of health. SRH impacts health-related behaviors affecting outcomes and provides coping mechanisms (23). Numerous studies have demonstrated the predictive ability of SRH in older populations with regard for foreseeable health status, functional decline, and death. SRH is a broad measure of general health state (109). Consequently, we advise adding the SRH score as an extra outcome measure to clinical trials and clinical practice (92). Besides its important predictive value, SRH also provides an opportunity for intervention. In an intervention study on the effect of counselling on SRH in cardiac patients, the authors reported that among anxious hospitalized individuals, there were notable improvements in SRH. The treatment could be a useful complement to an existing illness management program, according to the scientists (110).

When people are seriously ill or in pain, they are less happy. Exploring the link between happiness and health is important for several reasons. Not being depressed or anxious does not mean that one is happy. Happiness has the potential for intervention. If happiness promotes health, then techniques to improve well-being can have a positive impact on disease outcomes. Evidence showes that positive emotions, such as happiness, are associated with many health outcomes, including longer life expectancy. Positive emotions are inversely related to CVD risk. A Canadian study investigated young adults in order to determine whether baseline feelings of happiness over a 20-year period were linked to improved cardiovascular health. Over an extended period of time, positive emotions during early and middle adulthood were associated with improved cardiovasular health. Baseline cardiovascular health was also related to positive emotions during follow-up (111). Many factors appear to contribute to happiness or, more generally, subjective well-being (e.g. genetics, personality, education, socioeconomic status, social network, family). In the entire population and those with a confirmed diagnosis, a number of prospective observational studies have demonstrated a correlation between lower mortality and subjective well-being. Initial depression or negative affect measures were added to regression models to determine whether the magnitude of the correlation is decreasing or disappearing entirely, to investigate whether or not the defensive effect of higher subjective well-being is independent of depression or distress (112). There is evidence that depression is responsible for the association between well-being and lifespan (113), but there is also evidence to the contrary: depression and other negative states do not influence the link between well-being and survival (114, 115, 116). According to Steptoe and colleagues, the neuroendocrine, inflammatory, immunological, and cardiovascular systems may all benefit directly from pleasant feelings (117). It's possible that behavioral pathways play a role in mediating the relationship between positive psychological well-being and mortality. Positive attitudes are linked to longer survival predictors, such as quitting smoking, frequent exercise, consuming less alcohol, and getting better sleep. Psychologically balanced individuals may have higher adherence to medical treatment, as an inverse relationship between treatment adherence and depression has been described. Evidence has shown that other pathways may also play a role, for example direct physiological pathways. Joyful feelings increase parasympathetic activation and decrease sympathetic nervous system activity, which reduces susceptibility to illness. The strongest evidence suggests that reduced cortisol levels (a marker of reduced vulnerability to disease) are linked to well-being. Evidence for a link between happiness and lower inflammation is less consistent. Studies have shown different correlations between C-reactive protein and interleukin 6, with some demonstrating a reverse relationship in males and others in women (112). Metaanalyses of relationships between well-being and blood pressure have reported heterogenous results, although long term studies have revealed that psychological well-being is prospectively related to lower blood pressure (24). We showed that lower ratings of happiness significantly predicted longer ICU stay. Low levels of positive emotions do not necessary indicate depression and vice versa, since we found only a moderate inverse correlation between depression and happiness; however, the inverse correlation was stronger between anxiety and happiness (92). Anxiety is a known risk factor for cardiac mortality (78, 118). Happiness has the opposite effect of anxiety, which is known to enhance sympathetic activity and has negative effects on the cardiovascular system (119). Our second hypothesis regarding associations among different emotions and emotional distress could be confirmed.

The relationship between higher levels of depression (BDI > 10 points) and longer postoperative hospital stay in univariate analysis (92) is consistent with associations shown in previous cardiac research (120, 121, 122), however this could not be detected in multivariable analysis using continuous variables and adjusted for postoperative complications (92). Assuming that sadness plays a role, it might take longer for an unfavorable event to occur following heart surgery than, for example, five years following the procedure (123).

There are several limitations to this study, the most significant of which are the small sample size and the 42% of the population that declined to participate. In addition to having higher risk ratings, non-participants were more likely to be female and had higher prevalence rates of gastrointestinal disorders, stroke, diabetes, hypertension, and arrhythmia. Because SRH and happiness may be assumed to have been lower in non-participants, the current results may thus actually undervalue their significance. Institutional variables (number of beds, number of surgical patients, insurance, etc.) may have slightly influenced psychological aspects that predict length of stay in the intensive care unit. Therefore, our sample may not have been representative of the overall cardiac surgery population. Our single-center results require validation in a multicenter, broader population. Additionally, because they were unable to complete the questionnaires, patients with severe psychological or mental comorbidities were not eligible for enrollment in our study. Patients who have had valve surgery, CABG surgery, or both were recruited. The fact that we did not differentiate between these types of surgery in our analyses may have influenced our results, although previous reports have found no significant differences in mortality and morbidity (86), with only octogenarian patients showing differences in in-hospital mortality (87). Given that previous studies conducted in ICUs, hospitals, and prospective settings have assessed varying patient groups and cardiac surgery types, it may be challenging to interpret and integrate our findings. To identify as many predictors in a heterogeneous cardiac population as possible, we used a remarkably large collection of biological and psychological factors. We were unable to exclude the possibility that either sudden changes in health condition or, on the other hand, a chronic illness affected each test's preoperative score. Finally, because our study was entirely observational-that is, we had only one measurement point-we were unable to prove causality (92).

All the questionnaires used have the same problems as other self-report inventories, in that the person completing them can easily exaggerate or minimise the scores. However, they are widely acknowledged in psychological research and are utilized in therapeutic studies, frequently under identical conditions (e.g., before and after tough life situations, as in this case, before and after surgery) (92).

A number of clinical aspects impact how well men rate their overall health. For example, men's self-rating of health is a stronger predictor of death than women's, indicating that men and women have distinct perspectives on health. Obese people may include information on their obesity-related health risk in their assessment, independent of signs and symptoms. Patients with high cholesterol are also influenced by the diagnosis, even though the condition has no symptoms (124).

Results related to our article showed that preoperative anxiety symptoms were associated with longer lenght of stay after cardiac surgery in an Italian study in 2022. They also found an association between preoperative anxiety and depression with lower Health Related Quality of Life 3 months after surgery. The authors recommended a screening routine for symptoms of preoperative anxiety and depression in patients with CVD (125). Iranian researchers focused on clinical factors associated with prolonged ICU stay in their descriptive cross-sectional study. Patients were evaulated for ICU stays of less than 72 hours and more than 72 hours. Factors determining the lenght of ICU stay were older age, long cardiopulmonary bypass time, long intubation, low left ventricular ejection fraction, inotropic therapy, intra-aortic balloon pump use, blood products received and postoperative bleeding (126).

6. CONCLUSIONS

In summary, after controlling for biological variables, a higher incidence of MACCE five years following heart surgery was linked to depression, anxiety, illness intrusiveness, sleeping disorders, social inhibition, and worse SRH. By measuring psychosocial characteristics, it could potentially identify ”candidates” for future rehospitalization sooner and potentially prevent rehospitalization by addressing these risk factors. MACCE positive patients had increased severity of illness intrusiveness, sleeping problems and social inhibition between 2 to 5 years; 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 year five. The MACCE positive group had higher BDI, STAI-S and T test scores at baseline than the negative group, and this difference was maintained throughout the follow-up period. Depressed and anxious patients adapt poorly to stressful situations, like major cardiac surgery, and their altered mood contributes to prolonged or poor recovery. Sleeping problems and social inhibtion 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 more than 2 times the adjusted risk of adverse events at the end of the fifth year. Scores of illness intrusiveness, sleeping disorders and social inhibition were increased solely in MACCE positive patients. This suggests that patient personality may contribute to the development of major adverse events or even complicate recovery.

We found that STAI-T scores and low education level were linked to 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. Consistent with this, higher education level was linked to longer survival. Non-survivors had higher BDI and STAI-T scores before and after surgery than survivors. Within groups, pre- and postoperative BDI and STAI-t scores 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 to estimate the risk of cardiac surgery. The risk model may be further refined by including anxiety and education in relation to risk factors linked to higher mortality. Preoperative screening for anxiety is crucial in everyday clinical practice, as demonstrated by our findings that preoperative STAI-T scores were linked to an increase in 7.5-year mortality. In our study group, survivors were treated more frequently with anxiolytics and/or antidepressants than those who died during follow-up. However, levels of anxiety and depression remained high in the study population.

We found that long operation time, high NYHA levels and severe COPD were significantly associated with an ICU stay equal to or longer than three days after cardiac surgery. After adjustment for medical factors, lower SRH and low happiness levels were also independently associated with length of ICU stay. Longer hospital stay was associated with the same clinical factors and female sex, but among psychosocial factors, only SRH was predictive after adjusting for depression and anxiety. The primary finding of this study is that lower SRH and lower happiness significantly predicted prolonged ICU stay. Low SRH was also associated with longer hospital stay. Because each assessment just requires one question and a brief response time, it is a rapid, non-invasive tool for clinicians to use before surgery. Even after accounting for a large number of health parameters and mortality risk variables, SRH remained linked to mortality. SRH was an independent predictor of prolonged ICU and hospital stays in our study, but it was not the only one. For these reasons, we advise that in clinical trials and in clinical practice, the SRH score be used as a supplemental outcome measure. Apart from its significant predictive value, SRH offers options for intervention. We showed that lower ratings of happiness significantly predicted longer ICU stay. Low levels of positive emotions do not necessary indicate depression and vice versa, since we found only a moderate inverse 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 to complete. Measures of self-rated health, happiness, and depressed and anxious mood have not been studied simultaneously before; thus, this study may fill a gap in the field of emotional factors and chronic stressors in cardiac surgery. The reliability of our risk model for ICU stay and hospital stay with medical factors could be improved by adding psychosocial factors (BDI, STAI-T, SRH and happiness).

7. SUMMARY

In the MACCE study, we found that SRH, illness intrusiveness, depression, anxiety, sleeping disorders, social inhibition and negative affectivity, were independently associated with the occurrence of MACCE events after adjustment for biomedical factors and perioperative variables following cardiac surgery. We also demonstrated that severity of illness intrusiveness, sleeping problems and social inhibition increased in MACCE positive patients between 2 and 5 years, but did not change the event-free group. The MACCE positive group had higher BDI, STAI-S and T-test scores at baseline than the negative group, and this difference was maintained throughout the follow-up period. Both groups reported less social support at the end of year five. In our study, patients with Type D personality had more than 2 times the adjusted risk of adverse events at the end of the fifth year.

In the long term (7.5 years of follow-up after cardiac surgery), we found that STAI-T scores and low education levels were associated with a higher risk of mortality after adjustment for medical factors and MACCE after discharge. In accordance, higher education was associated with longer survival. We used additive EUROSCORE to estimate the risk of cardiac surgery. The risk model may be further refined including anxiety and education in relation to risk factors linked to higher mortality. The significance of preoperative anxiety screening in standard clinical practice is underscored by our findings.

We found that long operation time, high NYHA levels and severe COPD were significantly associated with an ICU stay equal to or longer than three days after cardiac surgery. After adjusting for medical factors, lower SRH and low happiness levels were also independently associated with length of ICU stay. Longer hospital stay was associated with the same clinical factors and female sex, but among psychosocial factors, only SRH remained a predictor after adjusting for depression and anxiety. The reliability of our risk model for ICU/prolonged hospital stay with medical factors could be improved by adding psychosocial factors: BDI, STAI-T, SRH and happiness.

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