# Supplementing prediction by EuroSCORE with social and patient reported measures among patients undergoing cardiac surgery

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**Abstract**

Objectives The risk of poor outcomes is traditionally attributed to biological and physiological processes in cardiac surgery. However, evidence exists that other factors, such as emotional, behavioural, social and functional, are predictive of poor outcomes. Objectives were to evaluate the predictive value of several emotional, social, functional and behavioural factors on four outcomes; death within 90 days, prolonged stay in intensive care, prolonged hospital admission and readmission within 90 days following cardiac surgery. Methods This prospective study included adults undergoing cardiac surgery 2013-2014, including information on register-based socio-economic factors and self-reported health in a nested subsample. Logistic regression analyses to determine the association and incremental value of each candidate predictor variable were conducted. Multiple regression analyses were used to determine the incremental value of each candidate predictor variable, as well as discrimination and calibration based on AUC and Brier score. Results Of 3217 patients, 3% died, 9% had prolonged intensive care stay, 51% had prolonged hospital admission and 39% were readmitted to hospital. Patients living alone (OR, 1.19; 95% CI, 1.02-1.38), with lower educational levels (1.27; 1.04-1.54) and low health-related quality of life (1.43; 1.02-2.01) had prolonged hospital admission. Analyses revealed living alone as predictive of prolonged ICU stay (Brier, 0.08; AUC, 0.68), death (0.03; 0.71) and prolonged hospital admission (0.24; 0.62). Conclusion Living alone was found to supplement EuroSCORE in predicting death, prolonged hospital admission and prolonged ICU stay following cardiac surgery. Low educational level and impaired health-related quality of life were, furthermore, predictive of prolonged hospital admission.

## Introduction

In cardiac surgery, surgical advances and an increasingly older population have resulted in more complex and high-risk patients being offered surgical procedures. Risk assessment in cardiac surgery aims to reduce poor outcomes by including individual differences in patient profiles and surgical complexity, as well as in surgeons' technical performance (1).

There are several prognostic screening tools currently available for patients undergoing cardiac surgery. Established clinical risk factors included are history of previous heart surgery, the severity of coronary artery disease, and the degree of comorbidity. In most of Europe, EuroSCORE (2,3) is used in clinical practice. The total risk is calculated by adding scores from several risk factors (e.g. chronic pulmonary disease, serum creatinine and left ventricular dysfunction) resulting in a predicted percentage of surgical mortality. The score is defined to distinguish low (<3), moderate (3-5) and high-risk (6+) groups (2,3). However, according to several validation studies (4–6) EuroSCORE is inaccurate in predicting mortality rates. Increasing evidence indicates that non-physiological factors, such as patients' emotional, behavioural, social and functional status are predictive of poor outcomes following cardiac surgery (7). Thus, disparities exist in traditional risk assessment in cardiac surgery designed to advise patients of their operative risk of death.

The complex nature of risk assessment and the lack of parameters representing the emotional, social, functional and behavioural lives of patients point toward the need for new definitions of risk and new approaches to risk management in cardiac surgery. The current study is a comprehensive research project developing a risk stratification model as a supplement to EuroSCORE. Emotional, social, functional and behavioural factors will be included to investigate the predictive value on mortality, prolonged stay in the intensive care unit (ICU), prolonged hospitalisation and readmissions within 90 days after cardiac surgery.

The aim of this study is therefore to describe the predictive value of emotional, social, functional and behavioural factors and outcomes of death, prolonged length of stay in the ICU, prolonged length of hospital admission and readmissions following cardiac surgery. The potential predictive factors are tested as a supplement to EuroSCORE.

# Methods

This is a prospective study with follow-up until 90 days after cardiac surgery. The protocol for this study has been published. (8)

## Study population and data sources

Patients having undergone cardiac surgery from April 2013 to 2014, aged 18 or above were eligible for inclusion. Information were obtained through national Danish registers for the total cohort: the Danish National Patient Register (DNPR) (cardiac surgery procedures, length of hospitalisation) (9), the Danish Civil Registration System (date of birth, sex, cohabitation status, migration, vital status) (10), Danish Education Registers (educational level) (11) and the Danish Register on Personal Income (disposable income) (12). Information on socio-economic factors included educational level, income and cohabitation status. Educational level was categorised as basic school ([?]10 years), upper secondary or vocational education, and higher education. Income was categorised in three groups according to median; [?]50%, >50%-150%, and >150%. Cohabitation was defined as being married or living with a partner. Living alone included singles, divorced and widowed.

Furthermore, analyses were done for a nested subsample of patients that participated in the national cross-sectional survey DenHeart (13). All patients discharged from a Danish Heart Centre were asked to fill out a questionnaire at hospital discharge to evaluate patient reported outcomes, reporting information on health-related quality of life (HRQoL), emotional and cognitive functioning, as well as questions about health behaviour. (13).

Information on EuroSCORE and length of ICU stay was received from two clinical databases (14).

### Patient-reported outcomes (DenHeart)

HRQoL was measured using the 12-Item Short-Form Health Survey (SF12) and the HeartQoL questionnaires.

The (SF-12) is a generic measure of self-rated health constituting a measure of mental (MCS) and physical (PCS) health. Higher scores (0-100) indicate better perceived health. (15) As recommended the cut-off was set as the mean minus one standard deviation, using the Danish normed score (16).

The HeartQol is a disease-specific tool, scored from 0 (poor) to 3 (best) (17). Scores are summarized in a global, a physical, and an emotional subscale score. For this study HeartQol quantities were converted to binary quantities based on the median score. Both the SF-12 and the HeartQoL questionnaires have a 4 week recall period.

Emotional and cognitive perceptions were measured by the Brief Illness Perception Questionnaire (B-IPQ). Higher scores (0-10) indicates stronger perceptions. (18). No clear cut-offs for screening have been determined for B-IPQ. To reduce the degrees of freedom only the summary score was included for the main analyses in three categories based on the $25^{\text{th}}$ and $75^{\text{th}}$ quartile in the studied sample.

Loneliness was assessed by two ancillary questions, which have previously been used and tested in the Danish National Health Survey (19). One question concerned whether patients experienced having someone to talk to if they needed support or were having problems, and the second question if they were alone, though preferring to be with others.

For health behaviour, patients reported status of current or previous smoking behaviour and alcohol intake during a typical week, as well as, current height and weight.

## Outcomes

Mortality is a reliable and clinically important outcome in cardiac surgery; however, duration of hospitalisation and stay in the ICU are common endpoints in cardiac surgical studies. The ICU stay is a standard component of the treatment and provides an indication of the patient's recovery profile and is in effect a composite measure of the entire perioperative process. (20). Readmission is frequent, why it is an outcome with significant health and economic implications. Readmission rates are about 15% at 30 days after discharge (21,22), but varies greatly after 30 days from 19 to 56% (22,23). Thus, four outcomes were included, 1) death within 90 days of cardiac surgery, 2) prolonged stay in the ICU ([?] 72 hours), 3) prolonged hospital admission ([?] 10 days) and 4) readmission within 90 days from the time of cardiac surgery. Each outcome was evaluated in separate models.

Death

From the Danish Civil Registration System information on all-cause mortality within 90 days from cardiac surgery was obtained.

Prolonged length of stay

Length of stay was included as number of days in the ICU (LOS-ICU), as well as total length of hospital stay (LOS-HOSP). Length of hospital stay, and ICU stay were dichotomised to designate normal and prolonged length of stay. There is no consensus on the definition of prolonged length of stay in hospital following cardiac surgery. Previous studies have adopted the $75^{\text{th}}$ percentile of the length of stay distribution, while others have defined prolonged length of stay as hospitalisation for 10 or more days following cardiac surgery (24,25), which was used in this study.

In previous studies, prolonged length of stay in the ICU has been defined as from >24 to as much as >96 hours (24,26–29). For the present study, based on the existing literature and clinical framework, prolonged length of stay in the ICU was defined as >72 hours.

Readmission

Information on rehospitalisation was obtained from the DNPR and was included as a dichotomous outcome of readmission within 90 days following cardiac surgery.

### Statistical analysis

Baseline characteristics at time of admission were described using means and standard deviations (SD) for continuous measures and percentages for categorical measures.

Initially, logistic regression analyses were conducted to investigate the association between each candidate predictor variable and outcomes for both the total and DenHeart population. Using logistic regression models, we estimated odds ratio (OR) for death, readmission, LOS-ICU and LOS-HOSP adjusting for (1) age (10 years intervals) and sex, and (2) EuroSCORE I.

The number of missing values in the register-based data was low for educational level (n = 110 (3%)) and income (n = 28 (<1%)), however, to determine the best model based on variable selection, data were imputed, by assigning missing for educational level to basic education and missing for income to the median value. For the DenHeart population of 982 patients, 456 patients had missing data in one or more variables. Thus, single mean imputation for each item was conducted for continuous variables whilst for categorical variables (smoking and loneliness), imputations were done by assigning missing to the category most frequently occurring, since missingness was <5% (see Supplementary Table 1).

To determine the incremental value of each candidate predictor variable, each of the predictor variables were excluded separately in a multiple regression model by using an automated backwards selection procedure with a set liberal significance level of 0.10. EuroSCORE was maintained in the models. The Receiver Operating Characteristic (ROC) curve including Area Under the Curve (AUC) and Brier score were used to determine discrimination and calibration, respectively (30,31).

All analyses were conducted using SAS version 9.4.

## Results

### Demographic and outcome distribution

Total cohort

The study population comprised 3217 (82%) of a total of 3904 patients aged 18 years or above having undergone cardiac surgery from April 2013 to April 2014 (Figure 1). Median age was 68 (range 23 – 95), with almost 70% being 60-79 years, 76% were male and 2085 (65%) had a spouse or partner. Most patients (2340 (73%)) had an income of 50-150% of the median for the total population. Isolated CABG were performed on 1548 (48%) patients and 707 (22%) had non-isolated procedures of cardiac surgery (Table 1). Of the total population, 110 (3.4%) patients died within 90 days, 286 (9%) patients experienced prolonged ICU stay, 1653 (51%) patients prolonged hospital admission and 1249 (39%) patients were readmitted to hospital within 90 days after cardiac surgery. A total of 542 (14%) patients were excluded due to lack of follow-up data in the national registers. Furthermore, we had to exclude 145 (3%) patients for whom we did not have information on EuroSCORE (Figure 1, flow-chart).

DenHeart cohort

In the nested DenHeart sub-sample, including a total of 982 patients, 771 (79%) were male, the median age was 67, 320 (33%) lived alone and 705 (72%) had an income between 50-150% of the median (Table 1). Only 1 patient in the nested subsample died, 63 (6%) patients experienced prolonged LOS-ICU, 443 (45%) patients experienced prolonged LOS-HOSP and 348 (35%) patients were readmitted to hospital within 90 days after cardiac surgery. Since only one patient died in the DenHeart nested sub-sample, death was not included as an outcome in these analyses. In total 1576 (49%) did not participate in the DenHeart cross-sectional survey and were therefore excluded from the nested sub-sample (see flow-chart, Figure 1).

### Individual candidate predictor associations in logistic models

Total cohort

Logistic analyses adjusted for EuroSCORE revealed that patients who were living alone (OR, 1.19; 95%CI, 1.02-1.38) and had a lower educational level (OR, 1.27; 95% CI, 1.04-1.54) were more likely to experience prolonged LOS-HOSP, whilst patients in the highest quartile for income were less likely to experience prolonged LOS-HOSP (OR, 0.83; 95% CI, 0.69-0.98) (Table 2).

Regarding prolonged LOS-ICU, patients who lived alone had an increased OR when adjusting for sex and age (OR, 1.33; 95% CI, 1.03-1.70), but the association was not present when adjusting for EuroSCORE (Table 2). The outcomes of readmission and death did not show any statistically significant associations.

DenHeart cohort

Logistic regression analyses in the nested DenHeart population revealed that a lower score on the physical component scale of the SF-12 was associated with LOS-HOSP when adjusting for age and sex, but not when adjusting for EuroSCORE. However, the mental component scale was associated with LOS-HOSP in both models (OR, 1.43; 95% CI, 1.02-2.01) and with LOS-ICU when adjusting for age and sex, but not when adjusted for EuroSCORE. Furthermore, a global score lower than the median on the HeartQoL questionnaire and a high score on the B-IPQ were associated with LOS-HOSP in both models (OR 1.35; 95% CI, 1.04-1.75 and OR, 1.58; 95% CI, 1.09-2.29, respectively). By contrast a medium score on the B-IPQ was found to be associated with LOS-ICU. Finally, being alone though preferring to be with others was associated with an increased OR for readmission within 90 days (OR, 1.41; 95% CI, 1.03-1.91) and not having someone to talk to was associated with an increased OR for LOS-HOSP (OR, 1.95; 95%CI, 1.25-3.04) when adjusting for EuroSCORE (Table 3).

### Prediction equation of emotional, social, functional and behavioural factors

Total cohort

The multiple regression models based on comprehensive data revealed low educational level and living alone as predictors of prolonged LOS-HOSP (Table 4). The discriminative value was acceptable based on AUC of 0.625, however, the Brier score of 0.238 indicates a poor informative model (Table 4). Furthermore, living alone was found to be a predictor of LOS-ICU with an acceptable Brier score of 0.078 and AUC of 0.676 (Table 4), and death with a Brier score of 0.032 and AUC of 0.710 (Table 4). None of the candidate variables were predictive of readmission including EuroSCORE, which did not predict readmissions either (AUC, 0.53; Brier score, 0.24) (Table 4 and Supplementary figure 1).

DenHeart cohort

The multiple regression model for prolonged LOS-HOSP included a low global HeartQoL score and not having someone to talk to as predictors (Table 5). The discrimination was acceptable (AUC 0.62), however, the informative value of the model was poor (Brier score of 0.24) (Table 5). None of the candidate predictors in the DenHeart study were found to be predictive of prolonged LOS-ICU (Table 5), however, being alone though preferring to be with others predicted readmission (Table 5). Model fit was found to be poor (Brier score of 0.23), and discriminating ability was low (AUC of 0.56) (Table 5 and Supplementary figure 2).

## Discussion

In this cohort study emotional, social, functional and behavioural prognostic factors were tested for patients undergoing cardiac surgery. The principal findings were that 1) living alone predicted both prolonged ICU stay and death for the total cohort of 3217 patients, and 2) low HRQoL and loneliness (not having someone to talk to) predicted prolonged hospital stay for the nested cohort of 982 patients undergoing cardiac surgery.

Thus, information on cohabitation status may potentially be added to existing risk evaluation models due to its predictive value.

The predictive value of living alone is supported by Murphy & colleagues who found patients undergoing CABG surgery and living alone, were more than three times more likely to be readmitted to hospital (OR, 3.42; 95% CI, 1.38– 8.48) than those living with others (32). Being married, especially being in a highly satisfying marriage, has been found to offer a significant benefit to long-term survival after CABG (OR, 2.49; 95% CI, 1.47–4.24) (33). The beneficial effect of cohabitation and relationship satisfaction on survival is likely multifactorial, which has been emphasised by earlier studies linking living alone with poor health outcomes. Patients who are socially isolated are more likely to smoke and have excessive alcohol intake (34,35), delay seeking treatment (36), and demonstrate non-compliance with medical regimens (37), which may be due to a lack of emotional or practical support gained through living with another person (32).

In earlier studies a feeling of loneliness has been linked to several adverse health outcomes. For example, endorsing "yes" to "I feel lonely" was associated with increased 30-day (Rate Ratio (RR), 2.61; 95% CI, 1.15-5.95) and 5-year (RR, 1.78; 95% CI, 1.17-2.71) mortality among patients undergoing CABG (38) , and a response of "often" to the question "do you feel lonely" was associated with increased cardiovascular mortality among elderly Danish men (Hazard Ratio, 1.70; 95% CI, 1.03-2.81) (39).

Several studies agree that HRQoL has become a necessary addition and key indicator of cardiac surgical outcomes (40–42). This study found that reduced health-related quality of life predicts prolonged LOS-HOSP. The predictive value of HRQoL has been confirmed in earlier studies that have found low HRQoL to be predictive of both mortality following CABG with a 10 point lower SF-36 Physical Component Summary score having an OR of 1.39; 95% CI, 1.11-1.77 (43) and of one year cardiac functional status (OR, 2.73; 95% CI, 1.43–5.23) (44).

For this study the intention was to investigate factors beyond the clinical indicators and physical health of the patients planned to undergo cardiac surgery. Traditional risk assessment in cardiac surgery has been a tool for patient selection and has been aimed at the perioperative patient pathways. With the proposed supplement the risk assessment can potentially be used to identify vulnerable groups of patients leading to improved patient management still with the overall aim to improve patient outcomes. Information on cohabitation status, loneliness and HRQoL could potentially be added to existing risk evaluation models in cardiac surgery. However, further research is warranted to validate the findings of the current study and to investigate interventions supporting the identified vulnerable groups of patients.

## Strength and limitations

This study has several limitations. Firstly, we were restricted to the use of predictor variables based on existing data measured in previously collected data sets, which is a beneficial way to make full use of already collected data to address potentially important new research questions and avoid disturbing patients unnecessarily. However, we may not have included important prognostic variables (e.g. cognitive status and frailty), because they were not measured in the original studies. Secondly, the present study used corresponding datasets. When doing this there is a risk that the datasets differ in important aspects, such as baseline risk. However, in the current study a prediction model was developed for each dataset reducing bias due to this.

Non-response for the DenHeart study was high at 49% which might bias the results. Responders and non-responders of the DenHeart study has earlier been established to be similar regarding socio-demographics, however, the non-responders were more severely ill, had more comorbidity and thus a much higher mortality rate compared to responders (45), which could have resulted in an underestimation of the associations between the predictor variables and the outcomes .

Imputations were utilised in the present study to maintain the sample size, assuming the missing values were missing at random. The use of mean imputations does not affect the estimate of the mean for the variable;

however, it reduces the variance of the imputed variables. Furthermore, it assumes that the mean value of the respondents was a good estimate of the missing values, which may have resulted in conservative bias.

We used an automated stepwise approach to specify the models, principally due to its objectivity and that it generally results in smaller, clinically applicable models (46), but stepwise methods have well-known limitations such as unstable variable selection (47) and biased coefficient estimation (46). It is therefore conceivable that our choice to use stepwise selection may have reduced the predictive performance of the models. The overall model fit statistics indicate that the variance explained by our prediction models is at best modest. Perhaps some factors that are yet to be tested thoroughly in cardiac surgery, for example, frailty and mental state, explain additional variance in cardiac surgery. Despite the limitations of the study the models made informative predictions that should be externally validated in a similar population of patients undergoing cardiac surgery.

### Conclusion

We tested several emotional, social, functional and behavioural prognostic factors as a supplement to EuroSCORE and reported different aspects of model performance that can be interpreted for further research applications. Based on the cohorts included, living alone predicts death, prolonged hospital admission and prolonged ICU stay following cardiac surgery. Low educational level and impaired HRQoL were, furthermore found to be predictive of prolonged hospital admission.

## Ethics approval

According to Danish legislation, surveys should only be approved by the Danish Data Protection agency (2007-58-0015/30-0937). Use of register data were permitted by The Danish national Board of health.

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## Declaration of conflicting interests

None

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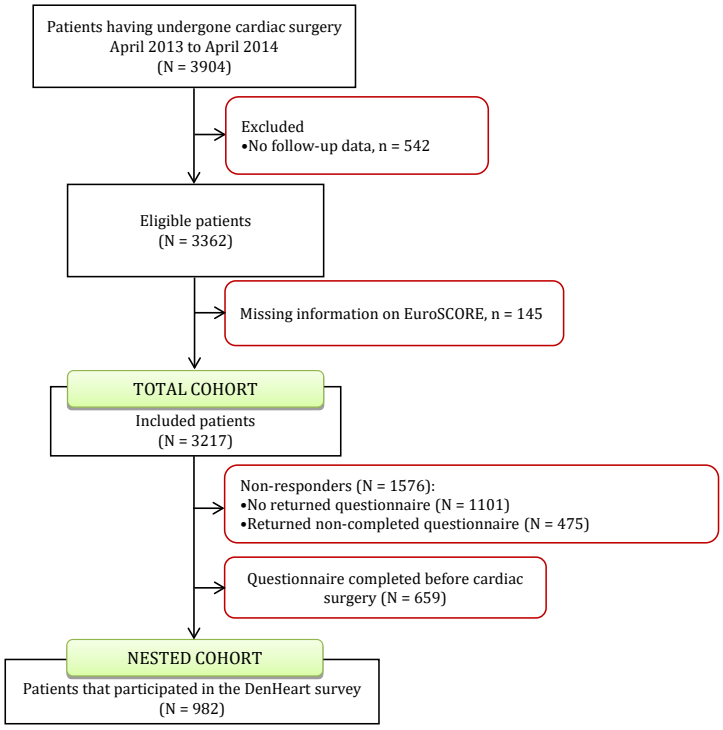


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