Predictors for long-term outcome and quality of life of patients after cardiac surgery with prolonged intensive care unit stay

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(Received: July 28, 2012; Accepted after revision: November 26, 2012)

Abstract: Objectives: This study investigated factors determining the long-term outcome and quality of life of patients with a prolonged intensive care unit (ICU) stay after cardiac surgery. Design: A retrospective analysis was performed in 230 patients that had undergone cardiac surgery and suffered from a post-operative ICU stay of 7 or more days at our institution. Among 11 pre-, 13 intra-, and 14 post-operative variables, factors influencing 5-year outcome were identified by logistic regression analysis. Quality of life was determined using the Short Form-36 questionnaire. Results: In-hospital mortality was 12%. One hundred and eleven of 187 patients (59%) were alive after 5 years. Non-survivors were older (70 vs. 65 years, \( p = 0.005 \)) and had a higher additive EuroSCORE (7 vs. 5, \( p = 0.034 \)). Logistic regression identified pre-operative atrial fibrillation (AF), (28 vs. 10%, \( p = 0.003 \)) as the strongest predictor for a 5-year outcome, followed by myocardial infarction (62 vs. 41%, \( p = 0.005 \)), and prolonged mechanical ventilation (8 vs. 5 days, \( p = 0.036 \)). Survivors did not show an impaired physical component summary SF-36 score (39 vs. 46, \( p = 0.947 \)) compared to an age-matched German Normative Sample. Conclusions: Pre-operative AF proved to be the most important factor determining the 5-year outcome of patients with a prolonged ICU stay after cardiac surgery. Neither physical nor mental health appeared to be impaired in these patients.

Keywords: prolonged intensive care unit stay, cardiac surgery, atrial fibrillation, quality of life, outcome

Introduction

Although the rate of cardiac surgery patients with a prolonged intensive care unit (ICU) stay varies due to different definitions of the term “prolonged,” it is estimated that up to 36% of patients undergoing cardiac surgery endure extended intensive care [1, 2]. Regarding the increase of high-risk patients in need of cardiac surgical procedures, information about relevant prognostic parameters shaping the overall outcome of these patients can be essential to medical decision proceeding and peri-operative management. Accordingly, this area of research has gained increased attention throughout the last years [3, 4]. In addition to pure long-term survival, quality of life after cardiac surgery has become a matter of growing concern especially with regard to the rising number of older patients referred to cardiac surgery. In fact, the actual physical and mental abilities may define the individual’s well-being more accurate than survival alone. Here, we investigated peri-operative factors determining the 5-year survival of patients who required prolonged intensive care after cardiac surgery at our institution. In addition, we aimed at assessing the quality of life (QoL) of this patient population.

Materials and Methods

Patient population

Clinical data of all adult patients (\( n = 5324 \)) who underwent cardiac surgery at our clinic between January 2000 and December 2004 were screened for a post-operative ICU stay of seven or more consecutive days. These patients (\( n = 230 \)) were included for further retrospective analyses. Patients who underwent thoracic organ transplantation were excluded as these patients consist of a small, exclusive group of individuals with long ICU stays.

A total of 38 pre-, intra-, and post-operative variables were extracted. The European System for Cardiac Operative Risk Evaluation (additive EuroSCORE) was calculated for each patient based on chart information. Patients or their relatives were contacted by phone to calculate the 5-year survival rate. If patients were unavailable, inquiries were sent to the civil registry offices. The 36-item Short Form (SF-36) questionnaire (German version) was sent to all patients who were alive at follow-up. Patients were sent letters requesting them to fill out the questionnaire and to return it by mail in...
the enclosed stamped and self-addressed envelope. The Short Form (SF)-36 questionnaire is a standardized survey measuring health-related quality of life. The answers are summarized as eight subscales, physical component summary score (PCS) and mental component summary score (MCS). In all scales, higher scores indicate better health. We compared our results of the quality of life assessment with data of a subgroup of the German normative sample aged 61–70 years. The German normative sample was collected in the scope of the German National Health Interview and Examination Survey from 1998, which was a representative investigation on the health status of the adult population of Germany [5]. The mean age of the whole German sample was 46.1 years, 51.4% were female and 48.6% were male. All patients provided written informed consent. The study was approved by the ethics committee of the medical faculty of the University of Kiel.

Statistical analyses

The continuous demographic and clinical patient data are described using mean and standard deviation or as median and range when data were not normally distributed. Categorical data were summarized using absolute and relative frequencies. Missing data were excluded case by case. The statistical comparison of parameters of those patients who survived the fifth post-operative year and those who were discharged from the hospital alive, but who died within the following 5 years was conducted as appropriate by t-test, Mann–Whitney U-test, Chi²-test or Fishers exact test. The statistical comparison of the eight subscales and two summary scores with the subgroup of the German population was conducted by one-sample Wilcoxon test. All tests were conducted two-tailed at a level of significance of 5%. Surgery of the thoracic aorta was excluded for modelling because its frequency was too rare such that parameter estimation was not reliable. In addition, EuroSCORE and post-operative atrial fibrillation could not undergo multiple logistic regression analysis due to critical collinearity with other variables (Table I). Every other parameter with a significant relation to the 5-year survival rate was included into a multiple logistic regression analysis to assess their relative importance (adjusted odds ratio) with a goodness of fit, described by Cox-Snell-R-Squared, of 0.166. The survival curves were estimated non-parametrically from, as available, right or interval-censored data and described with a 95% confidence interval. Statistical analyses were performed using the statistical software SPSS (17.0) and the free programming language R (2.12.2, package SURVIVAL).

Results

5324 patients underwent cardiac surgery at our hospital between January 2000 and December 2004. 230 of all patients (4.3%) had a post-operative ICU stay of seven or more days. 28 of the 230 patients (12.2%) died during their hospital stay. The 5-year follow-up could be completed in 92.6% of the cases (187/202). Fifteen patients could not be found. Since it was uncertain as to whether these patients were still alive at the time of follow-up, they were not included in the statistical analyses. The 187 patients with a complete 5-year follow-up had to stay in the ICU for an average of eleven days (range 7–85 days). 142 (75.9%) patients were male. The mean age at the date of cardiac surgery was 67.1 ± 10.2 years. The median additive EuroSCORE was 6 (range 0–16).

111 of 187 patients (59.4%) were still alive 5 years post-operatively (Fig. 1). Survival of patients with a prolonged stay in the ICU is shown in the Kaplan–Meier curve in Fig. 2.

Pre-operative parameters influencing long-term outcome after prolonged ICU stay

The pre-operative parameters of long-term survivors (n=111) were compared to those of patients who were discharged from the hospital alive but died within the first 5 years post-operatively (n=76) as presented in Table II. Non-survivors were significantly older (69.6 vs. 65.4 years, p=0.005) and showed a higher additive EuroSCORE in comparison to long-term survivors (7 vs. 5, p=0.034). In addition, more of them had experienced atrial fibrillation ((AF), 27.6 vs. 9.9%, p=0.003)

![Fig. 1. Survival rates of the patients with prolonged intensive care stay. The survival rates are shown at the date of hospital discharge (87.8%) as well as 1 year (73.1%) and 5 years (59.4%) post-operatively](image-url)
and a history of myocardial infarction (61.8 vs. 40.5%, \(p = 0.005\)). Both variables reduced survival as demonstrated in the Kaplan–Meier curves in Figs 3 and 4.

**Intra-operative parameters influencing long-term outcome after prolonged ICU stay**

Surgery of the thoracic aorta – mainly surgery of the ascending aorta and the proximal aortic arch due to aneurysm or dissection (0 vs. 8.1%, \(p = 0.012\)) and intra-operative circulatory arrest (5.3 vs. 18.9%, \(p = 0.008\)) were significantly less frequent in non-survivors (Table II).

**Post-operative parameters influencing long-term outcome after prolonged ICU stay**

Post-operatively, non-survivors demonstrated a prolonged mechanical ventilation duration (8 vs. 5 days, \(p = 0.036\), Table II) and had to undergo a rethoracotomy significantly less frequently than long-term survivors (18.4 vs. 33.3%, \(p = 0.030\)). Patients with new-onset post-operative AF showed a disastrous long-term survival (0% of survivors, 65.3% of non-survivors, \(p < 0.001\)).

**Atrial fibrillation as a strong predictor of poor long-term outcome after prolonged ICU stay**

The logistical regression identified pre-operative AF, followed by a history of myocardial infarction (MI) and with less effect post-operative mechanical ventilation duration as the most significant predictors for a poor long-term outcome (Table III).

**No physical or mental health impairment in long-term survivors of prolonged ICU stay**

The SF-36 questionnaire was returned by 49 patients (44.1%). Thirty-seven (75.5%) of the questionnaires could be fully evaluated and the PCS score and MCS score calculated. The long-term survivors did not show any physical or mental limitations compared to the subgroup aged 61–70 years of the German normative sample. Table IV demonstrates the eight subscales of the SF-36 in detail.
Discussion

A prolonged ICU stay after cardiac surgery is associated with enhanced mortality [6]. Even if patients survive, severe post-operative complications, physical, and/or mental limitations may permanently impair the individual QoL [7]. Thus, a detailed characterization of these patients may facilitate peri-operative, individualized medical decision making and thereby improve survival as well as QoL. In addition, intensive care resources may be distributed more efficiently [8]. We here investigated peri-operative parameters determining the outcome of patients who survived an ICU stay of at least 7 days for 5 years. We show that in concordance with the data of other groups, survivors tended to be younger with less pre-existing risk factors as determined by the additive EuroSCORE. Surprisingly, pre-operative AF proved to be the most significant risk factor for 5-year mortality in this study.

In contrast to post-operative AF, the importance of pre-operative AF for the general outcome of patients undergoing cardiac surgery has been divergently discussed so far [9, 10]. To our knowledge, even less data about the impact of this parameter on patients with a complicated post-operative course have been gathered.

Surely, the underlying causes for this finding are complex and the present study was not designed to investigate this observation any further. However, AF indicates pathological cardiac remodelling, involving inflammation, fibrosis, apoptosis and ageing [11]. Cardiac remodelling may be due to ischemia, arterial hypertension, or valvular disease. Even though coronary artery bypass surgery or valve repair treats the underlying pathology of AF, cardiac remodelling may persist. Thus, AF indicates and promotes chronic, advanced structural cardiac disease. In addition, several studies demonstrated that oral anticoagulation bears a considerable risk of bleeding but also of thrombo-embolic events due to insufficient monitoring and/or patient compliance [12, 13]. These factors most likely contribute not only to the overall impaired life expectancy of patients suffering from AF but may have significantly influenced the survival of our patient population, too [14].

As stated above, new-onset post-operative AF has already been demonstrated to severely modulate the outcome of patients after cardiac surgery. In our study, none of these patients survived the 5-year follow-up period. Although the absolute number of subjects is low, this observation further underlines the functional im-

| Table I | P-values of corresponding tests. The table demonstrates associations between some peri-operative parameters |
|---------|---------------------------------------------------------------------------------------------------|
|         | Age (years) | Gender | Additive EuroSCORE | History of myocardial infarction | Atrial fibrillation | Surgery of the thoracic aorta | Circulatory arrest | New-onset post-operative atrial fibrillation | Rethoracotomy | Duration of mechanical ventilation |
| Age (years) | 0.176 | <0.001 | 0.473 | 0.182 | 0.265 | 0.047 | 0.003 | 0.208 | 0.667 |
| Gender | 0.006 | 0.282 | 0.892 | 0.143 | 0.994 | 0.847 | 0.295 | 0.698 |
| Additive | 0.782 | 0.206 | 0.857 | 0.514 | 0.405 | 0.167 | 0.019 |
| EuroSCORE | History of myocardial infarction | 0.773 | 0.019 | 0.323 | 0.048 | 0.310 | 0.200 |
| Atrial fibrillation | 0.624 | 0.874 | 0.002 | 0.104 | 0.173 |
| Surgery of the thoracic aorta | <0.001 | 0.014 | 0.236 | 0.735 |
| Circulatory arrest | 0.015 | 0.012 | 0.646 |
| New-onset post-operative atrial fibrillation | 0.084 | 0.053 |
| Rethoracotomy | 0.025 |
| Duration of mechanical ventilation |
## Table II: Pre-, intra- and post-operative patient characteristics

|                              | Survivors $(n=111)$ | Non-survivors $(n=76)$ | $p$  |
|------------------------------|---------------------|------------------------|------|
| **Pre-operative patient characteristics** |                     |                        |      |
| Age (years)                  | 65.4±10.8           | 69.6±8.5               | 0.005|
| Gender (male/female)         | 74.8/25.2           | 77.6/22.4              | 0.729|
| Body mass index              | 26.4±3.9            | 26.6±3.6               | 0.768|
| Additive EuroSCORE           | 5 (0–13)            | 7 (0–16)               | 0.034|
| Ejection fraction <50 (%)    | 28.9                | 43.9                   | 0.065|
| History of myocardial infarction (%) | 40.5               | 61.8                   | 0.005|
| Atrial fibrillation (%)      | 9.9                 | 27.6                   | 0.003|
| Pulmonary hypertension (%)   | 29.2                | 51.4                   | 0.067|
| Creatinine > 1.2 mg/dl (%)   | 22.4                | 31.0                   | 0.224|
| History of stroke (%)        | 14.4                | 18.4                   | 0.544|
| Mechanical ventilation (%)   | 8.1                 | 7.9                    | 1.000|
| **Intra-operative details**  |                     |                        |      |
| CABG (%)                     | 49.5                | 56.6                   | 0.374|
| Aortic valve procedure (%)   | 6.3                 | 7.9                    | 0.772|
| Mitral valve procedure (%)   | 2.7                 | 2.6                    | 1.000|
| CABG and valve procedure (%) | 13.5                | 17.1                   | 0.536|
| Surgery of the thoracic aorta (%) | 8.1               | 0                      | 0.012|
| Other cardiac procedure* (%) | 19.8                | 15.8                   | 0.565|
| Reoperation (%)              | 22.5                | 18.4                   | 0.584|
| Emergency operation (%)      | 20.7                | 13.2                   | 0.241|
| Operation duration (min)     | 240 (125–723)       | 239 (95–695)           | 0.728|
| Cardiopulmonary bypass time (min) | 131.5±52.5         | 129.7±63.7             | 0.838|
| Cross-clamp time (min)       | 67 (0–179)          | 63 (0–191)             | 0.751|
| Circulatory arrest (%)       | 18.9                | 5.3                    | 0.008|
| Continuous application of catecholamines (%) | 71.2               | 72.4                   | 1.000|
| **Post-operative details**   |                     |                        |      |
| Intensive care unit stay (days) | 11 (7–85)           | 12 (7–71)              | 0.431|
| New-onset post-operative atrial fibrillation (%) | 0                  | 65.3                   | 0.000|
| Rethoracotomy (%)            | 33.3                | 18.4                   | 0.030|
| Intra-aortic balloon pump (%) | 14.4                | 5.3                    | 0.055|
| Myocardial infarction (%)    | 5.4                 | 5.3                    | 1.000|
| Catecholamines (d)           | 4 (0–17)            | 4 (0–48)               | 0.071|
| Cardiopulmonary resuscitation (%) | 17.1               | 15.8                   | 0.844|
| Ventricular fibrillation (%) | 11.7                | 9.2                    | 0.638|
| Reintubation (%)             | 47.7                | 56.6                   | 0.297|
| Duration of mechanical ventilation (days) | 5 (1–83)           | 8 (1–71)               | 0.036|
| Hemodialysis (%)             | 25.2                | 38.2                   | 0.075|
| Stroke (%)                   | 9.0                 | 10.5                   | 0.803|
| Tracheotomy (%)              | 29.7                | 43.4                   | 0.062|
| Pneumonia (%)                | 18.0                | 18.4                   | 1.000|

*The term “other cardiac procedure” summarizes all procedures that could not be assigned to the named procedures, for example, CABG with simultaneous surgery of the carotid artery as well as very complex procedures as, for instance, CABG combined with repair of a ventricular septal defect.
Prior MI also impaired the long-term outcome of the patients included in this study. The importance of this factor in this patient population has already been reported by other groups [15, 16]. The underlying causes for this finding may involve advanced cardiac disease with myocardial tissue scaring resulting in incomplete revascularization and/or increased susceptibility for hemodynamically relevant arrhythmias as well as recurrent ischemic events and progression of heart failure [17].

Surprisingly, intra-operative circulatory arrest needed to repair/replace the thoracic aorta due to aneurysmatic malformation or dissection was more often performed in survivors than non-survivors. On the one hand, we speculate that despite these positive results an early mortality might exist among these patients that we did not detect based on the fact that we chose an ICU stay of 7 days or longer as the inclusion criterion for our patient population. However, as indicated by Griep and demonstrated by Achneck et al., the midterm-survival of patients with aneurysms or dissections of the ascending aorta (not including the arch) may indeed be similar to the normal population [18].

Prolonged mechanical ventilation is also a known factor influencing the outcome of patients after cardiac surgery [1]. It may either be the result of extra-pulmonary overall systemic instability preventing weaning but also indicates primary pulmonary failure due to pneumonia, emphysema, or pulmonary hypertension.

Especially in consideration of the growing number of older, high-risk patients referred to cardiac surgery, the question of post-operative QoL has become an important, but complex issue [19, 20]. On the one hand, obtaining reliable information about the actual, post-operative QoL of patients after cardiac surgery with or without a complicated post-operative course remains difficult as reviewed by Noyez et al. [21]. On the other hand, the term “quality of life” is a sensitive aspect as the definition of this term may vary essentially from patient to family member to the treating physician. This consideration becomes even more problematic during the management of critically ill patients. In our study, long-term survivors showed neither mental nor physical restrictions as determined by using the PCS and MCS score. Both scores were slightly higher than those observed by Lagercrantz et al. [22]. Unfortunately, the response rate of the questionnaire used in the present study was below 50%. Although follow-up drop-outs and incomplete data about the QoL in this patient population have already been described as a common problem in other studies, any conclusions must be regarded with the appropriate care [21]. Nevertheless, our findings may contribute to peri-operative patient care and guidance/counselling by extending as well as supporting the current knowledge about future QoL when facing severe post-operative complications.

To conclude, the long-term survival of this patient population after cardiac surgery with a prolonged ICU stay is strongly determined by prior AF. A history of MI as well as post-operative duration of mechanical ventilation also influence patient outcome. Therefore, patients with these risk factors should be evaluated and treated with particular care and attention peri-operatively.

### Table III Risk factors for a negative long-term prognosis

| Risk Factor                          | Odds Ratio | 95% CI           | p   |
|-------------------------------------|------------|------------------|-----|
| **Pre-operative**                   |            |                  |     |
| Atrial fibrillation                 | 4.030      | 1.668–9.737      | 0.002|
| Myocardial infarction               | 2.389      | 1.256–4.579      | 0.008|
| **Post-operative**                  |            |                  |     |
| Duration of mechanical ventilation  | 1.031      | 1.003–1.059      | 0.027|

### Table IV Quality of life compared with a normative German sample

|                      | Study group (n=37) | Normative German sample (n=969) | p    |
|----------------------|--------------------|---------------------------------|------|
| Physical functioning | 57 (5–100)         | 85 (0–100)                      | 0.483|
| Physical role        | 25 (0–100)         | 100 (0–100)                     | 0.244|
| Bodily pain          | 92 (31–100)        | 62 (0–100)                      | 0.724|
| General health       | 56 (15–97)         | 62 (0–100)                      | 0.728|
| Vitality             | 50 (0–95)          | 60 (10–100)                     | 0.772|
| Social functioning   | 87.5 (0–100)       | 100 (0–100)                     | 0.303|
| Emotional role       | 100 (0–100)        | 100 (0–100)                     | 0.432|
| Mental health        | 76 (32–100)        | 76 (12–100)                     | 0.971|
| Physical component   | 38.6 (20.6–59.9)   | 46.0 (10.4–65.1)                | 0.737|
| Mental component     | 55.4 (26.1–67.2)   | 54.6 (28.1–70.7)                | 0.947|

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Study Limitations

Overall, the definition, analysis, as well as the dissociation of cause and effect of peri-operative factors and their influence on patient outcome remains difficult due to possible significant interactions. In particular, conclusions drawn from small-scaled studies, such as the one presented here, have to be regarded with care. The present study is also limited by its retrospective design. No statements on the cause of death can be made. The response rate of the Short Form-36 questionnaire to determine quality of life was below 50%.

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