Determinants of mortality in patients requiring prolonged intensive care unit stay after elective isolated on-pump coronary artery bypass grafting surgery

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Abstract

Background: In up to 36% of patients undergoing cardiac surgery prolonged intensive care unit stay may be necessary. Mortality rates of these patients range from 11% to 94%, causing enormous clinical and ethical issues.

Aim: To identify preoperative, perioperative and postoperative risk factors of mortality in patients with prolonged intensive care unit stay after elective, isolated on-pump coronary artery bypass grafting surgery.

Methods: Clinical data of 137 patients who underwent an elective, isolated on-pump coronary artery bypass grafting operation, and had an intensive care unit stay of ≥ 3 days were retrospectively evaluated. Survivors and non-survivors were compared with regard to preoperative, perioperative and postoperative characteristics to identify the risk factors for mortality.

Results: Multivariate analysis demonstrated that diabetes mellitus (OR = 3.62, 95% CI 1.07-12.26, p = 0.039), postoperative renal dysfunction (OR = 3.86, 95% CI 1.26-11.75, p = 0.018), postoperative intra-aortic balloon pump use (OR = 3.47; 95% CI 1.01-13.24, p = 0.048), prolonged intubation (OR = 3.90, 95% CI 1.19-12.69, p = 0.024) and re-intubation (OR = 14.83, 95% CI 4.35-50.55, p = 0.001) were significant and independent risk factors of mortality.

Conclusion: The present study found that the preoperative presence of diabetes mellitus, and postoperative multiorgan failure syndrome decreased the probability of survival in patients with prolonged intensive care unit stay after elective isolated on-pump coronary artery bypass surgery.

Key words: prolonged ICU stay, CABG, mortality

Kardiol Pol 2010; 68: 257-262

Introduction

Coronary artery bypass grafting (CABG) is an established treatment for patients with ischaemic heart disease [1]. Although the number of older, sicker and high-risk patients undergoing CABG has been increasing, the mortality rates of this procedure have declined significantly over the last decade [2]. The Society of Thoracic Surgeons (STS) database has documented that 87% of patients undergoing CABG can expect to survive without a major morbid event [3]. However, up to 36% of patients undergoing cardiac surgery require prolonged intensive care unit (ICU) stay. Prolonged ICU stay not only results in higher mortality rates, ranging between 11% and 94% [4], but also raises enormous clinical and ethical issues [5]. The costs of CABG are determined by the costs of the operation itself, and the length of hospital and ICU stay [6]. Several studies have reported independent risk factors [4] and parameters affecting the duration of ICU stay [7], and the predictors of hospital mortality in patients with prolonged ICU stay after cardiac surgery [8].

The aim of the present study was to identify preoperative, perioperative and postoperative risk factors of hospital mortality in patients with prolonged ICU stay after elective, isolated on-pump CABG.

Methods

Patients

Between September 2001 and May 2009, elective isolated on-pump CABG was performed in 5648 patients in our department. Among them, 137 (2.5%) patients, who required prolonged ICU stay after CABG, were included in the study.

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Received: 12 July 2009. **Accepted:** 18 November 2009.

Data collection

Preoperative, perioperative and postoperative data of the patients who underwent isolated on-pump CABG with prolonged ICU stay were retrospectively collected for analysis as risk factors of hospital mortality. Prolonged ICU stay was defined as an ICU stay ≥ 3 days [6, 7].

Preoperative risk factors

This analysis included: age, gender, body mass index, previous myocardial infarction (MI) (presence of Q wave positive MI within the last 3 months), previous invasive coronary procedure (percutaneous transluminal coronary angioplasty and/or intracoronary stent implantation), left main coronary (LMC) artery lesion (≥ 50 % stenosis of LMC), poor left ventricular (LV) function [ejection fraction (EF) ≤ 30%], LV end-diastolic pressure (LVEDP), congestive heart failure, cerebrovascular disease (≥ 50% stenosis of carotid artery system), peripheral artery disease (≥ 50% stenosis of peripheral artery system), preoperative renal dysfunction (serum creatinine level > 1.20 mg/dl), smoking (current smoking and/or cessation of smoking within 3 months), hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD) and the number of diseased coronary arteries.

Perioperative risk factors

Left internal thoracic artery usage, postoperative extracorporeal membrane oxygenator (ECMO) support, cardiopulmonary bypass and aortic cross-clamping times as well as the number of grafts were analysed.

Postoperative risk factors

The following parameters were analysed: inotropic support (any inotropic agent usage other than dopamine at renal dose), intra-aortic balloon pump (IABP) usage, blood transfusion (to maintain the haematocrit level at or above 30%), prolonged mechanical ventilation (not weaning the patient from mechanical ventilation within the first 24 h after operation), re-intubation (need of repeat mechanical ventilation after weaning once), chest re-exploration, new-onset arrhythmia (onset of new arrhythmia requiring use of an anti-arrhythmic agent), cerebrovascular event (any neurological dysfunction except for delirium), postoperative renal dysfunction (serum creatinine level > 1.20 mg/dl), fever (sublingual temperature > 37.8°C or rectal temperature > 38.2°C [9] after the second postoperative day) or gastrointestinal complications (paralytic or mechanical ileus, gastrointestinal haemorrhage).

Statistical analyses

The NCSS 2007 & 2008 Statistical Software (Utah, USA) was used. Besides descriptive statistics (mean ± standard deviation), quantitative data were compared using Student's t test or Mann–Whitney U test, where appropriate. For the comparison of qualitative variables, Chi-square test or Fisher's exact test was used. Effects on mortality were evaluated by logistic regression in a multivariate analysis. Results were evaluated at 95% confidence intervals and a p value < 0.05 was considered significant.

Results

Out of the 137 patients with prolonged ICU stay, 84 (61%) were discharged (survivor group) whereas 53 (39%) died (non-survivor group). The mean age of the patients was 62.63 ± 11.03 years and 42.3% of them were female. The patients from the non-survivor group were significantly older than those in the survivor group (66.10 ± 9.74 vs. 60.49 ± 11.29, p = 0.004) (Table I).

The mean duration of ICU stay for all patients was 7.87 ± 5.9 days. Mean duration of ICU stay time for the survivor group was significantly longer than the non-survivor group (Table II).

The leading reasons for prolonged ICU stay for all patients were low cardiac output syndrome (45%) and respiratory failure (37%). Postoperative renal dysfunction (9%), cerebrovascular accident (7%), and gastrointestinal complications (2%) were the other major reasons for prolonged ICU stay. The majority of deaths in the non-survivor group occurred between postoperative days 3 and 9. The time course of mortality in the non-survivor group is presented in Figure 1. The deaths in the non-survivor group were due to multi-organ failure and all deaths occurred during the ICU stay.

Univariate analysis demonstrated that mortality was significantly associated with LMC disease, advanced age (≥ 65 years), peripheral artery disease, diabetes mellitus, preoperative renal dysfunction, postoperative inotropic agent usage or IABP usage, prolonged intubation, re-intubation and postoperative renal dysfunction (Tables I and II). In the multivariate analysis, using a backward stepwise logistic regression model, only diabetes mellitus (OR 3.62; 95% CI 1.07-12.26, p = 0.039), postoperative renal dysfunction (OR 3.86; 95% CI 1.26-11.75, p = 0.018), postoperative IABP usage (OR 3.47; 95% CI 1.01-13.24, p = 0.048), prolonged intubation (OR 3.90; 95% CI 1.19-12.69, p = 0.024) and re-intubation (OR 14.83; 95% CI 4.35-50.55, p = 0.001) were significant and independent factors of mortality. The model was highly significant (p < 0.001), with a Nagelkerke R square value of 0.838 and determination coefficient of 91.3%.

Discussion

In this retrospective study we aimed at identifying the risk factors of mortality among patients who underwent elective isolated on-pump CABG with prolonged (≥ 3 days) ICU stay. Among a total of 5648 patients who underwent

Table I. Demographic and baseline clinical characteristics

	Non-survivors (n = 53)	Survivors (n = 84)	Overall (n = 137)	p
Age, n (%) ≥ 65 years	37 (69.8)	29 (34.5)	66 (48.2)	0.001
< 65 years	16 (30.2)	55 (65.5)	71 (51.8)	
BMI [kg/m^2]	26.96 ± 4.85	26.29 ± 6.09	26.54 ± 5.67	0.529
Gender, n (%) female	25 (47.2)	33 (39.3)	58 (42.3)	0,363
male	28 (52.8)	51 (60.7)	51 (57.7)	
Previous MI, n (%)	27 (50.9)	31 (36.9)	58 (42.3)	0.105
Left main coronary disease, n (%)	9 (17)	5 (6)	14 (10.2)	0.038
PCI, n (%)	3 (5.7)	4 (4.8)	7 (5.1)	1.000
EF < 30%, n (%)	13 (24.5)	18 (21.4)	31 (22.6)	0.673
Cerebrovascular disease, n (%)	3 (5.8)	4 (4.8)	7 (5.1)	1.000
Peripheral artery disease, n (%)	10 (19.2)	5 (6.0)	15 (11.0)	0.023
Congestive heart failure, n (%)	5 (9.6)	3 (3.6)	8 (5.9)	0.259
Smoking, n (%)	10 (18.9)	16 (19.3)	26 (19.1)	1.000
Diabetes mellitus, n (%)	20 (37.7)	14 (16.9)	34 (25.0)	0.006
Hypertension, n (%)	28 (52.8)	38 (45.8)	66 (48.5)	0.423
Preoperative renal dysfunction, n (%)	9 (17.0)	4 (4.8)	13 (9.6)	0.019
COPD, n (%)	5 (9.4)	5 (6.0)	10 (7.3)	0.445
LVEDP, mmHg (mean ± SD)	13.08 ± 4.14	14.81 ± 6.29	14.07 ± 5.45	0.417
No. of diseased coronary arteries, n (%)				
1-vessel disease	2 (4.4)	6 (8.6)	8 (7.0)	0.333
2-vessel disease	6 (13.3)	15 (21.4)	21 (18.3)	
≥ 3-vessel disease	37 (82.2)	49 (70.0)	86 (74.8)	

Abbreviations: BMI – body mass index, COPD – chronic obstructive pulmonary disease, EF – ejection fraction, No. – number, LVEDP – left ventricular end-diastolic pressure (physiological range, 5-12 mmHg), MI – myocardial infarction, PCI – percutaneous coronary intervention

isolated elective on-pump CABG surgery, the mortality rate of the patients with prolonged ICU stay was 38.7%, while for the remaining 5511 patients without prolonged ICU stay, mortality rate was 1.2%. All of the deaths occurred during ICU stay and were due to multi-organ failure. Most of the deaths occurred between postoperative days 3 and 9 and the most common reason for prolonged ICU stay was low cardiac output syndrome.

The mean ICU stay was significantly longer in non-survivors, presumably because of complications leading to death while staying in the ICU (all deaths occurred in the ICU). Re-intubation increased mortality risk 15 times; diabetes mellitus, development of postoperative renal failure, IABP usage and prolonged intubation increased the mortality risk more than 3 times.

The STS database showed that 87% of patients scheduled for CABG are expected to survive the procedure without a major morbid event [3]. However, prolonged ICU stay, and poor outcomes were reported to occur in up to 36% of the patients [10], and were associated with higher mortality rates (11 to 94%) [4]. Ghotkar et al. examined the preoperative predictors of prolonged ICU stay and found that age, body mass index, Canadian Class IV angina pectoris, NYHA class IV functional status, previous MI, smoking, hypertension, diabetes mellitus, peripheral artery disease, COPD, low LVEF, emergency surgery and renal dysfunction were significant predictors [11]. Janssen et al. reported that lung disease, absence of sinus rhythm and emergency surgery were independent risk factors for prolonged ICU stay after CABG [6]. Prolonged hospital and ICU stay times after cardiac surgery were reported to be associated with higher mortality rates in older patients [4]. Legare et al. demonstrated that preoperative renal failure was a determinant of length of hospitalisation, prolonged mechanical ventilation and ICU stay time [1]. They also reported that female patients had longer durations of intubation, prolonged ICU and hospital stay time [1].

Michalopoulos et al. and Weintraub et al. also identified serious intraoperative complications responsible for prolonged ICU stay [7,12]. Weintraub et al. reported low cardiac output syndrome and the amount of inotropic agents administered during the first 6 h after the operation as the most important predictors of prolonged ICU stay [7]. We also found that low cardiac output syndrome, characterised by inotropic agent and IABP usage, was significantly more often encountered in the non-survivor group ($p = 0.007$ and $p = 0.043$, respectively). Weintraub et al. and Wong et al. also

Table II. Perioperative and postoperative characteristics

	Non-survivors (n = 53)	Survivors (n = 84)	Overall (n = 137)	p
Perioperative characteristics				
Use of LITA, n (%)	33 (62.3)	56 (66.7)	89 (65.0)	0.599
ECMO support, n (%)	8 (15.1)	8 (9.5)	16 (11.7)	0.323
Total duration of perfusion [min]	124.47 ± 62.10	105.07 ± 46.73	112.58 53.72	0.090
Duration of cross-clamp [min]	81.57 ± 42.75	78.45 ± 36.28	79.64 38.69	0.710
Number of grafts	2.85 ± 0.79	2.69 ± 0.77	2.77 ± 0.75	0.642
Postoperative characteristics				
Inotropic support, n (%)	49 (92.5)	62 (73.8)	111 (81.0)	0.007
IABP, n (%)	19 (35.8)	17 (20.2)	36 (26.3)	0.043
Blood transfusion, n (%)	51 (96.2)	73 (86.9)	124 (90.5)	0.070
Prolonged intubation, n (%)	27 (50.9)	24 (28.6)	51 (37.2)	0.008
Re-intubation, n (%)	35 (66.0)	15 (17.9)	50 (36.5)	0.001
Chest re-exploration, n (%)	8 (15.1)	13 (15.5)	21 (15.3)	0.952
New-onset arrhythmia, n (%)	32 (60.4)	49 (59.0)	81 (59.6)	0.876
Cerebrovascular accident, n (%)	18 (34.0%)	17 (20.2)	35 (25.5)	0.073
Postoperative renal dysfunction, n (%)	38 (71.7)	27 (32.1)	65 (47.4)	0.001
Fever, n (%)	7 (13.2)	12 (14.2)	19 (13.8)	0.969
Gastrointestinal complication, n (%)	8 (15.1%)	13 (15.5)	21 (15.3)	0.952
ICU stay time [days]	6.02 ± 4.43	10.96 ± 6.83	7.87 ± 5.9	0.034

Abbreviations: ECMO – extracorporeal membrane oxygenator, IABP – intra-aortic balloon pump, ICU – intensive care unit, LITA – left internal thoracic artery

emphasised the association between prolonged ICU stay and preoperative factors including age, female gender, previous MI as well as several intraoperative and postoperative factors (IABP, postoperative inotropic agent use, amount of drainage). On the other hand, they failed to find an association between mortality and cardiopulmonary bypass, cross-clamping times or number of grafts [7, 13]. Rosenfeld et al. reported increased age, COPD, emergency surgery and increased duration of cardiopulmonary bypass as risk factors for prolonged ICU stay [10]. Inotropic agent or IABP usage, dialysis-dependent renal failure (ARF-D), respiratory failure and chest re-exploration were also found responsible for either prolonged ICU stay or mortality after open heart surgery [4, 8, 14].

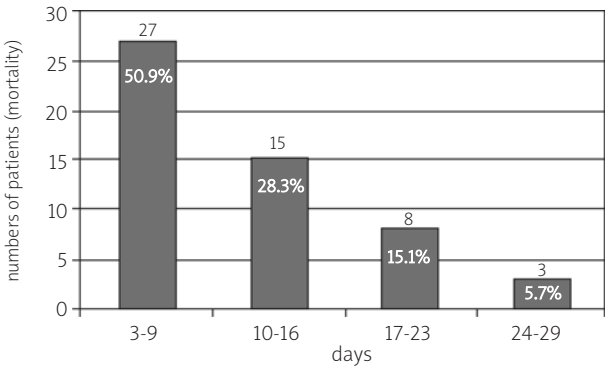

Figure 1. Time course of deaths in the non-survivors group

Ishikawa et al. reported low cardiac output, infection, renal failure, and gastrointestinal complications as the major morbidities for prolonged ICU stay after cardiac surgery [15]. Several studies have reported that patients who required prolonged mechanical ventilation after cardiac surgery had an unfavourable prognosis, with a hospital mortality rate of 50% [1, 16]. In our study, prolonged intubation (p = 0.008), re-intubation (p = 0.001), and postoperative renal dysfunction (p = 0.001) were found as risk factors for mortality. Hein et al. reported higher ICU and hospital mortality rates among patients with prolonged ICU stay, mainly due to multi-organ failure [4]. They also reported that the risk factors for mortality in patients who required prolonged ICU stay after cardiac surgery were renal and respiratory dysfunctions, congestive heart failure and chest re-exploration [4]. Ishikawa et al. found that postoperative respiratory failure and gastrointestinal complications were much more common in non-survivor patients [15]. In a similar study, the presence of valvular intervention, chest re-exploration, congestive heart failure, renal dysfunction and blood transfusion was found to increase mortality [16]. According to Tu et al., mortality and prolonged ICU stay were affected by age, female gender, LV dysfunction, type of surgical intervention, emergency surgery and re-operation [17].

In conclusion, diabetes mellitus, postoperative renal dysfunction, postoperative IABP usage, prolonged intubation, and re-intubation were significant and

independent factors of mortality in patients with prolonged ICU stay after elective isolated on-pump CABG.

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Czynniki ryzyzka zgonu pacjentów wymagających przedłużonego pobytu na oddziale intensywnej opieki medycznej po planowej operacji pomostowania aortalno-wieńcowego z użyciem krążenia pozaustrojowego

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Streszczenie

Wstęp: Do 36% pacjentów po przebytej operacji kardiochirurgicznej może wymagać przedłużonego pobytu na oddziale intensywnej opieki medycznej (OIOM). Umieralność w tej grupie sięga od 11% do 94%, co jest przyczyną poważnych dylematów klinicznych i etycznych.

Cel: Identyfikacja przed-, około- i pooperacyjnych czynników ryzyka zgonu u pacjentów wymagających przedłużonego pobytu na OIOM-ie po elektywnej izolowanej operacji pomostowania aortalno-wieńcowego (CABG) z użyciem krążenia pozaustrojowego.

Metody: Przeprowadzono retrospektywną ocenę danych klinicznych 137 chorych po elektywnej izolowanej operacji CABG z użyciem krążenia pozaustrojowego, których okres pobytu na OIOM-ie wyniósł ≥ 3 dni. Porównano przed-, około- i pooperacyjne cechy pacjentów, u których wystąpił zgon i którzy przeżyli, w celu zidentyfikowania czynników ryzyka zgonu.

Wyniki: Analiza wieloczynnikowa wykazała, że cukrzyca (OR 3,62, 95% CI 1,07–12,26, p = 0,039), pooperacyjne zaburzenia czynności nerek (OR 3,86, 95% CI 1,26–11,75, p = 0,018), pooperacyjne zastosowanie wspomagania wewnątrzaortalnego (OR 3,47, 95% CI 1,01–13,24, p = 0,048), przedłużona intubacja (OR 3,90, 95% CI 1,19–12,69, p = 0,024) oraz reintubacja (OR 14,83, 95% CI 4,35–50,55, p = 0,001) były istotnymi i niezależnymi czynnikami ryzyka zgonu.

Wnioski: W badaniu stwierdzono, że przedoperacyjna diagnoza cukrzycy oraz pooperacyjny zespół niewydolności wielonarządowej zmniejszały prawdopodobieństwo przeżycia pacjentów wymagających przedłużonego pobytu na OIOM-ie po elektywnej izolowanej operacji CABG z użyciem krążenia pozaustrojowego.

Słowa kluczowe: przedłużony pobyt na OIOM-ie, CABG, umieralność

Kardiol Pol 2010; 68: 257-262

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Praca wpłynęła: 12.07.2009. **Zaakceptowana do druku:** 18.11.2009.