Does diabetes mellitus increase the mortality risk in coronary artery disease patients undergoing coronary artery bypass grafting surgery at the National Heart Institute of Kuala Lumpur?

Abstract

Background: Multiple studies had shown that coronary artery disease (CAD) has been the principal cause of mortality in patients with diabetes mellitus (DM). Furthermore, DM has always been a major risk predictor for unfavorable outcomes in patients undergoing cardiac revascularization either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) surgery.

Objective: To investigate whether the presence of DM increase mortality risk in patients undergoing CABG.

Methods: A retrospective single-center study was performed. A special database was created to include all EuroSCORE II variables, EuroSCORE II predicted mortality and actual mortality of 1718 patients undergoing Coronary Artery Bypass (CABG) surgery in Malaysia from 1st January 2016 till 31st December 2016. Univariate and multivariate logistic regressions were done to identify significant predictors of in-hospital mortality among this group of patients.

Results: More than half of the patients undergoing CABG surgery are diabetic (56.3%) while 20.3% are on long-term insulin. In terms of mortality, a significantly higher proportion of in-hospital mortality was observed among patients with DM (5.7%) compared to those without DM (3.4%). On univariate logistic regression analysis, both non-insulin dependent DM (OR: 1.737, 95% CI 1.072-2.815, *p*=0.025) and insulin-dependent DM (OR: 1.960, 95% CI: 1.209-3.179, *p*=0.006) are significant predictors of in-hospital mortality in this group of patients undergoing CABG surgery. However, in multivariate logistic regression, which took into consideration of other related variables in the EuroSCORE II, only female gender, age more than or equal to 65 years old, serum creatinine more than 120 mol/litre and longer ICU stays are significant predictors of in-hospital post-CABG mortality.

Conclusion: In conclusion, a significant proportion of patients undergoing CABG surgery in JIN are actually diabetics while a higher in-hospital mortality risk post-CABG was observed in patients with DM. However, insulin-dependent diabetes mellitus was not a significant risk factor for in-hospital mortality in this group of patients.

Keywords: coronary artery disease (CAD), diabetes mellitus (DM), EUROScore II, mortality

Introduction

Globally, the number of patients with diabetes mellitus (DM) has increased to almost 451 million in 2017, and has become a worldwide epidemic. Even more worrisome is that 49.7% of them remain undiagnosed. Studies have shown that coronary artery disease (CAD) is the principal cause of mortality in DM patients and linked with significantly higher cardiovascular mortality due to myocardial infarction and stroke. DM has always been a major risk predictor for unfavourable outcomes in patients undergoing cardiac revascularization either percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG), surgery.

Methodology

We have undertaken a single-centre retrospective study on the validation of EuroSCORE II among 1718 patients undergoing CABG surgery at the National Heart Institute (JIN) of Kuala Lumpur from 1st January to 31st December 2016. EuroSCORE II is a risk evaluation tool that included ten patient-related factors, five cardiac-related factors, and three operation-related factors with the aim of determining in-hospital mortality after cardiac surgery. Patient-related factors include age (year), gender (male /female), renal impairment (creatinine clearance), extracardiac arteriopathy, poor mobility, previous cardiac surgery, chronic lung disease, active endocarditis, critical preoperative state and diabetes on insulin. Cardiac-related factors include the New York Heart Association (NYHA) stages, Canadian Cardiovascular Society (CCS) class 4 angina, Left Ventricular (LV) function (ejection fraction > 50%, 31-50%, 21-30%, <20%), recent myocardial infarction (MI) (within 90 days) and pulmonary hypertension (31-55mm Hg/>55mm Hg). Operation-related factors include urgency (elective, urgent, emergency, salvage), weight of the intervention (isolated CABG, isolated single non-
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CABG, 2-procedures, and 3-procedures) and surgery on thoracic aorta. Details regarding EuroSCORE II calculation are available from the EuroSCORE site.

**Results**

Many international studies have examined the validity of EuroSCORE II in predicting in-hospital mortality post-CABG. Most of the validation studies in Europe including Spain, Italy, Greece, Serbia and Hungary have an area under the receiver operating characteristic (ROC) curve (AUC) of more than 0.7, indicating good discriminatory power and calibration. However, there was a collaborative study between two centres in the Netherlands and United Kingdom, which showed that EuroSCORE II was not good in predicting mortality in patients undergoing cardiac operation. It showed an unsatisfactory AUC of 0.67, indicating poor discriminatory power. Among our own population of CABG patients in IJN, we observed an AUC of 0.7, which is deemed to be satisfactory in predicting in-hospital mortality.

In this review, we aim to use the data collected based on the EuroSCORE II variables to investigate whether the presence of DM increase the mortality risk in patients undergoing CABG.

Our results showed that more than half of the patients undergoing CABG surgery are diabetic (56.3%) while 20.3% are on long-term insulin. This once again proved the known correlation between CAD and DM, in which patients with DM will definitely have a greater burden of atherogenic risks, as compared to patients without DM.

Table 1 shows the relationship between DM status and in-hospital post-CABG mortality. A significantly higher proportion of in-hospital mortality is observed among patients with insulin dependent DM (7.4%), followed by non-insulin dependent DM (4.7%) and patients, with no DM (3.3%).

**Table 2** Multiple logistic regression between independent variables and in-hospital post-CABG mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>p value</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 65 years</td>
<td>0.004</td>
<td>2.27</td>
<td>1.303–3.954</td>
</tr>
<tr>
<td>Female gender</td>
<td>&lt;0.001</td>
<td>3.118</td>
<td>1.701–5.718</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>&lt;0.001</td>
<td>3.54</td>
<td>2.024–6.19</td>
</tr>
<tr>
<td>ICU stays (days)</td>
<td>&lt;0.001</td>
<td>1.093</td>
<td>1.061–1.127</td>
</tr>
<tr>
<td>Poor Mobility</td>
<td>&lt;0.001</td>
<td>5.896</td>
<td>2.297–15.135</td>
</tr>
</tbody>
</table>

On univariate binary logistic regression analysis, non-insulin dependent DM (OR: 1.425, 95% CI 0.826 - 2.460, p=0.203) is not significant in predicting in-hospital mortality. However, insulin-dependent DM (OR: 2.334, 95% CI: 1.327-4.105, p=0.003) is a significant predictor of mortality in this group of patients undergoing CABG surgery. On multivariate binary logistic regression, which took into consideration other related variables in the EuroSCORE II, only age≥65 years, female gender, serum creatinine ≥ 120 μmol/litre, longer ICU stay and poor mobility are significant predictors of in-hospital post-CABG mortality (Table 2).

On a side note, in our EuroSCORE II study, analysis of the discriminatory power was done on specific subgroups. It showed that the AUC was 0.672 in diabetic patients (95% CI 0.602–0.741, p < 0.001) and 0.728 in patients without DM (95% CI 0.614–0.841, p < 0.001). Therefore, the EuroSCORE II has a better discriminatory power in patients without DM.

**Discussion**

As shown in our results, a higher proportion of mortality is observed among both patients with insulin dependent DM and non-insulin dependent DM as compared to those who do not have DM. Compared with a previous literature, in a study done on about 1800 patients who underwent CABG, in-hospital mortality rate was about 5% in patients with DM while it was only 0.36% in non-diabetics. Multiple other studies have also verified that the mortality risk was higher in diabetic patients.

In our original study, we have determined both the calibration and discriminatory power of the EuroSCORE II in our local population undergoing CABG surgery. The Hosmer-Lemeshow goodness-of-fit test did not show any significant difference between expected and observed mortality in accordance to the EuroSCORE II model (Chi-square=13.758, p=0.089) suggesting good calibration of the model in this population. The Area under the ROC curve (AUC) for EuroSCORE II was 0.7 (95% CI 0.640–0.759) indicating good discriminatory power. Consistent with our study, most of the validation studies in Europe has an AUC of more than 0.7, which indicates good discriminatory power and calibration.

Logistic regression in this study had also shown that only age more than or equal to 65 years old, female gender, serum creatinine more than 120 micromole/litre, longer ICU stay and poor mobility are significant predictors of in-hospital mortality in patients post CABG surgery. In this context, independent variables were selected in line with the principle of parsimony so that our analysis can be more consistent and limited to as few variables as possible in the prediction model.

Few studies have identified the fact that EuroSCORE and EuroSCORE II risk model might not be as precise and accurate on older patients' populations. This is particularly important as a significant portion of the patients undergoing CABG are from the older age group. A study in France has shown that the EuroSCORE II performed not as good on patients more than 80 years old, showing overestimation. At the same time, another study in the United Kingdom has shown that both the original EuroSCORE and the EuroSCORE II has a ROC c-statistic value below 0.7 for patients more than or equal to 70 years of age, which indicates a potential issue with accuracy and validity of the risk prediction model. Lastly, among our own population in Malaysia, we have also identified that the AUC was 0.7 in those aged below 60 years while it was 0.673 in those aged 60 years and above.

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In the risk prediction model of EuroSCORE II, insulin-dependent diabetes was known as one of the many dichotomous variables (yes/no) in predicting mortality after cardiac surgery. According to the EuroSCORE database, diabetes on insulin recorded 1.43 times higher risk of in-hospital mortality after surgery. Wang et al. specifically looked into the significance of diabetes on post-operative outcomes. It was shown that preoperative HbA1c was actually the only diabetic variable that managed to independently predict mortality post-CABG. This indicated that HbA1c value, rather than the presence of diabetes on insulin, might stand as a relatively better endpoint in predicting mortality, which also explained the non-significance of insulin-dependent variable in predicting mortality among our population.

**Conclusion**

In conclusion, a significant proportion of patients undergoing CABG surgery in IJN are actually diabetics while a higher in-hospital mortality rate post-CABG was observed in patients with DM. However, insulin-dependent diabetes mellitus was not a significant risk factor for in-hospital mortality in this group of patients.

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None.

**Conflict of interest**

Author declares there is no conflict of interest.

**References**