On-pump or off-pump? Impact of risk scores in coronary artery bypass surgery

Com ou sem CEC? Impacto dos escores de risco na cirurgia de revascularização miocárdica

Omar Asdrúbal Vilca Mejía¹, Luiz Augusto Ferreira Lisboa², Luiz Boro Puig³, Luiz Felipe Pinho Moreira⁴, Luis Alberto Oliveira Dallan⁵, Fabio Biscegli Jatene⁶

Abstract

Objective: Remain controversies about the use of cardiopulmonary bypass (CPB) in coronary artery bypass grafting (CABG). The aim of this study was to evaluate the impact of the 2000 Bernstein Parsonnet (2000BP) and EuroSCORE (EU) for choice CPB in CABG.

Methods: 1551 consecutive patients underwent CABG. CPB was used in 1,121 (72.3%) patients. The performance of 2000BP and EU was assessed by calibration, discrimination and correlation tests. For both risk scores, increasing the value of the score and presence of CPB were directly related to a higher risk of death (P <0.05). Therefore with these two variables was constructed a logistic regression model for each risk score, in order to determine in which value of score the presence of CPB increases significantly the risk of death.

Results: The calibration, like the area under the ROC curve for the group with CPB [2000BP=0.80; EU=0.78] and without CPB [2000BP=0.81; EU=0.85] were appropriate. The Spearman correlation for groups with and without CPB was 0.66 (P<0.001) and 0.62 (P<0.001), respectively. Using the 2000BP, for a value>17.75 the presence of CPB increased the chance of death to 7.4 [CI 95% (4.4-12.3), P<0.0001]. With the EU, for a value >4.5 the presence of CPB increased the chance of death to 5.4 [CI 95% (3.3-9), P<0.0001].

Conclusion: In decision making, the 2000BP>17.75 or the EU>4.5 guide to identify patients who underwent CABG with CPB increases significantly the chance of death.

**Resumo**

**Objetivo:** Permanecem as controvérsias sobre a utilização de circulação extracorpórea (CEC) na cirurgia de revascularização miocárdica (CRM). O objetivo deste estudo foi avaliar o impacto do 2000 Bernstein Parsonnet (2000BP) e EuroSCORE (EU) para escolha de CEC na CRM.

**Métodos:** Foram submetidos à CRM 1551 pacientes consecutivos. CEC foi utilizada em 1.121 (72,3%) pacientes. O desempenho do 2000BP e EU para a amostra foi avaliado mediante testes de calibração, discriminação e correlação. Para ambos os escores de risco, o aumento do valor do escore e a presença de CEC tiveram relação direta com maior chance de óbito ($P<0.05$). Portanto, com essas duas variáveis foi construído um modelo de regressão logística para cada escore de risco, com a finalidade de determinar em que valor do escore a presença de CEC aumenta significativamente a chance de óbito.

**Resultados:** A calibração, ao igual que a área abaixo da curva ROC para o grupo com CEC [2000BP=0,80; EU=0,78] e sem CEC [2000BP=0,81; EU=0,85] foram adequadas. A correlação de Spearman para os grupos com e sem CEC foi de 0,66 ($P<0,001$) e 0,62 ($P<0,001$), respectivamente. No 2000BP, para um valor>17,75, a presença de CEC aumentou a chance de óbito para 7,4 [IC95% (4,4-12,3), $P<0,0001$]. No EU, para um valor>4,5, a presença de CEC aumentou a chance de óbito para 5,4 [IC95% (3,3-9), $P<0,0001$].

**Conclusão:** Na tomada de decisões, o 2000BP>17,75 ou o EU>4,5 orientam a identificar pacientes que quando submetidos a CRM com CEC têm chance de óbito aumentada significativamente.

**Descritores:** Fatores de Risco. Circulação Extracorpórea. Ponte de Artéria Coronária. Mortalidade Hospitalar.
of Cardiology, Heart Institute of the Clinical Hospital of the School of Medicine, University of São Paulo (Incor-HCFMUSP). In the sample, 1551 patients underwent CABG sequentially in both modality elective, urgent and emergency care, from May 2008 to July 2010.

We excluded from the study: reoperations associated surgeries (including valve, and other thoracic aorta) and coronary insufficiency alternative procedures (laser, injection of stem cells and other).

**Gathering, defining and organizing the data**

Data were collected preoperatively and clinical evaluation system for electronic medical records InCor-HCFMUSP (SI3) and stored in a single spreadsheet. This worksheet was adapted to include all the variables described by the model 2000BP and the EU for each patient. Patients were sorted according to risk groups established by the scores and placed in the database made on Excel for this purpose. All patients were followed until hospital discharge. No patient was excluded from analysis due to missing data.

The outcome of interest was in-hospital mortality, defined as death occurring in the time interval between surgery and discharge.

**Surgical Technique**

After median sternotomy, the patients were operated with or without the use of CPB, this option by the surgeon in charge of the case. When operated using CPB, this was performed at normothermia or mild hypothermia and arterial cannulation had made in the ascending aorta and the right atrium vein. Cardiac arrest was induced by blood cardioplegia or crystalloid, always using the anterograde. Off-pump patients needed the Octopus device (Medtronic).

**Statistical Analysis**

For plausibility of the study was initially assessed the applicability of scores (2000BP and EU) in patients with and without CPB sample studied by testing calibration and discrimination. The correlation between both scores in patients with and without CPB was analyzed by the Spearman test and the presence of outliers via box plots. From the directly proportional relationship between the score and the presence of in-hospital death ($P <0.001$) and there is more on-pump CABG group died ($P <0.05$) was built a logistic regression model with two variables (score value + presence / absence of CPB) for each risk score. The purpose of the study was to examine whether the same score value (total value represented by the sum of the weights assigned to each variable) the presence of CPB would alter the estimated probability of death.

To better prognostic accuracy cutoff points were obtained by means of receiver operating characteristic curve (ROC). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 16.0 for Windows (IBM Corporation Armonk, New York). Abnormal distribution of continuous variables were described as medians. The standard deviation and categorical variables were described by absolute number and percentage. The comparison of categorical variables was performed by chi-square test. The value of $P <0.05$ was considered significant.

**Ethics and consent**

This study was approved by the Ethics Committee for Analysis of Research Projects (CAPPesq), Hospital das Clinicas, School of Medicine, University of São Paulo with the number 1575, which exempted the need for informed consent and informed by the type of design applied.

**RESULTS**

Mean age was $63 \pm 10$ years, and 27% of female patients. Overall mortality was 5%. In Figure 1, so informative and not comparative, is shown the prevalence of variables in patients with and without CPB. The pump CABG was performed in 1,122 (72.3%) patients and OPCAB in 429 patients, with a mortality of 5.7% and 6.9%, respectively.

**Table 1 - Prevalence of variables in patients with and without cardiopulmonary bypass for patients undergoing coronary artery bypass grafting**

<table>
<thead>
<tr>
<th>Variable</th>
<th>CABG w/CPB</th>
<th>CABG w/o CPB</th>
<th>p = 0.006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>62.3 ± 10</td>
<td>63.6 ± 10.5</td>
<td>0.054</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>36.4%</td>
<td>39.1%</td>
<td>0.275</td>
</tr>
<tr>
<td>Score PM</td>
<td>44.3 ± 8.4</td>
<td>41.3 ± 8.7</td>
<td>0.080</td>
</tr>
<tr>
<td>Score EU</td>
<td>3.7 ± 3.1</td>
<td>3.8 ± 3.2</td>
<td>0.374</td>
</tr>
<tr>
<td>Hypertension</td>
<td>81.6%</td>
<td>89.3%</td>
<td>0.265</td>
</tr>
<tr>
<td>Diabetes</td>
<td>47.3%</td>
<td>43.6%</td>
<td>0.167</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>36.1%</td>
<td>47.6%</td>
<td>0.002</td>
</tr>
<tr>
<td>Mortal obesity</td>
<td>11.6%</td>
<td>12.1%</td>
<td>0.779</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>2.2%</td>
<td>3.3%</td>
<td>0.244</td>
</tr>
<tr>
<td>Peripheral arterial</td>
<td>6.2%</td>
<td>8%</td>
<td>0.233</td>
</tr>
<tr>
<td>Ejection Fraction</td>
<td>54.1 ± 15.1</td>
<td>57.1 ± 12.3</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>atrial fibrillation</td>
<td>2%</td>
<td>12%</td>
<td>0.044</td>
</tr>
<tr>
<td>HFS&lt; 60</td>
<td>1.3%</td>
<td>0.7%</td>
<td>0.543</td>
</tr>
<tr>
<td>TBI on&lt; 50%</td>
<td>18.9%</td>
<td>18.0%</td>
<td>0.721</td>
</tr>
<tr>
<td>prior ami</td>
<td>18.4%</td>
<td>29%</td>
<td>0.010</td>
</tr>
<tr>
<td>IAPB preoperative</td>
<td>3.8%</td>
<td>1.9%</td>
<td>0.052</td>
</tr>
<tr>
<td>IOT preoperative</td>
<td>1%</td>
<td>0.7%</td>
<td>0.760</td>
</tr>
<tr>
<td>ungradable Angina</td>
<td>10.8%</td>
<td>9.8%</td>
<td>0.508</td>
</tr>
<tr>
<td>AMI &lt;48h</td>
<td>4.4%</td>
<td>2.1%</td>
<td>0.066</td>
</tr>
<tr>
<td>AMI &lt;90 days</td>
<td>27.5%</td>
<td>24%</td>
<td>0.159</td>
</tr>
<tr>
<td>cardiogenic shock</td>
<td>6.3%</td>
<td>9.5%</td>
<td>1.600</td>
</tr>
<tr>
<td>Creatine preoperative</td>
<td>12.8 ± 1.8</td>
<td>15 ± 4.7</td>
<td>0.039</td>
</tr>
<tr>
<td>BIC dialysis</td>
<td>1.2%</td>
<td>2.0%</td>
<td>0.045</td>
</tr>
<tr>
<td>price stroke</td>
<td>5.6%</td>
<td>6.5%</td>
<td>0.609</td>
</tr>
<tr>
<td>Emergency Surgery</td>
<td>2.9%</td>
<td>3.1%</td>
<td>0.548</td>
</tr>
</tbody>
</table>

| Total                           | 1122        | 429          |           |

COPD: Chronic obstructive pulmonary disease; HFS: systolic pulmonary Hypertension; TEC: Trunk of left coronary artery; IAB: IAB; IOT: intra-thoracic intubation; AMI: acute myocardial infarction; CRF: chronic renal failure; CVA: stroke; (1) Descriptive level of probability of Student's t test, (2) descriptive level of probability of the Fisher exact test.

Fig. 1 - Prevalence of variables in patients with and without cardiopulmonary bypass for patients undergoing coronary artery bypass grafting
3.2%, respectively. In the calibration of the models in the on-pump group, the Hosmer-Lemeshow test showed a $P = 0.864$ ($\chi^2 = 3.926$, df = 8) to 2000BP and $P = 0.442$ ($\chi^2 = 5.836$, df = 6) for the EU. In the calibration of the models in the off-pump group, the Hosmer-Lemeshow test showed a $P = 0.199$ ($\chi^2 = 11.046$, df = 8) to 2000BP and $P = 0.728$ ($\chi^2 = 3.623$, df = 6) for the EU. Discrimination (Figure 2), the area under the ROC curve for the group with CPB was 0.799 [95% CI (0.741 to 0.856), $P < 0.001$] for 2000BP and 0.775 [95% CI (0.711 to 0.838), $P < 0.001$] for the EU. The area under the ROC curve for the off-pump group was 0.807 [95% CI (0.677 to 0.936), $P < 0.001$] for 2000BP and 0.845 [95% CI (0.743 to 0.947), $P < 0.001$] for EU. Therefore, the applicability of the models in the overall sample and by groups was adequate. From this analysis were prepared curves of observed mortality for the groups with and without cardiopulmonary bypass and its relation to expected mortality by EU and 2000BP (Figure 3).

The Spearman correlation between 2000BP and EU was good in both groups, showing a coefficient of 0.657 ($P < 0.001$) in the on-pump group and 0.620 ($P < 0.001$) in the group without CPB. However, the presence of outliers was observed in the group with and without cardiopulmonary bypass when estimated values for both risk scores were very high (Figure 4).

In Table 1, the association was demonstrated CPB with in-hospital death ($P < 0.05$) and directly proportional relationship between the score and the presence of death ($P < 0.0001$). To study the 2000BP and the presence of CPB as predictors of mortality, we adjusted the logistic regression model presented in Table 2. In this table, we observe that, for a given value of 2000BP, patients operated with CPB have chance of death twice that without CPB [95% CI (1.1 - 3.8), $P < 0.02$] and each unit increase in score patients have increased risk of death of 1.1 [95% CI (1.09 to 1.14), $P < 0.0001$].

![Fig. 2 - ROC curve (Receiver Operating Characteristic) of the 2000 Bernstein Parsonnet (2000BP) and EuroSCORE (EU) for the groups with and without cardiopulmonary bypass for patients undergoing coronary artery bypass grafting](image)
Fig. 3 - Observed and expected mortality by 2000 Bernstein Parsonnet (2000BP) and EuroSCORE (EU) for the groups with and without cardiopulmonary bypass for patients undergoing coronary artery bypass grafting

Fig. 4 - Diagram showing the presence of outliers after application of the 2000 Bernstein Parsonnet (2000BP) and EuroSCORE (EU) in patients with and without cardiopulmonary bypass for patients undergoing coronary artery bypass grafting
For the study of the EU and the presence of CPB as predictors of mortality, we adjusted the logistic regression model presented in Table 3. In this table, we observe that, for a given value of the EU, patients operated with CPB have a chance of death twice that without CPB [95% CI (1.1 - 3.8), \( P < 0.001 \)] and each unit increase in score patients have increased risk of death 1.4 times [95% CI (1.3 - 1.4), \( P < 0.0001 \)].

Thus, through these logistic models, made using 2000BP (Figure 5) and EU (Figure 6), one can calculate the probability of death for an overall score value, and for each of the situations with and without cardiopulmonary bypass.

In the search for better prognostic accuracy 2000BP and the EU were obtained cutoff points (balance between sensitivity and specificity) by the ROC curve. Thus, in 2000BP, which have the value 73% sensitivity and specificity also is 17.75 and the EU, where we have the value 71% sensitivity and 69% specificity is 4.5. For both models, the calculation of the power of the sample as a function of proportion was > 90% (\( \alpha = 0.05 \)). From this, we have, with 2000BP, the chance of death in patients operated...
with CPB compared to off-pump increases from 1.9 to 7.4 times when the value of 2000BP stay above 17.75 [OR 7, 4, 95% CI (4.40 to 12.31), \( P < 0.0001 \)]. Likewise, the EU, the chance of death in patients operated with CPB compared to off-pump increases from 1.8 to 5.4 times when the value of the EU stay above 4.5 [OR 5.4, CI 95% (3.3 - 9), \( P < 0.0001 \)].

**DISCUSSION**

Several studies [2,3] confirm that significant reduction of the inflammatory response leads to reduced organ dysfunction in OPCAB.

The results of observational studies based on well-structured database (real world) do not overestimate the magnitude of treatment effects compared with randomized trials in the same clinical setting [17,18]. In CABG, retrospective analyzes in large populations describe a significant reduction in morbidity and mortality, especially in-hospital, when performed without CPB [6,7]. In this approach, a multicenter study of the four major EU centers showed benefit in the immediate postoperative period with OPCAB, especially in patients considered at high risk [12]. Furthermore, the use of CPB was an independent predictor of mortality in centers with significant experience in OPCAB. As in this study, without the artifice of randomization, found higher chance of death when patients underwent surgery with CPB compared to surgery without CPB, especially in considered high risk by the scores used. Similarly, a study odd authored by Buffolo et al. [19], revealing the experience of 30 years of OPCAB, demonstrated a significant reduction in hospital mortality outcomes, stroke, severe postoperative complications, length of hospital stay and decreased costs. Also, was described biggest difference in mortality among high-risk patients when operated with or without CPB. This corroborates our analysis, where as the score values increase (worsening of the risk profile of the patient), also increases the risk of death among patients who underwent surgery with or without CPB. This corroborates our analysis, where as the score values increase (worsening of the risk profile of the patient), also increases the risk of death among patients who underwent surgery with or without CPB (Figures 5 and 6).

A demonstration that this technique is reproducible was published by Lima et al. [20], in which 95% of patients undergoing CABG surgery without CPB were. Thus, it is revealed that virtually all patients with indication for CABG are potential candidates for OPCAB. In the study, the authors demonstrate that low-risk patients and patients without comorbidities also benefit from OPCAB, which was confirmed in our analysis, although to a lesser extent (Figure 5 and 6).

On the international scene, recent randomized studies that found differences in favor of OPCAB with regard to in-hospital mortality did not show statistical significance [21,22]. Unfortunately, randomized trials are composed of stable patients at low risk and do not reflect the reality of the current profile of patients referred for CABG. In this sense, the last work of the greatest impact was published by Lamy et al. [23], in which 4752 patients from 79 centers in 19 countries were randomized. In the results, no significant difference, up to 30 days between CABG with and without CPB, on death, myocardial infarction, stroke and renal dysfunction requiring dialysis. However, OPCAB resulted in lower rates of transfusion, reoperation for bleeding, respiratory complications and acute renal failure, although the increased risk of early revascularization. Nationally, a randomized, multicenter published by Gerola et al. [24] almost a decade ago, had no significant difference was found within 30 days, between CABG with and without CPB in morbidity and mortality in low-risk patients.

As we can see, these studies were not considered high-risk patients with significant comorbidities and, unlike the patients included in our sample (the real world).

Recently, in non-randomized study, Cantero et al. [25] reported a hospital mortality of 4.3% and 4.7%, respectively, in the group without CPB and CABG (\( P = 0.92 \)). However, the off-pump patients had fewer complications compared to perioperative infarction (\( P = 0.02 \)) and the use of intra-aortic balloon (\( P = 0.01 \)).

Moreover, the risk scores are predictive tools that can help patients and health professionals in decision making by informing about the likely risk of complications or death. In this setting, two of the most commonly performed procedures in the interventional cardiology world are influenced by risk scores. The Syntax score was developed from database to examine how best revascularization (CABG or PCI), based on the angiographic characteristics [26]. Moreover, the score Wilkins was created to orient the cases of mitral stenosis which would be better handled by conventional surgery as compared to balloon valvuloplasty [27].

Thus, in InCor-HCFMUSP, held after the statistical validation of models 2000BP and EU [28], even in patients with acute myocardial infarction [29], was of clinical interest and practical know the score (cutoff) that would have better prognostic accuracy to define which patients would benefit most from OPCAB those who could be safely treated using CPB.

To do so, he had to be confirmed the good performance of risk scores for both patients with and without CPB (Figure 2), and good correlation between both models for each patient sample. However, as is expected for samples in the real world, outliers are described for scores 2000BP and EU in our study, confirming a truth about the stability of risk scores: the loss of calibration in the evaluation of high-risk patients (Figure 4).

Importantly, even though the subjective choice of the current CPB in CABG, it is supported in patients with low
ejection fraction and should be avoided in patients with severe renal impairment. These data are consistent with that observed in our study (Figure 1).

Surely, this analysis is more objective evidence and practice, from the look of the risk scores, which justifies the preference for not using CPB in CABG in patients considered high risk by the scores 2000BP and EU.

Limitations of this study were: 1. is a study in a single center, where there was lack of randomization between both groups, 2. although hospital mortality (up to 30 days after surgery) appears to be more complete than the in-hospital mortality (until discharge), the current definitions suggest that both have equivalent accuracy, and in-hospital mortality was more practical and easy to use [30].

In summary, randomized controlled trials have found in the short term, statistically significant reductions in morbidity and mortality demonstrated in observational studies. These discrepancies may be due to differences in patient selection and study methodology. Future studies should focus on improving research methodology, recruiting high-risk patients and data collection in the long term.

Finally, it is important to reiterate that the current medical treatment must be integrated into individual clinical experience and the best available external evidence, therefore, risk scores cannot continue to be neglected [31].

CONCLUSION

The scores 2000BP and EU showed good performance in the evaluation of patients undergoing CABG with and without CPB. In the real world, patients with 2000BP > 17.75 and EU > 4.5 show, respectively, 7.4 and 5.4 times greater chance of death when operated with CPB regarding OPCAB.

REFERENCES


