Factors associated to hypoxemia in patients undergoing coronary artery bypass grafting

Fatores associados à ocorrência de hipoxemia em pacientes submetidos à revascularização miocárdica

Natália Pereira dos Santos¹, PT; Rodrigo Martins Mitsunaga¹; Daniel Lago Borges¹, PT, MsC; Marina de Albuquerque Gonçalves Costa¹, PT; Thiago Eduardo Pereira Baldez¹, PT; Ilka Mendes Lima¹, PT; Karol Cristina Fonseca Moura¹, PT; Josimary Lima da Silva Lula²

Abstract

Introduction: Hypoxemia is a frequent pulmonary complication in the postoperative coronary artery bypass graft. Detection of factors associated with their occurrence may indicate patients at risk for this complication, which allows tracing specific therapeutic and consequently reduce morbidity and mortality.

Objective: To identify related factors to hypoxemia occurrence in immediate coronary artery bypass graft postoperative.

Methods: In this retrospective cohort study, we studied 100 patients submitted to elective on-pump artery bypass graft, between April 2010 and December 2011, at a reference university hospital for cardiac surgery in the state of Maranhão. It was considered hypoxemia gas exchange ratio less than or equal to 300 mmHg. Associated variables with perioperative hypoxemia were defined by the Student T test, G or Mann-Whitney tests, Chi-square, or Fisher’s exact test and multiple linear regression.

Results: Among studied variables, high body mass index (P=0.036) and smoking (P=0.024) were significantly associated with hypoxemia in the immediate coronary artery bypass graft postoperative. Hypoxemia incidence in this period was 55% and did not affects mechanical ventilation duration and Intensive Care Unit length of stay.

Conclusion: In this sample, body mass index and smoking were associated to hypoxemia. These data reinforce the importance of clinical assessment to identify patients at risk for this complication, considering its high incidence in immediate postoperative period.


Resumo

Introdução: A hipoxemia é uma complicação pulmonar frequente no pós-operatório de revascularização miocárdica. A detecção de fatores associados a sua ocorrência pode indicar pacientes de risco para essa complicação, o que possibilita traçar terapêuticas específicas e, consequentemente, diminuir a morbimortalidade.

Objetivo: Identificar fatores relacionados à ocorrência de hipoxemia no pós-operatório imediato de revascularização miocárdica.

Métodos: Nesta coorte retrospectiva, foram estudados 100...
INTRODUCTION

Coronary artery bypass grafting (CABG) surgery, despite all the advances in clinical treatment and percutaneous interventions, is still used in coronary heart disease treatment [1]. Pulmonary complications in cardiac surgery postoperative period are very frequent and represent significant morbidity and mortality cause [2].

Hypoxemia is one of the main causes of pulmonary complications characterized by decrease of arterial oxygen partial pressure (PaO₂) [3,4]. Measuring severity of the pulmonary injury in mechanically ventilated patients is performed by PaO₂ and inspired oxygen fraction (FiO₂) ratio [5].

Diverse mechanisms have been accounted for its development on cardiac surgery postoperative, especially atelectasis, shunt increase, respiratory and thoracic mechanics alterations, capillary and pulmonary parenchyma changes secondary to the left ventricular (LV) dysfunction or pulmonary endothelium injury [3,6].

Elderly, obeses and patients with left ventricular dysfunction (ejection fraction of the left ventricle < 55%) and prolonged cardiopulmonary bypass (CPB) time (> 120 minutes) had higher risks to postoperative surgery hypoxemia [7]. Pulmonary chronic diseases, diabetes and preoperative acute myocardial infarction are independent risk factors for hypoxemia after CABG [8].

According to a recent study [7], predictor factors detection may indicate patients at high risk for postoperative hypoxemia that demand mechanical ventilation strategies, in order to prevent and treat pulmonary collapse during intra-operative period, to minimize hypoxemia impact on mechanical ventilation duration, to reduce morbidity and mortality related to cardiac intervention, to reduce length of stay at Intensive Care Unit (ICU), and hospital costs.

This study is designed to analyze factors related to hypoxemia in a specific population of patients undergoing CABG surgery, to determine its incidence in immediate post-operative period, and to evaluate if hypoxemia interfered on mechanical ventilation duration and length of stay in ICU.

METHODS

It is a retrospective descriptive cohort study conducted in a reference university hospital for cardiac surgery in São Luís, MA, Brazil, after Research Ethics Committee approval (Protocol Nº 0051/2012), as required by Resolution Nº 196/96 of the National Health Council.

Patients who underwent CABG between April 2010 and December 2011 and were admitted to the Cardio ICU in the referred hospital were included in research.

Adult patients (> 18 years old) from both genders were included in the study, with no prior cardiac surgery,
submitted to elective on-pump CABG not associated to other procedures and ventilated in assisted/controlled volume mode, with PEEP (positive end-expiratory pressure) 8 cmH\textsubscript{2}O and FiO\textsubscript{2} 40%.

Missing data related to \(\text{PaO}_2/\text{FiO}_2\) ratio, perioperative death and returning to operation room were exclusion criteria to this study.

Data were collected from Physical Therapy Evaluation form – divided in pre, intra and postoperative periods, filled with information from medical records – and registered in a specifically form designed for this study.

During study period, two hundred and fifty-five patients were admitted to Cardiovascular ICU after CABG (Figure 1). Among them, 100 patients fulfilled all criteria and general characteristics are described in Table 1.

**Preoperative data**

Preoperative variables were: age, considering as advanced age \(\geq 60\) years old; gender; nutritional status, determined by Body Mass Index (BMI) calculated by weight/height\(^2\) ratio, considered as eutrophic = 20 to 24.9 kg/m\(^2\), overweight = 25 to 29.9 kg/m\(^2\) and obese \(\geq 30\) kg/m\(^2\), established by the World Health Organization (WHO)\(^[9]\).

Other studied variables were risk factors to coronary diseases registered in anesthesiologist assessment available in medical records: diabetes mellitus (DM), hypertension, dyslipidemia (DLP), smoking (also were considered former smokers) and associative diseases: chronic obstructive pulmonary disease (COPD), acute renal failure (ARF), acute myocardial infarction (AMI) and prior angioplasty.

It was not possible to correlate left ventricular ejection fraction (left ventricular dysfunction evaluation) due lack of data, cause it is not a routine service to have an echocardiogram in all preoperative patients.

**Intraoperative data**

For CABG patients underwent general anesthesia, tracheal intubation, controlled mechanical ventilation, surgical access via median sternotomy and CPB, performed with graphs of the left internal thoracic artery (LITA) and/or saphenous vein and the placement of mediastinal and pleural drains.

Intraoperative analyzed variables were numbers of graphs, LITA use, number of drains, surgery time, considering a prolonged intervention \(\geq 210\) minutes; pump time, considering prolonged when above 120 minutes; aortic clamping time, considering prolonged when above 90 minutes; and mechanical circulatory assistance use (intra-aortic balloon pump).

**Postoperative data**

After surgery, patients were admitted to the Cardiovascular ICU still under anesthesia. They were intubated and mechanically ventilated (Evita 2 Dura\textsuperscript{a} - Dräger Medical, Lübeck, Germany) in assisted/controlled volume mode,
according to Unit protocol [volume tidal (VT) 8 to 10 ml/kg; respiratory rate (RR) 12 to 16 bpm; inspiratory flow from 8 to 10 times minute volume (VT x RR); inspiratory time 1.0 second; FiO$_2$: 40%; PEEP: 8 cmH$_2$O].

Twenty minutes after admission, arterial blood was collected for a blood gas analysis (ABL 800 FLEX$^*$ - Radiometer, Bronshoj, Denmark), in which PaO$_2$ was analyzed and, consequently, gas exchange ratio (PaO$_2$/FiO$_2$). Other postoperative variables studied were mechanical ventilation duration and length of stay in the ICU.

According to 3$^{rd}$ Brazilian Consensus Conference on Mechanical Ventilation Consensus [5], normal PaO$_2$/FiO$_2$ ratio is above 300 mmHg; as gas exchange deterioration value equal or lower than 300 mmHg; and extreme severity of respiratory condition below 200 mmHg.

Current Berlin definition [10] classifies hypoxemia according to its level: Mild Hypoxemia (PaO$_2$/FiO$_2$ ≤ 300 and > 200 mmHg), Moderate Hypoxemia (PaO$_2$/FiO$_2$ ≤ 200 and >100 mmHg) and Severe Hypoxemia (PaO$_2$/FiO$_2$ ≤ 100 mmHg).

To determine the presence of gas exchange deterioration in researched subjects, it was considered hypoxemia a PaO$_2$/FiO$_2$ ratio ≤ 300, being classified according to Berlin definition [10].

Statistical analysis

Quantitative variables are described as mean and standard deviation or median (minimum, maximum), according to data distribution. Qualitative variables are presented by frequency and percentage. To normality test of the quantitative variables, D’Agostino-Pearson’s test was used.

To test the relation between normally distributed quantitative variables and severe hypoxia occurence, non-paired Student’s t test was used. For quantitative variables of non-normal distribution, Mann-Whitney’s test was used. Association between categorical and outcome variables was done using Chi-square test or Fisher Exact test. Quantitative variables whose statistic univariate tests presented hypothesis that at least one of analyzed variables influenced hypoxemia occurrence. Among partial regression coefficients, only BMI and surgery time were considered.

Mean number of drains was 2.5±0.7, and LITA was used as graph in 91 patients. Remaining patients have received only venous graph. Average number of drains was 1.8±0.5. Twenty three percent used just one drain, seventy percent used two drains and 7% three drains. Mechanical circulatory assistance with intra-aortic balloon pump was used in only 3% of the subjects. None of these variables presented statistically association with hypoxemia in immediate postoperative period.

Mean surgical time was 3 hours and 45 minutes which was considered prolonged. Average pump time was 82.9±29 minutes. In 92% of the patients, pump time was shorter than 120 minutes. Mean aortic clamp time was 59.1±22.7, and 93% less than 90 minutes. These variables did not have any association with hypoxemia during CABG immediate postoperative.

For multiple regression, BMI and surgery time were considered. F value (regression) was significant (P=0.02), accepting the hypothesis that at least one of analyzed variables influenced hypoxemia occurrence. Among partial regression coefficients, only BMI was statistically significant (t=-2.66, P=0.009).

The median of time for interruption of ventilation device for the studied group lasted around 9 hours and 54 minutes and the ICU admission, two days. The presence of hypoxemia did not interfere with time of mechanical ventilation and ICU admission, as observed in Table 3.

### Table 2. Univariate Analysis of the intra-operative variables (n = 100).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hypoxemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO (n = 45)</td>
</tr>
<tr>
<td>Number of grafts</td>
<td>2.5 ± 0.8</td>
</tr>
<tr>
<td>LITA grafts (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6.7</td>
</tr>
<tr>
<td>No</td>
<td>93.3</td>
</tr>
<tr>
<td>Number of drains</td>
<td>1.8 ± 0.5</td>
</tr>
<tr>
<td>Surgery time (min)</td>
<td>217.1 ± 48.1</td>
</tr>
<tr>
<td>Pump time (min)</td>
<td>81.4 ± 29.8</td>
</tr>
<tr>
<td>Aortic clamp time (min)</td>
<td>56.7 ± 23.2</td>
</tr>
</tbody>
</table>

$^a$ Student’s T Test; $^b$ Fisher Exact Test; LITA – Left Internal Thoracic Artery.

RESULTS

The incidence of hypoxemia, i.e., in the presence of PaO$_2$/FiO$_2$ ≤300, in this study, was 55%.

About gender, most patients were male (76%). Mean age was 61.8±9.8 years (33-84 years) and 57% of them were elderly (≥ 60 years). There was no association between hypoxemia and these variables.

Mean BMI was 26.1±3.8 kg/m$^2$. Sixty percent of the sample were dystrophic. Among patients with hypoxemia in immediate postoperative period, 50.9% were overweight and 20% obese. This variable presented association to hypoxemia in this population (P=0.002).

Smoking was observed in 40% of patients. Among the patients who presented hypoxemia, 50.9% were smokers or former smokers. Mild level of COPD was prevalent in 4%. Hypertension prevailed in 78% of population and diabetes mellitus in 44%. Among comorbidities, smoking presents statistically association (P=0.024) for hypoxemia occurrence. Others variables were not statistically associated with development of hypoxemia in immediate postoperative period.

The univariate analysis of hypoxemia occurrence and preoperative variable of the study group are presented in Table 1. Assessed intraoperative characteristics are shown in Table 2. Among studied patients, seven percent used only one graph, 40% two graphs and 53% three or more. Mean graphs number was 2.5±0.7, and LITA was used as graph in 91 patients. Remaining patients have received only venous graph. Average number of drains was 1.8±0.5. Twenty three percent used just one drain, seventy percent used two drains and 7% three drains. Mechanical circulatory assistance with intra-aortic balloon pump was used in only 3% of the subjects. None of these variables presented statistically association with hypoxemia in immediate postoperative period.
Hypoxemia in patients undergoing coronary artery bypass grafting is strictly related to risk factors associated to prior comorbidities and surgical procedure [11]. Among these comorbidities, advanced age, overweight, left ventricular dysfunction were associated to hypoxemia according to Szeles et al. [7], which analyzed risk factors to hypoxemia in CABG immediate postoperative in 481 patients with no relevant respiratory medical history.

In other studies [3,7,12], age was also mentioned as a risk factor related to hypoxemia after CABG. For Szeles et al. [7], age was an independent risk factor for hypoxemia and each year after age 34 increased their risk in 0.32% [7].

In our study we did not observe a significant association between advanced age and hypoxemia. However, considering physiological aspects, pulmonary function deteriorates with aging and the primary modification that happens in healthy person lungs due to aging is a gradual elastic retraction loss, reducing expiratory flow and increasing ventilation-perfusion inefficiency [13].

Divergent outcome from previous studies may be related to cut-off point of advanced age in this research, equal or above 60 years.

About weight, significant association was verified between high BMI and hypoxemia. This result is corroborated other studies in which obesity is described as a risk factor for hypoxemia [3,7].

Proposed mechanism to explain this result is obese patients’ abdominal wall, in general, being thicker due to adipose panicle, contributing to increasing abdominal pressure over diaphragm and collapsed parenchyma volume in caudal and dependent lung areas [7].

Another associated factor with hypoxemia occurrence in this study was smoking. Ambrozin et al. [14] analyzed some pulmonary function aspects after CABG related to preoperative risks and verified that half of the cases presented decreased gas exchange ratio, influenced by comorbidities such as pre-existing lung disease, respiratory symptoms and smoking.

Smokers present higher respiratory complications risk during postoperative period, due not enough respiratory system integrity to maintain alveolar ventilation [15]. This data reinforces preoperative assessment importance to identify those patients [14].

According to Morsch et al. [16], damages in pulmonary function and respiratory muscle strength after CABG are associated to transoperative factors, such as sternotomy, CPB, and general anestheisa.

CPB has been considered important cause of hypoxemia in immediate postoperative CABG [3,7]. Szeles et al. [7] showed that CPB was an associated factor to severe hypoxemia in univariate analysis. Hypoxemia occurred in 37.9% of patients with pump time higher than 120 minutes; in 29.3% with pump time less than 120 minutes; and 20% in off-pump CABG.

In our research we did not observe an association between hypoxemia and CPB. This result may be related to lower pump time (less than 120 minutes) in 92% of patients, with mean time 82.9 minutes. According to Nozawa et al. [17], is highly probable that inflammatory aggression due longer pump time causes higher interstitial alveolar injury and edema.

However when Cox et al. [18] investigated effects of on and off-pump CABG on pulmonary function by an alveolar-arterial oxygen gradient in patients with adequate ventricular function and no pre-existing pulmonary disease, it was observed a similar level of pulmonary dysfunction in both groups. It suggests that pulmonary gas exchange deterioration associated with cardiac surgery is due to other factors, not only CPB. We highlight that in these patients, mean pump time was low (74.36 minutes), closer to our study time.

Szeles et al. [7] also demonstrated high incidence of hypoxemia (54.2%), even considering gas exchange lower than 200 mmHg. Among these, 27.3% presented PaO2/FiO2 ratio lower to 150, demonstrating higher hypoxemia severity in this group of patients when compared to our research, in which no one presented this ratio lower than 150 mmHg.

Some strategies to prevent hypoxemia have been used after cardio surgery, as alveolar recruitment with PEEP, showing gas exchange ratio improvement [19]. Almost half of patients needed some therapy to reverse hypoxemia such as alveolar recruitment, PEEP level elevation or oxygen therapy [20].

Table 3. Correlation between mechanical ventilation and permanence in the ICU, and hypoxemia time (N=100).

<table>
<thead>
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<th>Mechanical ventilation duration (min)</th>
<th>P</th>
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<tbody>
<tr>
<td></td>
<td>NO (n = 45)</td>
<td>Median (Minimum; Maximum)</td>
<td></td>
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<tr>
<td>Mechanical ventilation duration</td>
<td>YES (n = 55)</td>
<td>596 (88; 3872) 565 (120; 5425)</td>
<td>0,961*</td>
</tr>
<tr>
<td>duration (min)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ICU length of stay (days)</td>
<td>Med. (Min.; Max.)</td>
<td>2 (2; 7) 2 (2; 7)</td>
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Mann Whitney: ICU - Intensive Care Unit

Mean PaO2 quantified after ICU admission was 117.7 ± 35.3 mmHg; in no hypoxia patients was 150.6 ± 22.2 mmHg; and in patients with hypoxia was 72.1 ± 3.9 mmHg. Average PaO2/FiO2 ratio was 294.2 ± 88.2, ranging 165.3 to 510 mmHg.

When hypoxemia severity [10] was evaluated, 45% of 100 patients in the study had PaO2/FiO2 ratio classified as normal (> 300 mmHg). PaO2/FiO2 ratio greater than 200 mmHg and lower or equal to 300 mmHg (mild hypoxemia) was observed in 37% and 18% of them had moderate hypoxemia (100 mmHg < PaO2/FiO2 < 200 mmHg). None of the patients presented severe hypoxemia (PaO2/FiO2 < 100 mmHg).

DISCUSSION

Hypoxemia in CABG immediate postoperative is strictly related to risk factors associated to prior comorbidities and surgical procedure [11]. Among these comorbidities, advanced age, overweight, left ventricular dysfunction were associated to hypoxemia according to Szeles et al. [7], which analyzed risk factors to hypoxemia in CABG immediate postoperative in 481 patients with no relevant respiratory medical history.

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Laizo et al. [21] analyzed complications that increased ICU length of stay and found as cause those related to pulmonary function (COPD and smoking, pulmonary congestion, prolonged mechanical ventilation), besides infections, kidney failure, stroke and hemodynamic instability (as arterial hypotension, arrhythmia and AMI).

Weiss et al. [3] pointed hypoxemia as responsible for increase mechanical ventilation duration, ICU length of stay and hospital cost in CAGB postoperative patients. This association was not observed in our research. Perhaps this result is explained by transitory hypoxemia in the first few hours after ICU admission presented by a lot of patients, with no implication in those times, besides PEEP level applied in admission.

Limitations of this study are related to its design, since retrospective studies may present selection and measurement biases. Regarding data collection from medical chart, with no direct patient’s evolution follow-up may also be characterized as a limitation factor. In some included patients, variables related to lifestyle such as smoking habit and intensity, pre-existing diseases, and left ventricular function were only cited in a qualitative manner. While inevitable data fail, available variables were categorized in the best way possible.

CONCLUSION

In this sample, body mass index and smoking were associated to hypoxemia. These comorbidities are easy to be observed during preoperative assessment. For these high risk patients, implementation of mechanical ventilation strategies such as higher PEEP and alveolar recruitment, aiming to prevent and treat pulmonary collapse should contribute to minimize hypoxemia incidence and morbidity-mortality related to cardiac surgery. Therefore, there are many aspects to study, yet, searching for effective interventions able to improve the clinical outcomes for this group of patients.

REFERENCES


