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ORIGINAL ARTICLE

Risk Score for Prolonged Mechanical Ventilation in Coronary Artery Bypass Grafting

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Abstract

Background: Prolonged mechanical ventilation (MV) after cardiac surgery imposes a significant burden on the patient in terms of morbidity and financial hospital costs.

Objective: To develop a risk score model to predict prolonged MV in patients undergoing coronary artery bypass grafting (CABG) surgery.

Methods: This was a historical cohort study of 4165 adult patients undergoing CABG between January 1996 and December 2016. MV for periods ≥ 12 hours was considered prolonged. Logistic regression was used to examine the relationship between risk predictors and prolonged MV. The variables were scored according to the odds ratio. To build the risk score, the database was randomly divided into 2 parts: development data set (2/3) with 2746 patients and internal validation data set (1/3) with 1419 patients. The final score was validated in the total database and the model's accuracy was tested by performance statistics. Significance was established at $p < 0.05$.

Results: Prolonged MV was observed in 783 (18.8%) patients. Predictors of risk were age ≥65 years, urgent/emergency surgery, body mass index ≥ 30 kg/m², chronic kidney disease, chronic obstructive pulmonary disease, and cardiopulmonary bypass time ≥ 120 minutes. The area under the ROC curve was 0.66 (95% CI, 0.64-0.68; p<0.001), the Hosmer-Lemeshow chi-square test was χ^2: 3.38 (p=0.642), and Pearson's correlation was r = 0.99 (p<0.001), indicating the model's satisfactory ability to predict the occurrence of prolonged MV.

Conclusion: Selected variables allowed the construction of a simplified risk score for daily practice, which may classify the patients as having low, moderate, high, and very high risk. (Int J Cardiovasc Sci. 2021; 34(3):264-271)

Keywords: Respiration, Artificial; Myocardial Revascularization; Risk Factors; Thoracic Surgery; Coronary Artery Disease; Probability.

Introduction

Although there has been a substantial advance in the perioperative treatment of patients undergoing cardiac surgery, prolonged mechanical ventilation (MV) continues to be an important adverse outcome, with an incidence greater than 22%.[1,2] Prolonged MV has a notable impact on cardiac surgery outcome, increasing morbidity, hospital length of stay, and, consequently, hospital costs.[3-7]

In cardiac surgery, most patients receive mechanical ventilatory support, which should be withdrawn when the clinical situation is stabilized.[8] It should be considered that early extubation, within 8 to 12 hours after the patient's transfer to the postoperative ward, is associated with improved cardiovascular conditions.[9,10]

The construction of a risk score that incorporates pre- and intraoperative risk factors that seek to predict the need for prolonged MV, especially in coronary artery bypass grafting (CABG) surgery, may be useful for patient care. It is utterly important on the contemporary setting, where patient conditions become more complex due to aging and coexistence of multiple comorbidities.[3]

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Several studies have identified factors that predict the need for prolonged MV. The most frequently associated factors are sex, type of surgery, arterial hypertension, chronic kidney disease, chronic obstructive pulmonary disease, cardiopulmonary bypass time, and reduced left ventricular ejection fraction.[6,8,11] Evaluation and monitoring of risk scores with their respective rates of postoperative complications and mortality are considered excellent indicators of the quality of hospital services.[6] It should be noted that specific risk scores for prolonged MV in patients undergoing CABG in clinical practice are limited since those available refer to combined cardiac surgery[3] or valve replacement surgeries.[12]

The development of a risk model to identify the need for prolonged MV would potentially help to select high-risk patients and the need for preventive measures to be taken. It would also help to better allocate postoperative care resources that may be adopted for recovery and rehabilitation after a surgical procedure.[6,10] Therefore, this study aimed to build a risk score model for prolonged MV in patients undergoing CABG.

Methods

This was a historical cohort observational study. The data were prospectively collected and inserted in the database of the Cardiac Surgery Postoperative Unit of Hospital São Lucas of PUCRS. We included 4165 patients who underwent isolated CABG with cardiopulmonary bypass between January 1996 and December 2016. The study followed the tenets of the Declaration of Helsinki and was approved by the institution's Research Ethics Committee under no. 2.231.168 and CAAE 72189417.5.0000.5336. Patients who underwent congenital heart surgery, valve replacement, or combined surgery and those who died during surgery or within the first 12 hours were excluded.

Variables initially included in the logistic regression model were age (classified as ≥ 65 years or < 65 years), sex (male and female), previous cardiac surgery, elective surgery, urgent/emergency surgery (included as a single variable and defined as intervention required within 48 hours), chronic obstructive pulmonary disease (clinically diagnosed by chest X-ray and/or spirometry) and/or on drug treatment (corticosteroid or bronchodilator), asthma (reported previous history and/or chronic use of bronchodilators), heart failure by functional class II versus III-IV (NYHA criteria),[13] current smoking, body mass index (classified as ≥ 30 kg/m^2, defined by specific calculation for adults up to 59 years[14] and specific for adults aged 60 and over),[15] arterial hypertension, diabetes mellitus, previous myocardial infarction, previous stroke, chronic kidney disease (defined as hemodialysis and/or creatinine ≥ 1.5 mg/dL), preoperative use of beta-blockers, preoperative use of corticosteroids, left ventricular ejection fraction (classified as < 40% according to the Brazilian Guidelines for Chronic and Acute Heart Failure[13] and measured by echocardiography or myocardial scintigraphy), and cardiopulmonary bypass time (classified as ≥ 120 minutes).

The main outcome was prolonged MV time, defined as MV for ≥ 12 hours,[9,10] including patients who were continuously ventilated for ≥ 12 hours postoperatively and those who were intubated and then extubated and subsequently re-intubated, resulting in a total duration of ≥ 12 hours.

Anesthesia, cardiopulmonary bypass, and cardioplegia were conducted according to the standard procedures of Hospital São Lucas of PUCRS, as previously described.[16] After CABG, all patients were transferred to the postoperative intensive care unit.

Statistical Analysis

Distributional assumptions were assessed using the Kolmogorov-Smirnov test. Continuous data were described as mean and standard deviation. Categorical variables were presented as absolute counts and percentages. Univariate comparisons were conducted with the chi-square test or Fisher's exact test as appropriate.

To construct the risk score, the automatic random function within the select cases tool of SPSS was used, with a 1:2 distribution, so that the database was randomly divided into 2 portions: development data set (2/3), with 2746 patients, and internal validation data set (1/3), with 1419 patients.

The initial consideration of the variables followed a hierarchical model based on biological plausibility and external information (literature) on the relevance and power of the association between these potential risk factors and the occurrence of the outcome to be analyzed. Once these variables were listed, multiple logistic regression was used in a backward selection process and all variables with a level of significance $p < 0.05$ were maintained in the model. After that, a weighted risk score was built, based on the magnitude of the b coefficients of the logistic equation. After they were transformed (exp [b]) into odds ratios, the values were rounded to the closest whole number to create the score.[17]

The preliminary risk score was applied to the validation database and 2 performance statistics were obtained: area under the ROC (Receiver Operating Characteristic) curve, the Hosmer-Lemeshow chi-square goodness-of-fit test, and the consequent Pearson's coefficient of correlation between the observed events and those predicted by the model. The area under the ROC curve was calculated, indicating the model's satisfactory ability to predict the occurrence of MV.

Observing the appropriate performance of the preliminary model in validation process, databases (modeling and internal validation) were arranged to obtain the final risk score, that is, with the total sample of this study. In this process, variables that had been removed were not included, which simply resulted in the obtaining of more accurate estimates for the coefficients that had been previously calculated. A weighted risk score was created from this final model by rounding the adjusted odds ratio (OR) to the nearest integer. These values made it possible to construct the weighted risk score with punctuated variables according to the magnitude of its effect, and significance was established at $p < 0.05$.

The resulting logistic model presents direct estimates of outcome occurrence probability. This process is understood as more appropriate to obtain event estimates, although it has a certain degree of mathematical complexity for its use in daily medical practice. The use of the logistic model is more adequate for the prognosis of individual risk, mainly in patients with a very high risk in the additive model.[17]

Statistical analyses were performed using SPSS, version 22.0 (Chicago, IL, USA) and R for Windows, version 3.4.2 (R Development Core Team – www.r-project.org).

Results

A sample of 4165 patients with coronary artery disease underwent CABG. Mean age was 61.7 (SD, 9.9 years), 2807 (67.4%) were men, and 783 (18.8%) required prolonged MV. Table 1 shows the univariate analysis of the clinical characteristics of patients who required prolonged MV vs those who did not require MV. A multiple logistic regression model was fitted to the development data set, which consisted of 2746 patients. Eighteen variables were included, which resulted in 6 independent predictors of prolonged MV remaining in the model, considering statistical significance and clinical relevance. The resulting predictors were urgent or emergency surgery (OR, 2.94; 95% confidence interval [CI], 2.07-4.18), chronic kidney disease (OR, 2.00; 95% CI, 1.55-2.59), age ≥ 65 years (OR, 1.86; 95% CI, 1.52-2.26), cardiopulmonary bypass ≥ 120 minutes (OR, 1.92; 95% CI, 1.48-2.48), body mass index ≥ 30 kg/m² (OR, 1.71; 95% CI, 1.33-2.21), and chronic obstructive pulmonary disease (OR, 1.46; 95% CI, 1.13-1.87).

The performance of the development model was tested on the internal validation data set and showed an area under the ROC curve of 0.64 (95% CI, 0.60-0.68) and a Hosmer-Lemeshow chi-square goodness of fit of χ^2: 1.85 ($p = 0.870$). The Pearson's correlation coefficient between observed and predicted events was $r = 0.98$ ($p < 0.001$). A final model was obtained from combining the development and validation data sets that resulted in the estimates presented in Table 2. In the total sample data set, the area under the ROC curve was 0.66 (95% CI, 0.64-0.68; $p < 0.001$), the Hosmer-Lemeshow chi-square goodness of fit was χ^2: 3.38 ($p = 0.642$), and the Pearson's correlation coefficient between observed and predicted events was $r = 0.99$ ($p< 0.001$).

A final risk score was obtained for each patient by adding the points presented in Table 3. The resulting risk score was then classified into 4 levels: low (0 to 1 point), medium (2 to 4 points), high (5 to 7 points), and very high risk (8 or more points), representing different probabilities for prolonged MV (Table 4). Figure 1 represents the calibration of the logistic model, and Figure 2 shows the area under the ROC curve of the risk model's predictive capacity for prolonged MV for the total sample data set.

Discussion

This study identified 6 risk predictors of prolonged MV in a population of patients who underwent CABG: urgent or emergency surgery, age (≥ 65 years), chronic kidney disease, body mass index (≥ 30 kg/m²), cardiopulmonary bypass time (≥ 120 minutes), and chronic obstructive pulmonary disease were significantly associated with prolonged MV. A clinical practice instrument was developed from these predictors to calculate the risk of MV in patients undergoing CABG.

The score was developed according to the choice of variables based on scientific evidence[6,9,10] and data available from our database records. Statistical resources were used to validate the results and allowed the score to be classified as low, medium, high, and very high risk of prolonged MV according to the values obtained. Many

Table 1 - Clinical characteristics of patients underwent coronary artery bypass grafting surgery

Clinical characteristics	Total sample (n = 4,165)	Without Prolonged MV (n = 3,382)	With Prolonged MV (n = 783)	p
Age ≥ 65 years	1,694/4,163 (40.7%)	1,264/3,380 (37.4%)	430/783 (54.9%)	< 0.001[a*]
Male	2,807 (67.4%)	2,283 (67.5%)	524 (66.9%)	0.767[a]
Asthma	90 (2.2%)	72 (2.1%)	18 (2.3%)	0.785[a]
COPD	653 (15.7%)	494 (14.6%)	159 (20.3%)	< 0.001[a*]
Smoking	1,345 (32.3%)	1,143 (33.8%)	202 (25.8%)	< 0.001[a*]
BMI ≥ 30 kg/m²	629 (15.1%)	483 (14.3%)	146 (18.6%)	0.003[a*]
Diabetes	1,430 (34.3%)	1,128 (33.4%)	302 (38.6%)	0.006[a]
Hypertension	3,220 (77.3%)	2,589 (76.6%)	631 (80.6%)	0.016[a]
CKD	537 (12.9%)	368 (10.9%)	169 (21.6%)	< 0.001[a*]
Previous stroke	307 (7.4%)	225 (6.7%)	82 (10.5%)	< 0.001[a*]
Previous MI	1,985 (47.7%)	1,606 (47.5%)	379 (48.4%)	0.662[a]
LVEF ≤ 40%	3,317/4,147 (80.0%)	2,744/3,369 (81.5%)	573/780 (73.5%)	< 0.001[a*]
NYHA Class I	2,673/4,087 (65.4%)	2,239/3,313 (67.6%)	434/774 (56.1%)	< 0.001[b*]
NYHA Class II	868/4,087 (21.2%)	681/3,313 (20.6%)	187/774 (24.2%)	
NYHA Class III	434/4,087 (10.6%)	326/3,313 (9.8%)	108/774 (14.0%)	
NYHA Class IV	112/4,087 (2.7%)	67/3,313 (2.0%)	45/774 (5.8%)	
Previous CS	98 (2.4%)	78 (2.3%)	20 (2.6%)	0.695[a]
Urgent/emergency CS	223 (5.4%)	134 (4.0%)	89 (11.4%)	< 0.001[a*]
CPB ≥ 120 minutes	551 (13.2%)	395 (11.7%)	156 (19.9%)	< 0.001[a*]

*MV: mechanical ventilation; COPD: chronic obstructive pulmonary disease; BMI: body mass index; MI: myocardial infarction; LVEF: left ventricular ejection fraction; CKD: chronic kidney disease; NYHA: New York Heart Association; CS: Cardiac surgery; CPB: cardiopulmonary bypass. * p < 0.05 was deemed statistically significant; [a] chi-square tests; [b] Fisher's test.*

Table 2 – Predictor variables of prolonged mechanical ventilation in patients who underwent coronary artery bypass grafting in the total sample database

Predictor variables	OR	95% CI	p
Urgent/emergency surgery	2.79	2.09 – 3.73	< 0.001
CKD	1.98	1.61 – 2.44	< 0.001
Age ≥ 65 years	1.91	1.62 – 2.24	< 0.001
CPB ≥ 120 minutes	1.75	1.42 – 2.16	< 0.001
BMI ≥ 30 kg/m²	1.49	1.21 – 1.84	< 0.001
COPD	1.43	1.16 – 1.76	0.001

OR: odds ratio; 95% CI: 95% confidence interval; CKD: chronic kidney disease; CPB: cardiopulmonary bypass; BMI: body mass index; COPD: chronic obstructive pulmonary disease. p < 0.05 was deemed statistically significant.

Table 3 - Risk score of prolonged mechanical ventilation in patients who underwent coronary artery bypass grafting

Predictor variable	Score
Urgent/emergency surgery	3
CKD	2
Age ≥ 65 years	2
CPB ≥ 120 minutes	2
BMI ≥ 30 kg/m^2	1
COPD	1

CKD: chronic kidney disease; CPB: cardiopulmonary bypass; BMI: body mass index; COPD: chronic obstructive pulmonary disease.

patients undergoing CABG have multiple comorbidities and require adequate treatment to eliminate or reduce the risk of prolonged MV. The identification of these variables and their adequate stratification may provide important elements for different strategies to be followed, which can result in a favorable hospital stay and contribute to the improvement of clinical outcomes.[9]

In the present study, the definition used for prolonged MV was 12 hours or more and the incidence was 18.8%, which is lower than the results of studies by Cislagui et al.,[9,10] with the same criteria for prolonged MV. Patients requiring MV of 12 hours or more, compared to those requiring less than 12 hours, had higher mortality and morbidity, and longer hospital stays[18]. Therefore, the prolonged period of MV can be a marker of great impact and considered a predictor variable of hospital death.[8] When the threshold used for prolonged MV was 48 hours or more, the incidence was lower, from 2.6% to 7.3%.[6,8,11] In some studies using the 24-hour parameter, the need for prolonged MV ranged from 4.9 to 29.4%[19,20] in patients undergoing cardiac surgery. The main predictor variables for prolonged MV identified in the present study are in agreement with literature findings.[8,10,11,19,21]

Urgent or emergency surgery was considered the variable with the greatest impact on prolonged MV, obtaining the highest value in the proposed score, with an odds ratio of 2.79 (95% CI, 2.09-0.73), and this condition adds 3 points to the risk score. The need for an intra-aortic balloon or more intense circulatory support offers limited opportunities to optimize the preoperative period and may be responsible for the high morbidity of prolonged MV. This outcome after cardiac surgery can be accurately predicted by readily available pre- and intraoperative information.[6]

Chronic kidney disease in predicting prolonged MV was the second most relevant variable in the present study, with an odds ratio of 1.98 (95% CI, 1.61-2.44), and this condition adds 2 points to the risk score. Compared to other studies, this variable associated with prolonged MV shows high odds ratio values, ranging from 1.57 to 5.53, possibly related to different evaluation parameters. Patients with chronic kidney disease have other comorbidities, such as systemic atherosclerosis, diabetes and hypertension, which contribute to the increased risk of complications in surgical procedures.[6,8,10,21,22]

Regarding the variable age ≥ 65 years, we obtained in the present study an odds ratio of 1.91 (95% CI, 1.62-2.24), and this condition adds 2 points to the risk score, which was higher compared to other studies with values of 1.06[8] and 1.04.[21] Also, Fitch et al.,[23] found that for each additional year of age, patients were less likely to be extubated early. Totonchi et al.,[11] found no association between increased age and delayed extubation. It can be considered that in the aging process there is a reduced physiological reserve associated with the development of pulmonary complications and increased morbidity and mortality.[8,24]

Table 4 - Risk score classification of prolonged mechanical ventilation (MV) in patients who underwent coronary artery bypass grafting

Risk score	Sample	Prolonged MV		Classification
		n	%	
0 to 1	1,856	207	11.2	low
2 to 4	1,997	444	22.2	medium
5 to 7	290	120	41.4	high
8 or more	22	12	54.5	very high

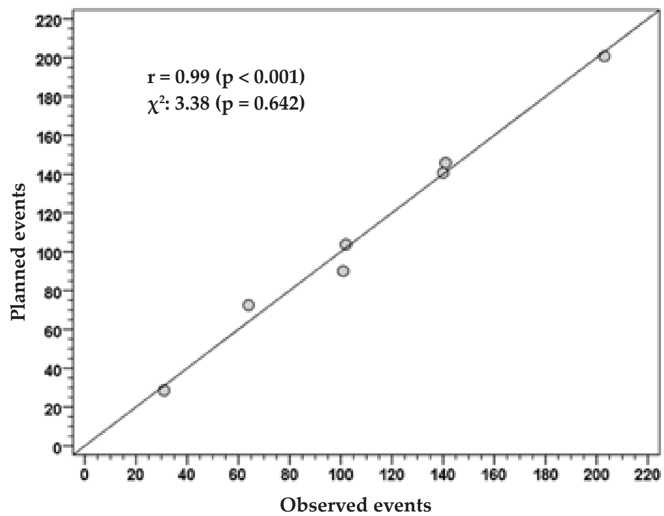

Figure 1 – Dispersion of points representing the outcome prolonged mechanical ventilation predicted and observed points

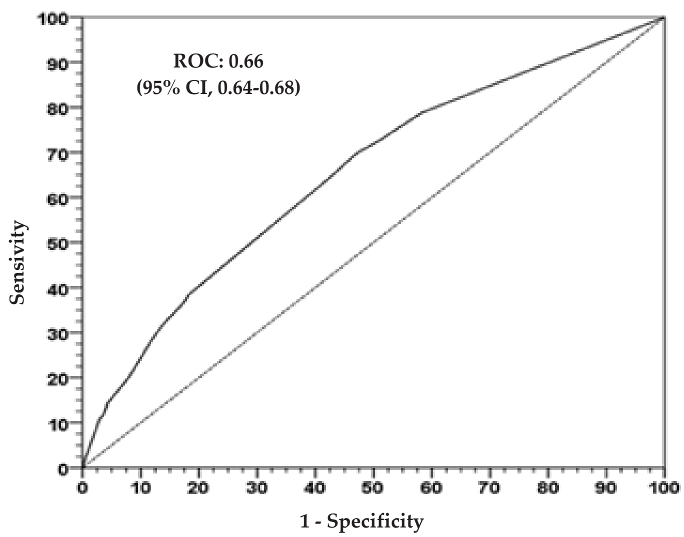

Figure 2 – Area under the Receiver Operational Characteristic (ROC) curve for predicting the occurrence of prolonged mechanical ventilation in the total data set

Cardiopulmonary bypass time was considered prolonged in our proposal (≥ 120 minutes), because beyond this limit, the complications inherent to procedure increase, and we obtained an odds ratio of 1.75 (95% CI, 1.42-2.16), condition that adds 2 points to the risk score. In view of the available data on prolonged cardiopulmonary bypass time in other studies, there are no differences regarding need for prolonged MV.[6,8,10] This technique provides an adequate surgical field, preserves functional characteristics of the heart, and provides safety for the surgical team, but when extubation is delayed, there is an increase in the intensity of inflammatory reactions and in the risk of respiratory problems.[5,19,25] Lung function and oxygenation are impaired in 20 - 90% of patients undergoing cardiac surgery with cardiopulmonary bypass.[26] Nozawa et al.,[27] consider that a cardiopulmonary bypass time greater than 120 minutes influences weaning from MV, and this is one of the factors that can increase surgical risk of patients.[27]

Obesity classified as body mass index ≥ 30 kg/m² was also a predictor of prolonged MV with an odds ratio of 1.49 (95% CI, 1.21-1.84), and this condition adds 1 point to the risk score; a similar impact was found by Wigfield et al.,[22] A high body mass index possibly increases the risk of pulmonary complications due to restrictive changes,[28] increasing complexity of the surgical procedure and hindering postoperative pulmonary rehabilitation.[21] Obesity proved to be a risk factor for pulmonary embolism after cardiac surgery, a condition that increases the duration of mechanical ventilation.[29] The impact of obesity on prolonged MV, however, still needs further studies for better understanding.

Chronic obstructive pulmonary disease was the lowest impact variable in our study, with an odds ratio of 1.43 (95% CI, 1.16-1.76), and this condition adds 1 point to the risk score. Regarding literature data, we found similar values with odds ratios ranging from 1.45 to 2.65.[8,10] This disease is considered a prothrombotic condition due to increased blood viscosity and endothelial dysfunction, which may contribute to postoperative complications.[8,11,19]

Performance analysis of weighted risk scores showed an area under the ROC curve with the model's satisfactory ability to predict prolonged MV, in agreement with literature findings. [3,6,19]

Limitations

Our risk model was constructed and validated in a single institution, a large university hospital in southern Brazil. In addition, we evaluated the results of patients from the same geographical area and who may have peculiar and distinct characteristics compared to other regions of Brazil. Therefore, validation in an external population with new data from other institutions is important so that the score has wide clinical use and can predict prolonged MV to optimize care resources and reduce hospital stay and costs in patients undergoing CABG.

Implications

As the score is based on a clinical database, the system offers an estimate of surgical risk in the "real world". The score can be used to monitor deficiencies of the hospital facility, the multidisciplinary team (surgeon, anesthesiologist, and postoperative team), and of the surgical indication. The model is accurate enough to be routinely employed at Hospital São Lucas of PUCRS and to be tested with data from other institutions.

Conclusion

Preoperative predictors (urgent / emergency surgery, age ≥ 65 years, chronic kidney disease, body mass index (≥ 30 kg/m²), chronic obstructive pulmonary disease, and perioperative variable (cardiopulmonary bypass time (≥ 120 minutes) were associated with prolonged MV. This risk score could be useful to predict the risk of prolonged MV and allow classifying patients as low, medium, high, and very high-risk.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the *Pontifícia Universidade Católica do Rio Grande do Sul* (PUCRS). under the protocol number 2.231.168/72189417.5.0000.5336 - 2017. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Author Contributions

Conception and design of the research: Dallazen-Sartori F, Guaragna JC, Bodanese LC. Acquisition of data: Dallazen-Sartori F, Guaragna JC, Magedanz EH, Bodanese LC. Analysis and interpretation of the data: Dallazen-Sartori F, Guaragna JC, Bodanese LC, Albuquerque LC, Wagner MB. Statistical analysis: Dallazen-Sartori F, Bodanese LC, Wagner MB. Writing of the manuscript: Dallazen-Sartori F, Guaragna JC, Bodanese LC, Wagner MB. Critical revision of the manuscript for intellectual content: Dallazen-Sartori F, Guaragna JC, Magedanz EH, Petracco JB, Bodanese R, Bodanese LC.

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