Original Article

Immediate Results after Multiple Arterial Grafts in Coronary Artery Bypass Graft Surgery in the São Paulo State: Cross Cohort Study

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Abstract

Background: **The short-term results after using arterial grafts still raise questions and doubts for medical society.**

Objective: **To compare the immediate outcomes of patients undergoing single arterial graft versus multiple arterial grafts coronary artery bypass grafting surgery.**

Methods: **Cross-sectional cohort study in the São Paulo Registry of Cardiovascular Surgery II (REPLICCAR II). Perioperative data from 3122 patients were grouped by the number of arterial grafts used, and their outcomes were compared: reoperation, deep sternal wound infection (DSWI), stroke, acute kidney injury, prolonged intubation (>24 hours), short hospital stay (<6 days), prolonged hospital stay (>14 days), morbidity and mortality. Propensity Score Matching (PSM) matched 1062 patients, adjusted for the mortality risk.**

Results: **After PSM, the single arterial graft group showed patients with advanced age, more former smokers, hypertension, diabetes, stable angina, and previous myocardial infarction. In the multiple arterial grafts, there was a predominance of males, recent pneumonia, and urgent surgeries. After the procedure, there was a higher incidence of pleural effusion (p=0.042), pneumonia (p=0.01), reintubation (p=0.006), DSWI (p=0.007), and sternal debridement (p=0.015) in the multiple arterial grafts group, however, less need for blood transfusion (p=0.005), extremity infections (p=0.002) and shorter hospital stays (p=0.036). Bilateral use of the internal thoracic artery was not related to increased DSWI rate, but glycosylated hemoglobin >6.40% (p=0.048).**

Conclusion: **Patients undergoing the multiarterial technique had a higher incidence of pulmonary complications, and DSWI, where glycosylated hemoglobin ≥6.40%, had a greater influence on the infectious outcome than the choice of grafts.**

Keywords: **Database; Myocardial Revascularization; Indicators of Morbidity and Mortality; Glycated Hemoglobin A.**

Introduction

Cardiovascular diseases are the leading cause of death in the world, and coronary artery disease has the greatest impact,[1] In this scenario, coronary artery bypass grafting (CABG) surgery has become a fundamental strategy, resulting in one of the most performed procedures in the world,[2,3] increasing long-term survival. Therefore, the patency of the chosen grafts becomes a fundamental point in decision-making.

Current evidence has recommended the greater use of arterial grafts, especially for the second-best coronary artery. In this scenario, prospective studies with large samples were able to state that using a bilateral internal thoracic artery (ITA) is better than using a single ITA in the long term, even when revascularization is incomplete.[4-7] However, the difficulty of the graft harvesting technique and, consequently, the increase in surgical time make some surgeons choose to use venous grafts instead of arterial grafts;[6,8,9] at the same time, deep sternal wound infection (DSWI), increased intraoperative bleeding, and longer healing time, among others, stand out as negative points.[9] These reasons may have contributed to low adherence in practice.

On the other hand, recent analyses showing the benefits of using a radial artery graft for the second-best coronary artery show a good alternative's impact. Potential reasons would be reduced surgery time, decreased risk of DSWI, and excellent long-term patency associated with using calcium channel blockers.[10] Although its choice for different patient profiles, including people with diabetes, seems greater, some questions related to the characteristics of the target coronary artery and the degree of obstruction are evident.

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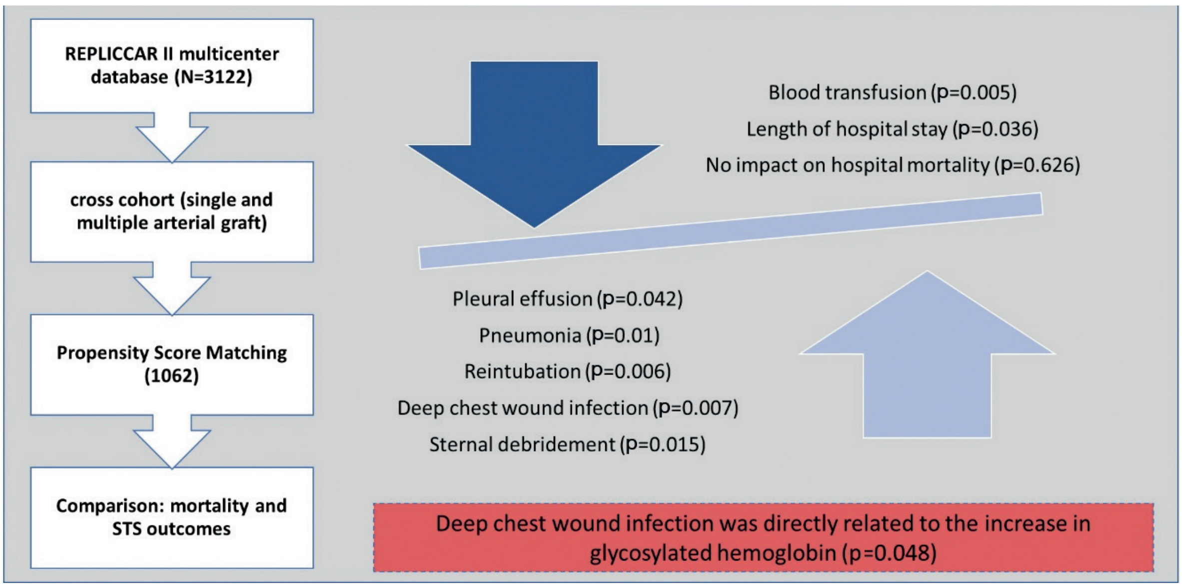
Central Illustration: Immediate Results after Multiple Arterial Grafts in Coronary Artery Bypass Graft Surgery in the São Paulo State: Cross Cohort Study



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Summarized results.

In this aspect, according to the results of the ART trial, patients treated with the multiple arterial grafts (MAG) option, regardless of whether it is bilateral or unilateral ITA with radial graft, had greater event-free survival when compared to the single arterial graft.[11] However, there are still controversies that the MAG option would increase the number of immediate complications.

Thus, this study aimed to compare the immediate results regarding morbidity and mortality of patients undergoing CABG procedure with single arterial graft (SAG) versus multiple arterial grafts in the Registro Paulista de Cirurgia Cardiovascular II/São Paulo Registry of Cardiovascular Surgery II (REPLICCAR II) project.

Methods

For this analysis, data from the REPLICCAR II were used. This is a prospective, observational, and multicenter registry with data from patients undergoing primary and isolated coronary artery bypass grafting surgery in 5 hospitals in the state of São Paulo between July 2017 and June 2019. The collection of perioperative variables was online in a registry built on the Research Electronic Data Capture (REDCap) platform and dedicated to the project, which followed the definitions of version 2.9 of the Society of Thoracic Surgeons (STS) data collection system.

The short-term results of using arterial grafts in CABG surgeries in hospitals in the state of São Paulo were evaluated, while immediate results were compared using 1 arterial graft versus ≥2 arterial grafts concerning the STS outcomes. Two analyses were performed, one with the total base and the other after adjustment with the Propensity Score Matching (PSM) technique, which used the STS predicted risk of mortality, resulting in the matching of 1062 patients (531 in each group, single arterial graft vs. multiple arterial grafts). The flowchart of methodologies addressed is shown in Figure 1. The characterization of the evaluated patients is represented in Material Supplementary – Table 1. The authors followed the criteria established by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative.[12]

Data used

Perioperative and follow-up data (collected in person or by phone) performed 30 days after surgery (if previous hospital discharge) were included in the REDCap platform built for this project. Quality audits were carried out periodically to verify the accuracy, integrity, and consistency of the data.[13]

The outcome variables analyzed were: reintervention, DSWI, stroke, kidney injury, prolonged intubation (>24 hours), short hospital stay (<6 days), prolonged hospital stay (>14 days), operative morbidity, and mortality.

All variable definitions followed the criteria from STS Adult Cardiac Surgery Database version 2.9.[14] The morbidity variable was a composite endpoint that included the five major endpoints: stroke, acute kidney failure, prolonged intubation, DSWI, and reoperation. Operative mortality

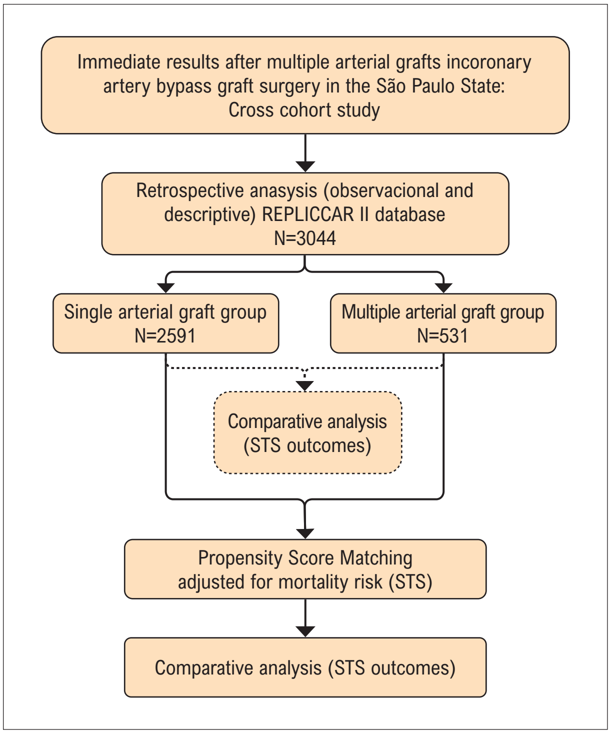

Figure 1 – *Study methodology flowchart.*

was defined as deaths that occurred after hospital discharge but before the 30th postoperative day and deaths that occurred during the hospital stay in which the operation was performed, even after 30 days.

All patients who underwent CABG surgery from July 2017 to 2019 in the 5 centers participating in this study were included in REPLICCAR II. Of this database (N=3122), 17% (N=531) received multiple arterial grafts. During the study, it was noticed that there was an increase in the use of radial and right thoracic artery grafts, as shown in Material Supplementary – Figure 1.

Ethics and consent

This is a sub-analysis of the REPLICCAR II project, approved by the local ethics committee. Informed consent was waived due to the research design applied to the project.

Statistical analysis

The R software version 4.0.2 was used to perform all of this study's analyses.

In the descriptive analysis, continuous variables were expressed as mean, median, standard deviation, and quartiles (25% and 75%), while categorical variables were expressed in frequencies and percentages. Due to missing data, the percentages were calculated as a function of the number (N) of responses obtained by variables instead of the total number of patients.

Propensity Score Matching was used to match the groups using the "nearest" method, available in the Matchit package of R software, by the STS predicted risk of mortality of the patients analyzed, creating both paired groups with N=531 (single and multiple arterial grafts).

For comparing two groups in continuous variables, the t-test was used for variables that followed the normal distribution (Anderson-Darling test), and non-parametric tests were used for the others. In the case of homogeneous variables, the Mann-Whitney test was used, and the Brunner-Munzel test was used for heterogeneous variables. Fisher's exact or the Chi-Square test was used for categorical variables. The significance level adopted in the tests was 0.05. Two-tailed hypotheses were considered. Furthermore, the confidence interval constructed was 95%.

Results

The general database showed that the cardiopulmonary bypass time was significantly longer in the single arterial graft group ($p=0.001$), as well as the anoxia time ($p=0.031$); on the other hand, the total surgery time was longer in the multiple arterial graft group ($p<0.001$). It is noticed that the profile patient in the SAG group had lower hematocrit ($p\leq0.001$) and hemoglobin ($p\leq0.001$) levels but a higher rate of blood transfusions during the procedure ($p\leq0.001$) compared to the MAG group. Intraoperatively, the radial artery was used in 30.32% of the patients who underwent MAG treatment, and the right internal thoracic artery in 79.28%, while the left internal thoracic artery was used in 100% of the cases; Thus, the left internal thoracic artery, the right internal thoracic artery and the radial artery were concurrently used in 9.06% of the patients (Material Supplementary – Table 2).

The SAG treatment group had a significantly higher predicted risk than the MAG group at all assessments ($p<0.001$), except for the prediction of hospital stay <6 days (STS) (Material Supplementary – Table 1). Regarding the outcomes observed in the complete database (Material Supplementary – Table 3), in the single arterial graft group, there was an increase in acute kidney injury ($p\leq0.001$), new atrial fibrillation ($p=0.006$), sepsis ($p=0.003$), intraoperative and postoperative transfusion of blood products ($p\leq0.001$), need for intra-aortic balloon pump ($p=0.008$) and need for dialysis in the postoperative period ($p=0.002$), as well as increased length of hospital stay (>14 days) ($p=0.036$) concerning the multiple arterial graft group.

After the Propensity Score Matching, matched by the STS predicted mortality risk, outcome comparisons were performed between the 531 patients in both groups.

Among the preoperative variables after PSM (Material Supplementary – Table 4), there was a higher prevalence of males in the multiple arterial graft group ($p<0.001$). The patient profile showed that patients in the single arterial graft group had older age ($p<0.001$), higher rate of diabetes mellitus ($p=0.008$), hypertension ($p<0.001$), previous myocardial infarction >21 days ($p=0.004$), and smoking ($p=0.027$). In contrast, the MAG group had a higher rate of surgeries with urgent status ($p=0.022$), family history of coronary heart disease ($p=0.011$), recent pneumonia ($p=0.007$), unstable angina or acute myocardial infarction with or without ST-segment elevation and symptoms at hospital admission (p=0.03). Despite the predicted risk of mortality being balanced between both groups, heterogeneity of risk probability was observed concerning the variables of evaluated outcomes.

Concerning intraoperative findings (Table 1), the single arterial graft group had slightly lower hematocrit and hemoglobin levels compared to the multiple arterial graft group (p=0.007 and p=0.006, respectively), which may have influenced a greater need for red blood cell transfusion (p=0.005). In the multiple arterial graft group, there was greater use of the skeletonized technique for dissection of the internal thoracic artery (p<0.001) and duration of surgery (p<0.001).

Regarding postoperative results (table 2), the multiple arterial graft group had a greater need for chest drainage due to pleural effusion (p=0.042), DSWI (p=0.007), pneumonia (p=0.01), need for reintubation (p=0.006), morbidity (p=0.028) and sternal debridement (p=0.015). However, there were lower rates of *saphenous* vein harvest site infection (p=0.002) and length of hospital stay <6 days (p=0.036). No statistically significant differences were observed regarding postoperative stroke, kidney injury, intubation time, mortality, and length of stay >14 days or mortality.

Investigating the findings in the multiple arterial graft group, an analysis was carried out relating the glycosylated hemoglobin level between patients who developed DSWI versus those who did not. In the group of patients with MAG, glycosylated hemoglobin was significantly higher in the DSWI group than in the non-DSWI group (p=0.048). However, there was no difference between the associations of arterial grafts used, even in the subgroup with the bilateral internal thoracic artery (Figure 2).

Discussion

The debate over the pros and cons of using multiple arterial grafts persists, where the best long-term results[9] are confronted by higher infection rates, the technical difficulty that requires the surgeon's experience, and the consequent increase in surgical time.[15,16] Our analysis is consistent with the literature and showed that most teams routinely prefer to use a single arterial graft in CABG surgeries (single arterial graft N=2591 vs. multi arterial graft N=531). In this cross-sectional study of the REPLICCAR II database, the group with MAG was associated with a higher rate of immediate pulmonary complications and DSWI.

Regarding pulmonary outcomes, there was an increase in the rate of pleural effusion (p=0.042), postoperative pneumonia (p=0.01), and the need for reintubation (p=0.006); however, it is important to note that this same group also had a higher incidence of pneumonia in the preoperative period (p=0.007), which may have contributed to these outcomes, as well as the use of the open pleural technique for dissection of intern thoracic arteries, and the increase in surgical time (p>0.001), consequently leading to longer anesthesia time,[17] however, it is important to emphasize that there was no impact on the mortality of this group and the time of hospitalization was reduced compared to the other analyzed group.

Rocha et al.[18] retrospectively evaluated the evolution of patients who underwent CABG with 2 or >2 arterial grafts; among its findings, the length of hospital stay between groups did not differ in the studied population (mean of 6 days in both groups). In our study, the multiple arterial graft group significantly reduced the length of hospital stay (p=0.036). This may be due to the greater availability of the patient to walk more efficiently in the postoperative period, resulting in the reduction of edema and pain, and stimulation of blood circulation, among others, which may have influenced a shorter hospital stay, considering that early ambulation is one of the most important items in contributing to the positive evolution of the patient, as recommended by protocols for rapid recovery after surgery.[19]

In this analysis, the single arterial graft group, even with a higher prevalence of diabetic patients (p=0.008) and a higher risk of DSWI (p=0.003), had a lower rate of DSWI (p=0.007) and debridement (p=0.015) than the group of patients with multiple arterial grafts, which is in line with the current literature.[15,16] We observed that glycosylated hemoglobin >6.40% was determinant for the development of DSWI, regardless of the graft used in the MAG group (p=0.048). This could also have been influenced by the fact that in the multiarterial group, there was a higher rate of patients operated on with an urgent status (p=0.022) and with more advanced age (p<0.001).

Considering that high glycosylated hemoglobin influenced the development of DSWI in the multiple arterial graft group, the question arises regarding the current conduct of medical teams, where patients with diabetes or increased levels of glycosylated hemoglobin are managed for alternative methods for the use of bilateral ITA, such as radial artery and/or saphenous graft, to reduce the probability of an outcome of infection.[20,21] However, our findings show that to avoid DSWI, glycemic values need to be strictly corrected before, during, and after surgery, regardless of the choice of grafts. In this way, we believe that the most careful optimization of blood glucose[22,23] may bring more benefits to the patient than simply avoiding the use of bilateral ITA.

Dorman et al.[24] retrospectively compared controlled and assisted diabetic patients after PSM who underwent SAG and MAG CABG surgery in a 30-year follow-up and showed that, even though the patients had diabetes, the use of bilateral ITA did not increase morbidity or mortality rates. Zhou et al.[25] also showed benefits in using the multiple arterial graft technique for properly controlled diabetic patients in their meta-analysis. These findings reinforce the theory put forward by the authors of this paper: the control of the patient's blood glucose is more important than the choice of grafts.

This study is a cross-sectional cohort in a database of patients undergoing CABG in the state of São Paulo, where the impact of choosing the type of graft used did not follow a pre-surgery standardization, which may have affected the findings. An adjustment was made using the Propensity Score Matching technique based on the STS-predicted mortality risk in our prospective and robustly structured records to reduce biases. Therefore, the results need to be validated in future research, preferably in randomized studies, considered the gold standard for the analysis profile.

Table 1 – Intraoperative variables of single and multiple arterial graft patients matched using the Propensity Score Matching technique

Variable	Single arterial graft treatment (N=531)		Multiple arterial graft treatment (N=531)		p-value
	N	%*	N	%*	
Cardiopulmonary bypass	491	92.47%	504	94.92%	0.129
Cardiopulmonary bypass time (minutes), median (interquartile range) †	74.00 (55.00-91.00)		70.00 (54.00-90.00)		0.184
Anoxia time (minutes), median (interquartile range) †	53.00 (41.25-71.00)		55.00 (40.00-70.25)		0.75
Porcelain aorta	9	1.69%	9	1.70%	1
Higher intraoperative blood glucose level, mean, ± standard deviation	180.58 ± 56.17		182.57 ± 52.81		0.359
Lower intraoperative hematocrit level, mean, ± standard deviation	28.04 ± 5.37		28.83 ± 4.76		0.007
Lower intraoperative hemoglobin level, mean, ± standard deviation	9.31 ± 2.59		9.44 ± 1.62		0.006
Intraoperative transfusion of blood components	80	15.15%	49	9.28%	0.005
Intraoperative transfusion of packed red blood cells (units), mean, ± standard deviation	1.35 ± 0.68		1.35 ± 0.68		0.61
Use of the right internal thoracic artery	5	0.94%	421	79.28%	<0.001
Use of the left internal thoracic artery	525	99.06%	531	100%	0.073
Use of the bilateral internal thoracic artery	0	0%	421	79.28%	<0.001
Skeletonized internal thoracic artery	185	34.84%	281	52.92%	<0.001
Pedicled internal thoracic artery	301	56.69%	233	43.88%	<0.001
Use of the radial artery	1	0.19%	161	30.32%	<0.001
Number of distal anastomoses with internal thoracic artery, mean, ± standard deviation	1.03 ± 0.18		1.75 ± 0.52		<0.001
Number of distal anastomoses with venous grafts, mean, ± standard deviation	1.76 ± 0.72		1.32 ± 0.56		<0.001
Surgery time (hours), median (interquartile range) †	4.31 (3.50-5.95)		5.00 (4.08-6.17)		<0.001
Cardiogenic shock (during the procedure or within 24 hours of the procedure)	1	0.19%	0	0%	1
Extubation in the operating room	27	5.09%	25	4.71%	0.778

** Percentages were calculated as a function of the number (N) of responses obtained due to missings; † Interquartile range 0.25-0.75.*

Conclusion

In the present analysis, it was identified that the use of multivessel grafts for patients undergoing coronary artery bypass graft surgery had a higher rate of pulmonary complications and deep chest wound infection, with glycosylated hemoglobin above 6.40% having a greater influence on the outcome of the than the choice of grafts itself. Strict blood glucose control is recommended in elective patients for glycated hemoglobin levels ≥6.40% and exhaustive control for patients operated under urgent conditions to avoid infectious outcomes that can significantly impact the patient's evolution.

Study funding

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Table 2 – Events and Postoperative variables of single and multiple arterial graft treated patients matched using the Propensity Score Matching technique

Variable	Single arterial graft treatment (N=531)		Multiple arterial graft treatment (N=531)		p-value
	N	%*	N	%*	
Need for intra-aortic balloon pump	17	3.20%	13	2.45%	0.579
Preoperative intra-aortic balloon pump	7	43.75%	2	18.18%	
Intra-operative intra-aortic balloon pump	4	25%	3	27.27%	0.375
Postoperative intra-aortic balloon pump	5	31.25%	6	54.55%	
Postoperative creatinine level (mg/dL), mean, ± standard deviation	1.31 ± 1.04		1.33 ± 0.62		<0.001
Postoperative hematocrit level before hospital discharge, mean, ± standard deviation	30.84 ± 4.22		30.95 ± 4.45		0.215
Postoperative hemoglobin level before hospital discharge, mean, ± standard deviation	10.32 ± 2.02		10.54 ± 2.57		0.072
Blood glucose peak 18-24 hours after anesthesia, mean, ± standard deviation	171.75 ± 47.38		174.15 ± 49.4		0.761
Postoperative left ventricular ejection fraction (%) mean, ± standard deviation	56.86 ± 9.78		57.97 ± 11.06		0.149
Peak CKMB, median (interquartile range) †	20.25 (13.10-38.98)		19.30 (12.90-32.60)		0.153
Peak troponin I, median (interquartile range) †	2.06 (1.04-6.89)		2.22 (0.97-7.36)		0.87
Abnormal heart rhythm requiring permanent device implantation (pacemaker)	1	0.20%	0	0%	1
Stroke	9	1.73%	4	0.79%	0.264
Postoperative atrial fibrillation	63	12.14%	61	12.10%	1
Sternal dehiscence	13	2.63%	18	3.89%	0.28
Sternal dehiscence without signs of infection	4	0.81%	3	0.66%	1
Deep sternal wound infection	12	2.26%	30	5.65%	0.007
Superficial surgical wound infection	64	13.06%	46	10.34%	0.223
Surgical site infection: thoracotomy	36	7.35%	45	10.14%	0.162
Saphenous vein harvest site infection	42	8.57%	16	3.60%	0.002
Sepsis	14	2.83%	9	1.94%	0.405
Acute kidney injury	25	4.82%	19	3.77%	0.444
Need for postoperative dialysis	7	1.43%	2	0.45%	0.182
Reoperation for bleeding with or without cardiac tamponade	4	0.77%	6	1.19%	0.541
Reoperation for myocardial ischemia	0	0%	1	0.22%	0.973
Reoperation for other cardiac problems	2	0.40%	2	0.43%	1
Sternal debridement	9	1.84%	21	4.72%	0.015
Reoperation for non-cardiac causes	14	2.83%	16	3.46%	0.584
Planned angioplasty after surgery	1	0.19%	3	0.57%	0.373
Acute limb ischemia	1	0.2%	0	0%	1
Pericardiocentesis	1	0.2%	0	0%	1
Pleural effusion with indication for drainage	4	0.81%	12	2.59%	0.042
Pneumonia	7	1.41%	20	4.32%	0.01
Pneumothorax with an indication for intervention	1	0.20%	6	1.30%	0.061
Venous thromboembolism	0	0%	1	0.22%	0.973
Postoperative transfusion of blood-derived components	126	23.82%	101	19.02%	0.061

Postoperative transfusion of packed red blood cells (unit), mean, ± standard deviation	1.66 ± 1.17		1.87 ± 1.23		0.193
Ventilation time (hours), median (interquartile range) †	7.10 (4.17-10.19)		6.38 (3.50-10.40)		0.125
Ventilation time >24 h	24	4.55%	29	5.47%	0.573
Reintubation	8	1.51%	24	4.52%	0.006
Length of stay in the intensive care unit (hours), median (interquartile range) †	65.28 (45.90-88.75)		65.80 (44.15-92.68)		0.439
Readmission to the intensive care unit	13	2.45%	18	3.39%	0.466
Postoperative length of stay (days), median (interquartile range) †	7.00 (5.00-8.00)		7.00 (6.00-9.00)		0.167
Long hospital stay (>14 days)	132	25.73%	134	27.35%	0.568
Short hospital stay (<6 days)	20	3.90%	34	6.94%	0.036
Total length of hospital stay (days), median (interquartile range) †	11.00 (8.00-15.00)		11.00 (8.00-15.00)		0.771
Hospital readmission to follow-up	18	3.88%	21	4.67%	0.625
Morbidity	59	11.94%	80	17.06%	0.028
Morbidity or mortality	64	12.90%	81	17.27%	0.059
Operative mortality	10	1.88%	10	1.88%	1
In-hospital mortality (up to 30 days after surgery)	7	1.32%	10	1.88%	0.626

** Percentages were calculated as a function of the number (N) of responses obtained due to missings; † Interquartile range 0.25-0.75.*

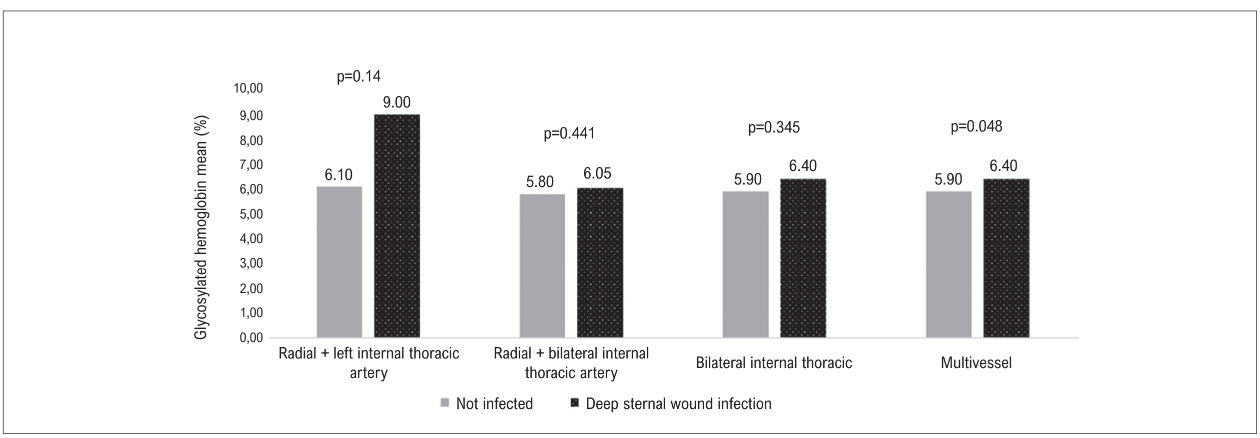

Figure 2 – *Glycosylated hemoglobin values and their relationship with DSWI according to the type of arterial graft used.*

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Author Contributions

Conception and design of the research: Mejia OAV; Acquisition of data: Paredes RAM, Borgomoni GB, Dallan LRP, Lisboa LAF, Dallan LAO; Analysis and interpretation of the data and Statistical analysis: Borgomoni GB, Mejia OAV; Writing of the manuscript: Paredes RAM, Borgomoni GB; Critical revision of the manuscript for important intellectual content: Borgomoni GB, Dallan LRP, Lisboa LAF, Dallan LAO, Mejia OAV; Methodology: Paredes RAM, Borgomoni GB, Micalay AKP, Camacho JCA, Dallan LRP, Mejia OAV; Project admnistration: Dallan LRP, Dallan LAO, Mejia OAV.

Potential conflict of interest

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

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Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo under the protocol number 2016/15163-0. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013.

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