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Skeletonized left internal thoracic artery is associated with lower rates of mediastinitis in diabetic patients

Artéria torácica interna esquerda esqueletizada é associada a menores taxas de mediastinite em diabéticos

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Abstract

Background: **Mediastinitis is a serious complication of median sternotomy and is associated to significant morbidity and mortality. Diabetes is a feared risk factor for mediastinitis and viewed with caution by cardiovascular surgeons.**

Objective: **To identify risk factors for mediastinitis in diabetics undergoing CABG surgery with use of unilateral ITA in the Division of Cardiovascular Surgery of Pronto Socorro Cardiológico de Pernambuco - PROCAPE.**

Methods: **Retrospective study of 157 diabetics operated between May 2007 and April 2010. Nine preoperative variables, five intraoperative variables and seven postoperative variables possibly involved in the development of postoperative mediastinitis were evaluated. Univariate and multivariate logistic regression analyses were applied.**

Results: **The incidence of mediastinitis was 7% (n=11), with a lethality rate of 36.1% (n=4). Variables associated with increased risk of mediastinitis were: use of pedicled ITA (OR 8.25, 95% CI 2.03 to 66.10, *P*=0.016), postoperative renal complications (OR 5.10, 95% CI 1.03 to 25.62, *P*=0.049) and re-operation (OR 7.45, 95% CI 1.24 to 42.17, *P*=0.023). In multivariate analysis using backward logistic regression, only one variable remained as independent risk factor: use of pedicled ITA (OR 7.64, 95% CI 1.95 to 61.6, *P*=0.048), in comparison to skeletonized ITA.**

Conclusions: **We suggest that diabetics should be considered for strategies to minimize risk of infection. In diabetics that undergo unilateral ITA, the problem seems to be related to how ITA is harvested. Diabetics should always be considered for use of skeletonized ITA.**

Descriptors: **Mediastinitis. Myocardial Revascularization. Diabetes Mellitus. Mammary Arteries.**

Resumo

Introdução: **Mediastinite é uma complicação séria da esternotomia mediana e está associada a significativa morbidade e mortalidade. Diabetes é um temido fator de risco para mediastinite, visto com cautela pelos cirurgiões cardiovasculares.**

Objetivo: **Identificar fatores de risco para mediastinite em diabéticos submetidos à CRM com uso unilateral da ATI na Divisão de Cirurgia Cardiovascular do Pronto Socorro Cardiológico de Pernambuco - PROCAPE.**

Métodos: **Estudo retrospectivo de 157 pacientes diabéticos operados entre maio de 2007 e abril de 2010. Nove variáveis pré-operatórias, cinco variáveis intraoperatórias e sete variáveis pós-operatórias possivelmente envolvidas no desenvolvimento de mediastinite foram avaliadas. Análises univariada e multivariada por regressão logística foram aplicadas.**

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Resultados: **A incidência de mediastinite foi de 7% (n=11), com taxa de letalidade de 36,1% (n=4). Variáveis associadas com maior risco de mediastinite foram: uso de ATI pediculada (OR 8,25, IC 95% 2,03-66,10, *P*=0,016), complicações renais (OR 5,10, IC 95% 1,03-25,62, *P* = 0,049) e reoperação (OR 7,45, IC 95% 1,24-42,17, *P*=0,023). Na análise multivariada por regressão logística, apenas uma variável permaneceu como fator independente de risco: uso ATI pediculada (OR 7,64, IC 95% 1,95-61,6, *P* = 0,048), em comparação à ATI esqueletizada.**

Conclusões: **Sugerimos que diabéticos devem ser considerados para estratégias de minimização do risco de infecção. Nos diabéticos que recebem ATI unilateral, o problema parece estar relacionado à forma como a ATI é dissecada. Diabéticos devem sempre ser considerados para utilização da ATI esqueletizada.**

Descritores: **Mediastinite. Revascularização Miocárdica. Diabetes Mellitus. Artéria Torácica Interna.**

INTRODUCTION

Mediastinitis is a deep wound infection after median sternotomy, with clinical evidence and / or microbiological commitment of the retrosternal space, associated with sternal osteomyelitis with or without its instability [1-4]. It is one of the most serious complications of median sternotomy and is associated to significant morbidity and mortality [5]. It is also known as deep sternal wound infection [5].

This is an entity with low incidence, occurring in only 1% to 3% of patients after cardiac surgery [6]. However, when it occurs, is associated with high mortality rates, reaching 35% [7].

It has been shown that coronary artery bypass grafting (CABG) is associated with a higher risk of developing mediastinitis compared to other procedures in cardiovascular surgery (valve surgery, correction of congenital heart disease) [8].

Diabetes is always a feared risk factor for mediastinitis and viewed with caution by cardiovascular surgeons, because, as a result of its pathophysiology, microvascular changes and high levels of blood glucose, may adversely affect the healing process [9,10].

In recent years, studies [11-13] have emphasized the use of bilateral internal thoracic artery (ITA or mammary) as the major cause of higher incidence of mediastinitis in coronary artery bypass grafts. However, Sá et al. [8] performed a study in the Division of Cardiovascular Surgery of Pronto Socorro Cardiológico de Pernambuco - PROCAPE, noting an interesting aspect in comparison to these studies: in almost no patient in this service was performed bilateral ITA, performing mostly only unilateral ITA. Although we have performed almost exclusively CABG with unilateral ITA, this surgery was associated with increased risk of developing mediastinitis compared to other procedures.

Therefore, the aim of this study is to identify risk factors for mediastinitis in diabetics undergoing CABG with use of unilateral ITA in our institution.

METHODS

Source Population

After approval by the ethics committee (protocol number 322010), we reviewed the records of consecutive patients undergoing CABG at our institution from May 2007 to April 2010. At first, we identified 542 patients eligible for the study. Eight were excluded because they used bilateral ITA, 88 excluded because did not use any ITA (received only saphenous vein grafts), 255 excluded because were non-diabetics and 34 excluded due to lack of information from medical records, leaving 157 patients for data analysis (diabetics undergoing CABG with use of unilateral ITA). All of them used left ITA. Data collection was performed by trained staff (four people) and they did not know the purpose of the study (blind data collection).

Study Design

It was a retrospective cohort study.

The presence of diabetes was defined as reported by patient and/or use of oral hypoglycemic medication and/or insulin.

The dependent variable was mediastinitis after surgical procedure. This variable was categorized into yes or no. Mediastinitis were considered with those who met at least 1 of the criteria according to the Centers for Disease Control and Prevention (CDC) [14]:

1. Patient has organisms cultured from mediastinal tissue or fluid obtained during a surgical operation or needle aspiration;

2. Patient has evidence of mediastinitis seen during a surgical operation or histopathologic examination;

3. Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever (38ºC), chest pain, or sternal instability and at least 1 of the following:

a. purulent discharge from mediastinal area

b. organisms cultured from blood or discharge from mediastinal area

c. mediastinal widening on x-ray.

Isolated superficial infections from sternal wound with stable and/or sterile sternal dehiscence and/or no macroscopic evidence of deep infection (purulent drainage) were not considered as having mediastinitis.

The independent variables were divided into three categories:

1. Pre-operative factors

a. Age >70 years old

b. Gender (male or female)

c. Obesity (body mass index ≥ 30kg/m^2, BMI)

d. Hypertension (reported by patient and/or use of anti-hypertensive medication)

e. Smoking (reported by patient; active or inactive for less than 10 years)

f. Chronic obstructive pulmonary disease - COPD (dyspnea or chronic cough AND prolonged use of bronchodilators or corticosteroids AND/OR compatible radiological changes - hypertransparency by hyperinflation and/or rectification of ribs and/or rectification diaphragmatic)

g. Renal disease (creatinine ≥ 2.3 mg/dL or pre-operative dialysis)

h. Previous cardiac surgery

i. Ejection fraction < 50%

j. Acute myocardial infarction (AMI) <90 days

k. Insulin-dependent

2. Intra-operative factors

a. Emergency surgery (during acute myocardial infarction, ischemia not responding to therapy with intravenous nitrates, cardiogenic shock)

b. Concomitant cardiac surgery

c. Harvesting technique for ITA (PEDICLED - direct dissection of surrounding margin of tissue around the ITA with electrocautery - or SKELETONIZED - artery dissection with scissors and clipping intercostal branches with metal clips without involving any margins tissue around ITA)

d. Number of bypass

e. Use of cardiopulmonary bypass – CPB (on-pump or off-pump)

3. Postoperative factors

a. Low cardiac output (need for inotropic support with dopamine 4µg/kg/min at least for a minimum of 12 hours or intraaortic balloon)

b. Reoperation (new sternotomy for bleeding, tamponade, or other reasons during the intra-hospital period)

c. Respiratory complications (pulmonary infection, acute respiratory distress syndrome, atelectasis, need for intubation for more than 48 hours)

d. Renal complications (creatinine ≥ 2,3 mg/dL or postoperative dialysis)

e. Hyperglicemia (first blood glucose after closure of skin >200mg/dL)

f. Multiple transfusions (more than 3 units of any blood products in postoperative period before diagnostic definition of mediastinitis)

g. Infection at another site

We also assessed the following characteristics: intensive care unit length of stay (days) and hospital length of stay (days), outcome at hospital discharge (survival or death).

Data Analysis

The data were stored in SPSS program (Statistical Package for Social Sciences) version 15, from which calculations were performed with statistical analysis, and interpretation. The data storage was done in double-entry to validate and carry out analysis of data consistency, in order to ensure minimal error in recording information in software.

Univariate analysis for categorical variables was performed with the chi-square test or Fishers exact test as appropriate. For continuous variables we used t-Student test. Verification of the hypothesis of equality of variances was performed using the Levene F test. Potential risk factors with $P<0.20$ in univariate analysis were included in multivariate analysis, which was performed by stepwise forward logistic regression, remaining variables with $P<0.10$. P values <0.05 were considered statistically significant.

RESULTS

Incidence

Study population had a mean age of 61.6 years (± 9.0) and 49.7% (n = 78) were male and 50.3% (n = 79) were female. It was found incidence of 7.0% (n = 11) of cases of mediastinitis. The time between the date of surgery and symptom onset ranged from 8 to 30 days with a mean of 15.1 days (± 7.5).

Univariate Analysis

Variables that were associated with increased risk of mediastinitis with P <0.05 were use of pedicled ITA (OR 8.25, 95% CI 2.03 to 66.10, P=0.016), postoperative renal complications (OR 5.10, 95% CI 1.03 to 25.62, P=0.049) and reoperation (OR 7.45, 95% CI 1.24 to 42.17, P=0.023). Tables 1, 2 and 3 show the data from the univariate analysis.

Multivariate Analysis by Logistic Regression

We identified only one independent risk factor for postoperative mediastinitis: use of pedicled ITA (OR 7.64, 95% CI 1.95 to 61.6, P=0.048). This result is based on comparison with skeletonized ITA. Table 4 shows the data regarding the comparison of pedicled and skeletonized ITA group in relation to preoperative variables (there were no statistically significant differences between groups).

Evolution and Outcome

Diabetics who developed mediastinitis stayed more days in the intensive care unit (18.45 ± 14.54 versus 5.93 ± 7.96, P <0.001) and longer hospital stay (44.27 ± 23.99 versus 35.93 ± 23.08; P <0.001) compared with those who did not develop mediastinitis.

Four (36.4%) cases resulted in death.

Table 1. Incidence of mediastinitis according to preoperative variables (univariate analysis).

Variable	Mediastinitis		Total		*P* value	OR (CI 95%)
	N	%	N	%		
Age > 70						
Yes	3	9.7	31	19.7	0.519	1.58 (0.39-6.34)
No	8	6.3	126	80.3		1.00
Gender						
Male	4	6.4	78	49.7	0.237	0.83 (0.24-2.85)
Female	7	7.6	79	50.3		1.00
Obesity						
Yes	2	8.0	25	15.9	0.832	1.19 (0.24-5.86)
No	9	6.8	132	84.1		1.00
Hipertensyon						
Yes	10	6.7	149	94.9	0.540	0.50 (0.06-4.50)
No	1	12.5	8	5.1		1.00
Smoke						
Yes	6	10.9	55	35.0	0.170	2.38 (0.69-8.17)
No	5	4.9	102	65.0		1.00
Renal disease						
Yes	0	0.0	15	9.5	-	-
No	11	7.7	142	90.5		1.00
COPD						
Yes	0	0.0	9	5.7	-	-
No	11	7.4	148	94.3		1.00
Previous cardiac surgery						
Yes	1	4.8	21	13.4	0.668	0.63 (0.08-5.19)
No	10	7.3	136	86.6		1.00
EF < 50%						
Yes	2	7.2	32	20.4	0.851	0.86 (0.17-4.19)
No	9	6.2	125	79.6		1.00
AMI < 90 days						
Yes	4	6.3	64	40.8	0.511	0.82 (0.17-3.40)
No	7	7.5	93	59.2		1.00
Insulin-dependent						
Yes	2	7.2	32	20.4	0.851	0.86 (0.17-4.19)
No	9	6.2	125	79.6		1.00

COPD: chronic obstructive pulmonary disease; EF: ejection fractions; AMI: acute myocardial infarction

Table 2. Incidence of mediastinitis according to intraoperative variables (univariate analysis).

Variable	Mediastinitis		Total		*P* value	OR (CI 95%)
	N	%	N	%		
Number of bypass						1,00
1	3	9.7	31	17.7		0,77 (0,18-3,32)
2	6	7.7	78	49.7	0.609	0,41 (0,06-2,58)
3 or more	2	4.2	48	32.6		
Use of ITA						
Pedicled	10	11.1	90	57.3	0.016*	8.25 (2.03-66.10)
Skeletonized	1	1.5	67	42.7		1.00
Use of CPB						
Off-pump	5	5.9	84	53.5		1.00
On-pump	6	8.2	73	46.5	0.551	1.45 (0.42-4.98)
Additional procedure						
Yes	0	0.0	4	2.6	-	-
No	11	7.2	153	97.4		1.00
Emergency surgery						
Yes	0	0.0	1	0.6	-	-
No	11	7.0	156	99.4		1.00

*ITA: internal thoracic artery; CPB: cardiopulmonary bypass. *: Significant difference at 5.0%*

Table 3. Incidence of mediastinitis according to postoperative variables (univariate analysis).

Variable	Mediastinitis		Total		*P* value	OR (CI 95%)
	N	%	N	%		
Hyperglicemia						
Yes	5	6.7	75	47.8	0.873	0.90 (0.23-3.54)
No	6	7.3	82	52.2		1.00
Low cardiac output						
Yes	0	0.0	26	16.5	-	-
No	11	8.4	131	83.5		1.00
Renal complications						
Yes	3	23.1	13	8.3	0.049*	5.10 (1.03-25.62)
No	8	5.6	144	91.7		1.00
Respiratory complications						
Yes	3	16.6	18	11.8	0.116	3.28 (0.61-15.90)
No	8	5.7	139	88.2		1.00
Infection at another site						
Yes	3	21.4	14	9.8	0.060	4.60 (0.83-23.50)
No	8	5.6	143	90.2		1.00
Reoperation						
Yes	4	40.0	10	6.4	0.023*	7.45 (1.24-42.17)
No	7	4.8	147	93.6		1.00
Multiple transfusion						
Yes	2	6.4	31	19.7	0.626	0.90 (0.01-4.83)
No	9	7.1	126	80.3		1.00

**: Significant difference at 5.0%*

Table 4. Comparison of pedicled ITA group versus skeletonized ITA group in relation to preoperative variables.

Variable	Skeletonized (n=67)		Pedicled (n=90)		*P* value
	N	%	N	%	
Age > 70	13	19.4	18	20.0	0.926
Gender					
Male	27	40.3	51	56.7	0.061
Female	40	59.7	39	43.3	
Obesity	7	10.4	18	20.0	0.162
Hipertensyon	65	97.0	84	93.3	0.467
Smoke	19	28.3	36	40.0	0.388
Renal disease	8	11.9	7	7.7	0.546
COPD	5	7.5	4	4.4	0.497
Previous cardiac surgery	6	8.9	15	16.7	0.243
EF < 50%	12	17.9	20	22.2	0.643
AMI < 90 days	22	32.8	42	46.7	0.114
Insulin-dependent	11	17.9	21	22.2	0.387

COPD: chronic obstructive pulmonary disease; EF: ejection fractions; AMI: acute myocardial infarction

DISCUSSION

In our study, the incidence of mediastinitis was 7.0% (n=11), above the rates reported in other studies, ranging from 0.2% to 5.0% [15-17]. However, we should note two points. First, a previous study at our institution [8] showed an incidence of 2.4% between 1038 cardiovascular surgeries (involving all types of surgeries - within the range defined in the literature) and CABG was associated with increased risk compared with other cardiac surgeries (CI 3.44 to 8.30, $P = 0.0001$). Second, diabetes is recognized as an important risk factor for sternal wound infections after cardiac surgery [9,10]. So we are looking at a "doubled" risk group, justifying excess incidence in the present study.

Many factors have been associated with development of mediastinitis after cardiac surgery [18]. However, there is no consensus as to which factors are most important and how each is an independent predictor of risk for postoperative mediastinitis [18].

In our study, we observed only one independent risk factor for mediastinitis in diabetics after CABG: the use of pedicled ITA. We found there was higher incidence of mediastinitis in diabetics who used pedicled ITA compared with skeletonized ITA (statistically significant). Several studies have shown favorable results to the use of skeletonized ITA [19-21].

Saso et al. [19] demonstrated that skeletonization of ITA in patients undergoing CABG was associated with reduced incidence of deep sternal infection (OR 0.41, 95% CI 0.26 to 0.64) and this effect was even more evident when the specific analysis of diabetic patients (OR 0.19, 95% CI from 0.1 to 0.34).

Kai et al. [20] observed that incidence of deep sternal infection was significantly lower in diabetics that underwent CABG with use of skeletonized ITA compared to diabetics using pedicled ITA (0.6% versus 13.0%, $P = 0.01$).

Milani et al. [21] studied 70 diabetic patients submitted to CABG, dividing them into 2 groups: in group A, thoracic arteries were dissected as a pedicle, while in group B they were skeletonized. Three patients (8.57%) from group A presented with mediastinitis. The use of skeletonized ITA significantly decreased the incidence of mediastinitis (P = 0.044). They concluded that the utilization of skeletonized ITA significantly decreases the incidence of mediastinitis.

These results were found probably as a result of better sternal perfusion after ITA skeletonization compared to the pedicled ITA [22-24].

Boodhwani et al. [22] conducted a study with 48 patients, in which each individual was submitted to CABG using bilateral ITA, and all ITAs were dissected skeletonized in left side and pedicled in right side. Patients were then evaluated for sternal perfusion through scintigraphy (radionuclear image). The authors found that sternal perfusion was increased in skeletonized side compared with pedicle side (increase of 17.6%, P = 0.03).

Kamiya et al. [23] showed that the oxygen saturation and blood flow in the microcirculation of the sternum tissue were better when using the skeletonized ITA compared to pedicled ITA.

Santos Filho et al. [24] studied 35 patients submitted to CABG, dividing them into two groups: group A (n=18) had ITA dissected using skeletonization technique and group B (n=17) as pedicle preparation. There was no difference in the two groups relating gender, age and demographic characteristics. On the seventh postoperative day the patients underwent bone scintillography. They observed that group A (skeletonized ITA) showed higher perfusion than group B (pedicled ITA) patients, however, it was not statistically significant (P = 0.127). On the other hand, comparing the diabetic population, seven in each group, there was a marked 47.4% higher perfusion of the sternum in group A (skeletonized ITA) comparing to group B (pedicled ITA) and this difference reached statistical significance (P = 0.004). They concluded that in diabetic subgroup, a significant preservation of the sternal perfusion was observed in patients that undergone skeletonized ITA.

Our study showed that patients who developed mediastinitis stayed more time in the intensive care unit and had higher length of hospital stay (statistically significant) compared with those who did not developed mediastinitis, which reflects the high morbidity and high costs involved with this complication. The lethality rate found (36.4%) was similar to that observed in other study [25].

Other risk factors may be involved, but they are difficult to be measured. The aspect of the bone, which can sometimes show signs of osteoporosis, ischemia, the surgeon's ability, failure to follow the antisepsis procedures, errors in the sternotomy and in the sternum rewiring, and excessive use of an electric scalpel are factors that are very often not mentioned but can be important factors in the pathophysiology of mediastinitis [25].

CONCLUSION

We suggest that diabetics should be considered for strategies to minimize risk of infection. In diabetics that undergo unilateral ITA, the problem seems to be related to how ITA is harvested. Diabetics should always be considered for use of skeletonized ITA.

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