ORIGINAL ARTICLE

EMC

Rev Bras Cir Cardiovasc 2012;27(3):377-82

Long term mortality of deep sternal wound infection after coronary artery bypass surgery

Mortalidade em longo prazo da infecção esternal profunda após cirurgia de revascularização do miocárdio

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DOI: 10.5935/1678-9741.20120065

RBCCV 44205-1396

Abstract

Background: **Deep sternal wound infection and mediastinitis determine high in-hospital mortality. International studies show that these patients are also at increased cardiovascular mortality risk in long-term follow-up. However, data are scarce and there is no national data.**

Objectives: The aim of this study is to evaluate the mortality and incidence of cardiovascular events in long-term follow-up of patients suffering from deep sternal wound infection and mediastinitis.

Methods: **Case-control study, matched by propensity score in a 1:1 proportion, in patients submitted to coronary artery bypass grafting between 2005 and 2008 at the Institute Dante Pazzanese of Cardiology (São Paulo, SP, Brazil). The primary outcome was death. As a secondary outcome, we analyzed the composite event of myocardial infarction, new revascularization, stroke or death.**

Results: **Of 1975 patients, 114 developed one of the infections. During the mean follow up of 3.6 years, deep sternal wound infection and mediastinitis increased the risk of death by 8.26 (95% CI 1.88-36.29, *P* = 0.005) and the incidence of combined end point by 2.61 (95% CI 1.2-5.69, *P* = 0.015). The Kaplan-Meier curves for both outcomes demonstrated that the greatest risk occurs in the first six months, followed by a period of stabilization and further increase in the incidence of events after 4 years of hospital discharge. The similarity between the curves of primary and secondary outcomes may be consequent to the predominance of death on the combined cardiovascular events.**

Conclusion: **The presence of deep sternal wound infection or mediastinitis increased mortality in long-term follow-up in this sample of the Brazilian population according to the same pattern displayed by the developed countries.**

Descriptors: **Mediastinitis. Mortality. Myocardial revascularization. Coronary artery bypass. Surgical wound infection.**

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Article received on May 24th, 2012
Article accepted on August 21st, 2012

Abbreviations, Acronyms and Symbols	
AMI	Acute myocardial infarction
BMI	Body mass index
CABG	Coronary artery bypass graft
CVA	Cerebrovascular accident
DSWI	Deep sternal infection and mediastinitis
EF	Ejection fraction
ESRD	End-stage renal disease
ITA	Internal thoracic artery
PAD	Peripheral artery disease
MR	Myocardial revascularization

Resumo

Introdução: **A infecção esternal profunda e a mediastinite determinam elevada mortalidade intra-hospitalar. Estudos prévios demonstram que esses pacientes também apresentam maior mortalidade cardiovascular em longo prazo. No entanto, os dados são escassos para o Brasil.**

Objetivo: **O objetivo deste estudo é avaliar a mortalidade e a incidência de eventos cardiovasculares em longo prazo em pacientes acometidos de infecção esternal profunda e mediastinite.**

Métodos: **Estudo de caso-controle com pareamento 1:1 por meio de *propensity score*, em pacientes submetidos à cirurgia de revascularização do miocárdio entre 2005 e 2008, no Instituto Dante Pazzanese de Cardiologia (São Paulo, SP, Brasil). O desfecho primário avaliado foi óbito. Como desfecho secundário, analisou-se o composto de infarto agudo do miocárdio, nova revascularização miocárdica, acidente vascular encefálico ou óbito.**

Resultados: **De 1975 pacientes avaliados, 114 desenvolveram infecção esternal profunda ou mediastinite. Durante o seguimento médio de 3,6 anos, as infecções conferiram razão de risco de óbito de 8,26 (IC 95% 1,88-36,29, *P* = 0,005), tendo sido a razão de risco de desfecho combinado de 2,61 (IC 95% 1,2-5,69, *P* = 0,015). A curva de Kaplan-Meier para ambos os desfechos demonstra que o maior risco ocorre nos primeiros 6 meses, seguindo-se um período de estabilização e novo aumento na incidência de eventos após 4 anos da alta hospitalar. A semelhança entre as curvas dos desfechos primário e secundário pode ser consequente à predominância do óbito sobre os demais eventos cardiovasculares.**

Conclusão: **A presença de infecção esternal profunda ou de mediastinite aumentou a mortalidade em longo prazo nesta amostra da população brasileira, de acordo com o mesmo padrão exibido nos países desenvolvidos.**

Descritores: **Mediastinite. Mortalidade. Revascularização miocárdica. Ponte de artéria coronária. Infecção da ferida operatória.**

INTRODUCTION

Deep sternal wound infection and mediastinitis (DSWI) are serious postoperative complications in patients undergoing coronary artery bypass graft surgery (CABG) [1-4]. Patients suffering from DSWI have high morbidity and mortality, with the in-hospital deaths occurring in up to 20% of those subjects [5].

Studies show that the increased mortality is also observed in long-term follow-up [6]. The leading cause of death is cardiovascular disease, particularly acute myocardial infarction [6,7]. Compared with individuals who had no infection, patients suffering from DSWI have a 13% increased risk of cardiovascular death in 10 years following surgery [7].

These studies, however, enrolled a small sample of patients and possess methodological limitations, due in part to the low incidence of mediastinitis. In our setting, in-hospital mortality varies between 23% [8] and 32% [9] in patients suffering from mediastinitis, but there are no data on long-term mortality of DSWI in the Brazilian population.

The aim of this study was to evaluate the long-term mortality of patients with deep sternal wound infection in a public service in Brazil. As a secondary objective, we evaluated the incidence of cardiovascular events in the same population.

METHODS

Case-control study with prospective follow-up based on a database of 1975 patients undergoing CABG at our institution between 2005 and 2008. Cases were defined as patients who developed DSWI according to Centers for Disease Control and Prevention criteria [10]. In order to guarantee the comparability between groups, a propensity score analysis was performed.

Propensity score

In observational studies, randomization to different treatments is not possible. Thus, the different characteristics of the populations can insert bias in the interpretation of results. Multivariate analysis is the most known technique

to exclude the interference of the covariates on the results of a study. The disadvantage of this feature is that the number of variables analyzed is limited to the number of patients enrolled in the study. Thus, in studies of rare diseases, where there are few patients enrolled, multivariate analysis may not eliminate all the confounding factors. If the selection of the control group is made using the propensity score analysis, it is possible to select patients for the control group that have similar characteristics to the affected group disease. This guarantees the pairing of as many features as necessary to ensure adequate comparability between groups.

Controls were defined through a propensity score analysis in a 1:1 ratio, in accordance with the following characteristics: age, gender, body mass index (BMI), chronic kidney disease defined as creatinine clearance less than 30 ml/min/1.73m^2, smoking, previous heart surgery, acute myocardial infarction, prior stroke, diabetes mellitus, peripheral arterial disease, ejection fraction lower than 50% defined by ventriculography, number of diseased vessels, injury in the left main coronary artery and the use of bilateral internal thoracic artery bypass.

The notification of the infection was performed by the method of active surveillance for 30 days, by the Hospital Infection Control Service. Treatment included antibiotic therapy, drainage of collections, debridement of necrotic tissue and subsequent wound closure. The pectoralis major muscle flap was performed in accordance with the evaluation of the surgical team. The dehiscences were closed by bilateral pectoralis major muscle flap. The rotation of the rectus abdominis muscle flap or omentum and composed of breast tissue were used when necessary [11-13].

Outcome data were collected from medical records or telephone contact.

Table 1. Propensity score pairing for baseline characteristics.

	Controls n (%) 114	DSWI n (%) 144	*P*
Age	61.86 ± 8.52	62.5 + 8.57	0.56
Female sex	55 (48)	59 (51.8)	0.59
BMI (kg/m^2)			
	26 (22.8)	28 (24.6)	
< 25			
	45 (39.5)	42 (36.8)	
25 to 30			0.97
	36 (31.6)	36 (31.6)	
31 to 40			
	7 (6.1)	8 (7)	
> 40			
Diabetes mellitus	74 (64.9)	76 (66.7)	0.78
Tobacco smoking			
	42 (36.8)	33 (28.9)	
Previous			0.3
	29 (25.4)	27 (23.7)	
Current			
Stroke	2 (1.8)	4 (3.5)	0.68
ESRD	16 (14)	13 (11.4)	0.55
AMI	60 (52.6)	62 (54.4)	0.79
Previous CABG	2 (1.8)	3 (2.6)	NA
Vessel disease extent			
	61 (53.5)	60 (52.6)	
Three-vessel			0.35
	13 (11.4)	21 (18.4)	
Left main			
Bilateral ITA bypass	5 (4.4)	16 (14)	0.33
EF < 50%	43 (37.7)	41 (36)	0.78
PAD	21 (18.4)	24 (21.1)	0.61

DSWI: deep sternal wound infection; ESRD: end-stage renal disease, AMI: acute myocardial infarction, CABG: coronary artery bypass graft, ITA: internal thoracic artery, EF: ejection fraction, PAD: Peripheral artery disease

Outcomes

Primary outcome was death from any cause. As a secondary outcome, we evaluated the combined event of acute myocardial infarction (AMI), new myocardial revascularization, cerebrovascular accident (CVA) and death.

Statistical analysis

Analysis of event-free survival was performed by the Kaplan-Meier and the Cox models after exclusion of patients that presented cardiovascular event within 30 days of the surgery. Continuous variables were analyzed by Student's t test or Mann-Whitney test when necessary. We analyzed categorical variables using the X^2 test or Fisher's exact test. The significance level was 5% and bilateral tests evaluate hypotheses. The software used was SPSS 19 and R 2.5.1 for Windows.

Ethical aspects

This study followed the principles of the declaration of Helsinski and was approved by the local research ethics under the protocol number 1443.

RESULTS

Of 1975 patients that underwent CABG, 114 developed DSWI, corresponding to an infection incidence of 5.77%.

The propensity score paired 114 patients not affected by wound infection in the control group, ensuring comparability of baseline characteristics, as described in Table 1. Both groups had increased cardiovascular risk. The mean age was 62 years, there was a high prevalence of diabetes mellitus (65.8%), obesity (38.2%), smoking (57.5%), previous myocardial infarction (53.5%), triple vessel disease (53.1%) and 36.8% had ventricular dysfunction.

Mean follow-up was 3.6 years, counted from the hospital discharge. Minimum follow-up was 10 months and the maximum was 6 years and 3 months. Excluding the 11 deaths occurred during in-hospital period, the follow-up was complete for 95.1% of patients. Analysis was based on 204 individuals, 109 from the DSWI group and 95 from the control group. The propensity score was revalued after exclusion of those patients and its validity was reaffirmed.

The 3.6 year survival of patients suffering from infection was significantly lower in the control group, 86.3% versus 96.8%, respectively. Infection conferred an odds ratio for death of 8.26 (95% CI 1.88 - 36.29, $P = 0.005$). The Kaplan-Meier curve showed an increased mortality in the group suffering from infection during the first six months after discharge, following a period of stabilization, and further increase in death after a four years follow-up (Figure 1).

Event-free survival was 89.5% in the control group and 79.8% for patients who had infection. The AMI, stroke, revascularization or death risk was 2.61 times greater for this group when compared with controls (95% CI 1.2 - 5.69, $P = 0.015$) (Figure 2).

Among the combined endpoints, the most common was death. Stroke also had a high incidence, though not significant, with an odds ratio of 5.43 (95% CI 0.63-46.71, $P = 0.12$) (Table 2).

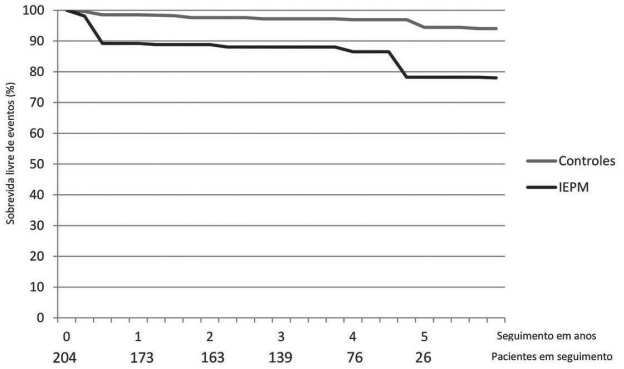

*Fig. 1 - Kaplan-Meier curves for death. Mortality rates are higher in the group suffering from infection in the first 6 months and 4 years after discharge (*P *= 0.001)*

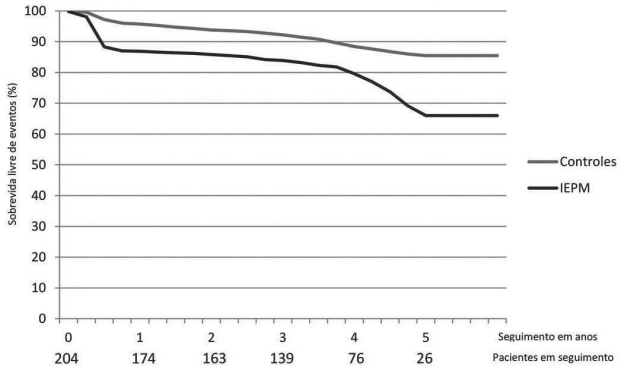

*Fig. 2 - Kaplan-Meier curves for combined cardiovascular events. There is a higher incidence of combined cardiovascular events in the group suffering from infection in the first 6 months and 4 years after discharge (*P *= 0.012)*

Table 2. Results.

	Control (n)	DSWI (n)	*P*
AMI	3	2	0.75
MR	3	1	0.37
Stroke	1	5	0.07
Death	3	15	0.001
Composite	10	23	0.42

DSWI: deep sternal wound infection; AMI: acute myocardial infarction; MR: myocardial revascularization

DISCUSSION

In this case-control study, we selected 114 patients who developed deep sternal wound infection or mediastinitis after CABG and compared with 114 controls identified by a propensity score analysis. In the 3.6 years follow-up, we demonstrated higher mortality and incidence of combined cardiovascular events in the group affected by infection.

We emphasize the high cardiovascular risk presented by the study population. The prevalence of diabetes mellitus, usually around 40% in the population undergoing CABG at our institution [14], was 65.8% in the population of this study. Of the study population, 38.2% were obese, while this incidence is 23% of the usual population submitted to CABG at our institution [14]. These findings probably reflect the more complex clinical preoperative profile presented by patients at risk of developing mediastinitis.

We used the propensity score analysis in order to select the control group, which ensured comparability between the two groups regarding the long-term risk of cardiovascular events, as described in Table 1.

Our mean follow-up was 3.6 years, resembling that of Braxton et al. [6]. In our study, the survival rate of infection in the affected group was significantly lower, 86.3% versus 96.8%, with the odds ratio of death being 8.26 (95% CI 1.88 - 36.29, $P = 0.005$). The distribution of the death risk occurred in a bimodal fashion. There was an increased mortality in the DSWI group during the first 6 months, followed by a stabilization period and a new increase 4 years after discharge (Figure 1).

Infection also resulted in an increase of the composite outcome of AMI, stroke, new myocardial revascularization or death, with an odds ratio of 2.61 (95% CI 1.2 to 5.69, $P = 0.015$). Distribution of the combined event risk by the Kaplan-Meier method was similar to that observed for mortality (Figure 2). However, these findings probably reflect the fact that death was the most frequent cardiovascular event of the secondary outcome. The short follow-up period and the non-knowledge of the cause of death may justify the low incidence of the other components of the combined outcome.

Some hypotheses are suggested to explain the greater cardiovascular risk of patients suffering from mediastinitis. The infectious process leads to a chronic inflammatory process that could accelerate atherogenesis and increase thrombogenicity, resulting in plaque instabilization [7,14]. Thus, the chronic inflammatory process could compromise graft patency and increase mortality and cardiovascular events years after CABG [7,15]. Information regarding the long-term patency of coronary artery grafts in patients who had DSWI is still scarce [16].

Limitations

We were unable to verify the cause of death of our patients, but none of them were violent.

The study was unicentric, so careful must be taken not to generalize the data for the Brazilian population.

The loss of follow-up for 4.9% of patients initially enrolled in the study is low, especially considering that our institution serves patients from all over Brazil.

CONCLUSIONS

We conclude that the DSWI increased mortality in this Brazilian long-term analysis in a similar manner to the few data found in the literature. Since this was a single center study, studies in other institutions are needed before these findings can be generalized to the Brazilian population.

REFERENCES

1. Tiveron MG, Fiorelli AI, Mota EM, Mejia OAV, Brandão CMA, Dallan LAO, et al. Fatores de risco pré-operatórios para mediastinite após cirurgia cardíaca: análise de 2768 pacientes. Rev Bras Cir Cardiovasc. 2012;27(2):203-10.

2. Sá MPBO, Soares EF, Santos CA, Figueiredo OJ, Lima ROA, Escobar RR, et al. Fatores de risco para mediastinite após cirurgia de revascularização miocárdica. Rev Bras Cir Cardiovasc. 2011;26(1):27-35.

3. Magedanz EH, Bodanese LC, Guaragna JCVC, Albuquerque LC, Martins V, Minossi SD, et al. Elaboração de escore de risco para mediastinite pós-cirurgia de revascularização do miocárdio. Rev Bras Cir Cardiovasc. 2010;25(2):154-9.

4. Sá MPBO, Figueira ES, Santos CA, Figueiredo OJ, Lima ROA, Rueda FG, et al. Validação do MagedanzSCORE como preditor de mediastinite após cirurgia de revascularização miocárdica. Rev Bras Cir Cardiovasc. 2011;26(3):386-92

5. Rahmanian PB, Adams DH, Castillo JG, Carpentier A, Filsoufi F. Predicting hospital mortality and analysis of long-term survival after major noncardiac complications in cardiac surgery patients. Ann Thorac Surg. 2010;90(4):1221-9.

6. Braxton JH, Marrin CA, McGrath PD, Morton JR, Norotsky M, Charlesworth DC, et al. 10-year follow-up of patients with and without mediastinitis. Semin Thorac Cardiovasc Surg. 2004;16(1):70-6.

7. Risnes I, Abdelnoor M, Almdahl SM, Svennevig JL. Mediastinitis after coronary artery bypass grafting risk factors and long-term survival. Ann Thorac Surg. 2010;89(5):1502-9.

8. Abboud CS, Wey SB, Baltar VT. Risk factors for mediastinitis after cardiac surgery. Ann Thorac Surg. 2004;77(2):676-83.

9. Sá MP, Silva DO, Lima EN, Lima EC, Silva FP, Rueda FG, et al. Postoperative mediastinitis in cardiovascular surgery postoperation. Analysis of 1038 consecutive surgeries. Rev Bras Cir Cardiovasc. 2010;25(1):19-24.

10. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control. 1988;16(3):128-40.

11. Anger J, Farsky PS, Amato VL, Abboud CS, Almeida AFSA, Arnoni RT, et al. Use of a flap composed of skin and breast tissue for repairing a recalcitrant wound resulting from dehiscence of sternotomy in cardiac surgery. Arq Bras Cardiol. 2004;83(6):43-5.

12. Sampaio DT, Alves JCR, Silva AF, Lobo Jr NC, Simões D, Faria W, et al Mediastinite em cirurgia cardíaca: tratamento com epíploon. Rev Bras Cir Cardiovasc. 2000;15(1):23-31.

13. Brito JD, Assumpção CR, Murad H, Jazbik AP, Sá MP, Bastos ES, et al. One-stage management of infected sternotomy wounds using bilateral pectoralis major myocutaneous advancement flap. Rev Bras Cir Cardiovasc. 2009;24(1):58-63.

14. Farsky PS, Graner H, Duccini P, Zandonadi EC, Amato VL, Anger J, et al. Risk factors for sternal wound infections and application of the STS score in coronary artery bypass graft surgery. Rev Bras Cir Cardiovasc. 2001;26(4):624-9.

15. Ross R. Atherosclerosis: an inflammatory disease. N Engl J Med. 1999;340(2):115-26.

16. Mansuroglu D, Omeroglu SN, Kaya E, Kirali K, Sismanoglu M, Mataraci I, et al. Does mediastinitis affect the graft patency? J Card Surg 2005;20(3):208-11.