

Sepsis in the Postoperative Period of Cardiac Surgery: Problem Description

Dinaldo Cavalcanti de Oliveira^{1,2,3}, João Bosco de Oliveira Filho¹, Rogério Ferreira Silva¹, Simone Soares Moura¹, Diego Janstk Silva¹, Enilton Sergio Tabosa Egito¹, Stevan Krieger Martins¹, Luis Carlos Bento Souza¹, Adib Domingos Jatene¹, Leopoldo Soares Piegas¹

Hospital das Clínicas - Universidade Federal de Pernambuco¹, Recife, PE; Hospital do Coração - Associação Sanatório Sírio²; Hospital São Paulo - Universidade Federal de São Paulo³, São Paulo, SP - Brazil

Abstract

Background: In spite of the advances in sepsis diagnosis and treatment in the last years, the morbidity and mortality are still high.

Objective: To assess the prevalence, in-hospital evolution and prognosis of patients that presented sepsis in the postoperative period of cardiac surgery.

Methods: This is a prospective study that included patients (n = 7,332) submitted to cardiac surgery (valvular or coronary) between January 1995 and December 2007. The classic criteria of sepsis diagnosis were used to identify the patients that developed such condition and the preoperative comorbidities, in-hospital evolution and prognosis were evaluated.

Results: Sepsis occurred in 29 patients (prevalence = 0.39%). There was a predominance of the male when compared to the female sex (79% vs. 21%). Mean age was 69 ± 6.5 years. The main preoperative comorbidities were: systemic arterial hypertension (79%), dyslipidemia (48%) and family history of coronary artery disease (38%). The mean Apache score was 18 ± 7, whereas the Sofa score was 14.2 ± 3.8. The primary infectious focus was pulmonary in 19 patients (55%). There were 19 positive cultures and the mean IV hydration during the first 24 hours was 1,016 ± 803 ml. The main complications were acute renal failure (65%), low cardiac output syndrome (55%) and malignant ventricular arrhythmia (55%). Mortality was 79% (23 patients).

Conclusion: The occurrence of sepsis after cardiac surgery was a rare event; however, its occurrence showed catastrophic clinical outcomes. The high morbidity and mortality showed the need to improve treatment, aiming at patients' better clinical evolution. (Arq Bras Cardiol 2010; 94(3):332-336)

Key words: Sepsis; postoperative care; heart / surgery; thoracic surgery.

Introduction

The advent of cardiac surgery represents a milestone in Medicine, as this procedure can prolong the patient's life and decrease the morbidity of the coronary atherosclerotic disease¹.

In the last years, the advances in this surgery have been striking, which has determined an improvement in the results and the progressive increase in the number of patients submitted to this procedure².

In the United States, in 2006, 700,000 Americans had a heart attack and around 500,000 had a recurrent attack. The direct and indirect expenses with coronary artery disease

(CAD) were US\$ 142.5 billion dollars. More than a million cardiac catheterisms and more than 400,000 myocardial revascularization surgeries were performed³.

The cardiac surgery, in most cases, is a clean surgery with a low rate of infectious complications; however, when these do happen, they contribute to patients' unfavorable evolution⁴.

Patients that develop sepsis, regardless of the infectious focus and the subjacent disease, present high morbidity and mortality, which vary from 17% to 65%⁵.

Recently, recommendations that standardize the diagnosis and treatment of this disease have been published, aiming at improving the clinical evolution of patients⁶.

In spite of the increasing information on sepsis, there is not a relevant number of recent publications that standardize the diagnosis and treatment in the context of the in-hospital postoperative period of patients submitted to cardiac surgery.

Mailing address: Dinaldo C. Oliveira •

Rua Abílio Soares, 625, apto 64 A - Paraíso - 04005002 - São Paulo, SP - Brazil

E-mail: dinaldo@cardiol.br, dinaldoc@ig.com.br

Manuscript received December 17, 2008, revised manuscript received July 10, 2009; accepted August 19, 2009.

The main objective of the present study was to evaluate the morbidity and mortality of patients submitted to cardiac surgery (clean) that developed sepsis during the in-hospital postoperative period, whereas the secondary objective was to assess the prevalence of this type of sepsis.

Methods

This study was approved by Ethics Committee in Research of our Institution and carried out based on a dynamic real-world registry that started in January 1995, which includes all adult patients submitted to elective cardiac surgery.

From January 1995 to December 2007, we studied 7,332 patients from this registry submitted to surgery for the correction of acquired valvulopathy ($n = 1,366$ patients) or to myocardial revascularization surgery ($n = 5,966$ patients), classified as clean surgeries.

Prophylactic antibiotic therapy was prescribed according to the institution protocol, from the anesthetic induction to the second postoperative day.

Sepsis in the postoperative period was defined as evidence of infection associated with two or more criteria of systemic inflammatory response syndrome (SIRS): body temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, heart rate >90 bpm, respiratory rate >20 bpm or $\text{PaCO}_2 <32$ mmHg, leukocytes $>12,000$ cells/ mm^3 , $<4,000$ cells/ mm^3 or >10 young forms⁷.

We assessed the hospital evolution of patients in order to identify those that developed sepsis at the in-hospital postoperative phase (post-op).

The assessed pre, intra and postoperative characteristics of the patients with sepsis were: age, sex, body mass index (BMI), previous myocardial revascularization surgery (MRS), previous percutaneous coronary intervention (PCI), previous acute myocardial infarction (AMI), diabetes mellitus, systemic arterial hypertension (SAH), dyslipidemia, smoking status, previous cerebrovascular accident (CVA), chronic renal disease (creatinine ≥ 1.5 mg/dl), dyslipidemia, chronic obstructive pulmonary disease, family history of CAD, deaths, post-op CVA, post-op acute renal failure (ARF), low cardiac output syndrome, bleeding episode that needed blood derivative transfusion in the post-op period, prolonged respiratory support (>48 hrs), post-op heart failure, malignant ventricular arrhythmia (ventricular tachycardia and/or fibrillation), acute respiratory failure, positive cultures, identified microorganisms, primary focus of infection, variation in glycemia and mean arterial pressure (MAP), heart rate (HR), partial oxygen pressure (PO_2), partial pressure of carbon dioxide (PCO_2) (6, 24, 48 hours after the sepsis diagnosis) antibiotic therapy, Intensive Care Unit stay duration and hospital stay duration. We assessed the APACHE and SOFA scores when the sepsis was diagnosed.

The morbidity was evaluated through the measurement of the occurrence of previously described post-op complications and mortality was measured by the number of deaths. The categorical variables were described as percentages and the continuous variables as means and standard deviations. The ANOVA test was used for the statistical analysis of some of

the numerical variables and statistical significance was set at $p \leq 0.05$.

Results

Of the 7,332 patients submitted to cardiac surgery during the analyzed period, 29 developed sepsis during the in-hospital post-op period (prevalence = 0.39%).

There was a predominance of male patients with sepsis during the post-op period when compared to female patients (79% vs. 21%); the patients' mean age was 66 ± 6.5 years and the mean BMI was 22.6 ± 6.2 kg/ m^2 . The main preoperative comorbidities were SAH in 79% of the patients, dyslipidemia in 48%, family history of CAD in 38% and smoking habit in 34% of the patients (Table 1). The mean APACHE score was 18 ± 7 , and the mean SOFA score was 14.2 ± 3.8 .

The primary infectious foci identified in the patients were: pulmonary in 19 patients (55%), cardiac valve in 3 (10%), abdominal in 2 (6.8%) and bone in 2 (6.8%).

The frequency of distribution of positive cultures was as follows: blood cultures = 11, pulmonary secretion = 6, uroculture = 1 and surgical wound = 1.

The main isolated microorganisms were: *Pseudomonas MR* in 4 patients, *Candida glabrata* in 3, *Staphylococcus epidermidis* in 3, *Stenotrophomonas maltophilia* in 3, *Candida albicans* in 3, *Streptococcus viridans* in 3, *Staphylococcus coagulase negative* in 3, *Flavobacterium* in 1, *Acinetobacter calcoaceticus* in 1, *Streptococcus faecalis* in 1, *Neisseria sp* in 1 and yeast in 1.

The antibiotic agents that were most frequently used for the treatment were: vancomycin in 11 patients, ceftazidime in 11, ceftriaxone in 9, meropenem in 7, cefepime in 5, gentamycin in 4 and teicoplanin in 3.

The mean hydration in the first 24 hours after the sepsis diagnosis was $1,016 \pm 803$ milliliters. Table 2 shows the comparative analysis of glycemia, BP, HR, PCO_2 and PO_2 in the first 6, 24 and 48 hours of sepsis evolution.

The main post-op complications were: post-op ARF in 65% of the patients (all of them needed dialysis), low-cardiac output syndrome (55), malignant ventricular arrhythmia (55) and CVA (20%) (Table 3).

The in-hospital mortality was 79% (23 patients). The mean time of ICU stay was 45 ± 55 days, whereas the mean hospital stay duration was 54 ± 55 days.

Discussion

The infectious complications after clean cardiac surgeries occur in up to 3.5% of the patients, and the main ones are: mediastinitis, infection at the site of the removal of the saphenous vein graft, endocarditis, sternal infection, chest surgical wound infection, sepsis, pulmonary infections, vascular access site infections, urinary tract infections, gastrointestinal tract infections, etc⁸⁻¹³.

The cardiac surgery postoperative infections contribute to the increase of the morbidity and mortality, the hospital and ICU stay duration and costs¹⁴.

The main predictors of infections in the postoperative period are: body mass index ≥ 40 kg/m², hemodialysis in the preoperative period (pre-op.), pre-op cardiogenic shock, age ≥ 85 yrs, pre-op treatment with immunosuppressive agents, diabetes mellitus, ECC time ≥ 200 minutes, use of intra-aortic balloon 3 or more revascularized vessels¹⁵⁻²⁰.

The sepsis after cardiac surgery has been described as a low-prevalence infectious complication, albeit with tragic consequences²¹⁻²⁴.

Toumpoulis et al²⁵ studied 3,720 patients submitted to cardiac surgery, with the objective of identifying risk factors for sepsis and endocarditis. The prevalence of sepsis in the post-op was 1.2%; however, the in-hospital mortality was $> 70\%$ and there was an increase in costs and time of hospitalization associated with the occurrence of sepsis.

Michalopoulos et al²² evaluated 2,615 patients submitted to cardiac surgery and verified a low prevalence of sepsis (2%). During sepsis, the patients presented the following picture: hypoxemia (41%), fever (39%), metabolic acidosis (36%), acute renal failure (36%), tachycardia (33%), arterial hypotension (28%) and mental confusion (22%).

In the present study, which assessed more than 7,000 patients submitted to cardiac surgery, sepsis also presented a low prevalence. However, the rates of complications, which were high, and mainly the mortality rate of 79%, suggest that patients that presented such infectious complication represent a group of very-high risk.

The BP and PCO₂ goals in the present study were reached at the sixth hour (and maintained up to the end of the second day), whereas the PO₂ goal was reached only at the 48th hour. Glycemic control was not reached until 48 hours of sepsis evolution. It is possible that the lack of early goal-reaching has contributed to the high mortality rate.

Fowler et al²⁶ analyzed 331,429 patients submitted to myocardial revascularization surgery between January 2002 and December 2003, with the objective of developing an infection risk score. The prevalence of major infections was 3.5%: septicemia in 1.2% of the patients, infection at the site of the removal of the saphenous vein graft in 1.1%, mediastinitis in 0.9% and multiple-site infection in 0.2%. The mortality of patients with infection was higher when compared to those without infection (17% vs. 3%, $p < 0.001$).

In the present study, the temporal onset of complications, that is, the occurrence of adverse events after the onset of sepsis, suggests that the patients with this disease are more vulnerable and thus, present such high rates of complications. We believe, for instance, that the patient with sepsis has a higher chance of presenting acute renal failure, heart failure, etc.

The current treatment of severe sepsis must be based on the following procedures: aggressive and early (first six hours) volemic resuscitation (colloid or crystalloid), early antibiotic therapy (preferably at the first hour of septic shock), maintenance of hemoglobin > 8 g, administration of blood derivatives, adequate mechanical ventilation (when necessary), sedation, analgesia, no muscular blockers (whenever possible),

Table 1 – Clinical profile of patients

Variable	Prevalence
Systemic Arterial Hypertension, n	23 (79%)
Dyslipidemia, n	14 (48%)
FH of coronary artery disease, n	11 (38%)
Smoking, n	10 (34%)
Cerebrovascular accident, n	8 (27%)
Previous Acute myocardial infarction, n	7 (24%)
Previous PCI, n	6 (20%)
Previous MRS, n	5 (17%)
Diabetes mellitus, n	5 (17%)
Chronic obstructive pulmonary disease, n	3 (10%)
Chronic renal disease, n	2 (7%)

MRS - myocardial revascularization surgery, PCI - percutaneous coronary intervention, FH - family history, n - number of patients.

Table 2 – Temporal variation of hemodynamic, respiratory and glycemia parameters

Variable	6 h	24 h	48 h	p Value
HR, bpm	116 \pm 21	115 \pm 21	118 \pm 23	0,8
BP, mmHg	60 \pm 10	61 \pm 10	62 \pm 12	0,8
PCO ₂ , mmHg	48 \pm 53	38 \pm 6	40 \pm 10	0,4
PO ₂ , mmHg	82 \pm 26	88 \pm 18	99 \pm 6	0,3
Glycemia, mg/dl	183 \pm 124	158 \pm 47	195 \pm 75	0,3

HR - heart rate, BP - blood pressure, PCO₂ - partial pressure of carbon dioxide in blood, PO₂ - partial pressure of oxygen in blood.

Table 3 – Complications in the postoperative period

Variable	Prevalence
Bleeding with need for blood derivative transfusion, n	23 (79%)
Prolonged ventilatory support, n	21 (72%)
Acute renal failure, n	19 (65%)
Low cardiac-output syndrome, n	16 (55%)
Malignant ventricular arrhythmia, n	16 (55%)
Acute respiratory failure, n	16 (55%)
Cerebrovascular accident, n	6 (20%)
Congestive heart failure, n	5 (17%)

strict glycemia control (blood glucose < 150), dialysis therapy (there is an equivalence between the classic and the new modalities), corticoid administration when there is inadequate response of BP to fluid therapy and/or vasopressors, recombinant activated protein C if APACHE score is ≥ 25 or when there is multiple-organ failure, administration of sodium bicarbonate to patients with hypoperfusion induced by lactic acidosis with pH ≥ 7.15 and prophylaxis for deep venous thrombosis and stress ulcer⁶.

The objectives in the first 6 hours of volemic resuscitation are: central venous pressure between 8 and 12 mmHg, mean BP ≥ 65 mmHg, urinary output ≥ 0.5 ml/kg/hour and central venous oxygen saturation (ScvO₂) $\geq 70\%$. In cases where the administration of fluids does not reach the target ScvO₂, a red blood cell transfusion must be considered (if the hematocrit is < 30%) as well as the intravenous infusion of dobutamine⁶.

The implementation of this treatment contributes to decrease morbidity and mortality of severe sepsis in several clinical situations⁶. These measures must be adopted for patients submitted to cardiac surgery that develop severe sepsis, as they are capable of reducing morbidity and mortality.

In spite of its low prevalence, the sepsis that occurs in the post-op of cardiac surgery significantly contributes to patients' high morbidity and mortality. Therefore, the current recommendations for the treatment of severe sepsis represent a treatment strategy that is potentially capable of improving the hospital evolution of patients and need to be evaluated concerning the sepsis that occurs after cardiac surgery.

The present study presents some limitations: the study was carried out in a single center and modifications in sepsis diagnosis and treatment were verified during the assessed period.

Conclusions

Sepsis has always been a rare complication in the postoperative period of cardiac surgery. However, when observed, the result is catastrophic: 79% of the patients who presented such complication died during the hospitalization phase.

The therapeutic measures recommended by the international guidelines⁶ for the treatment of sepsis must be applied to patients that present sepsis after cardiac surgery, as they are potentially capable of reducing morbidity and mortality.

Potential Conflict of Interest

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

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.

References

1. Morrow DA, Gersh BJ. Chronic coronary artery disease. In: Libby P, Bonow RO, Mann DL, Zipes DP (eds). Braunwald's heart disease: a textbook of cardiovascular medicine. 8th ed. Philadelphia: Saunders Elsevier; 2008. p. 1353-405.
2. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Gardner TJ, Hart JC, et al. ACC/AHA 2004 Guideline update for coronary artery bypass graft surgery: report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to update the 1999: Guidelines for Coronary Artery Bypass Graft Surgery. *Circulation*. 2004; 110: e340-437.
3. Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, et al. Heart disease and stroke statistics. 2006 Update: a report from the American Heart Association Statistics Committee and stroke Statistics Subcommittee. *Circulation*. 2006; 113: e85-151.
4. Slaughter MS, Olson MM, Lee JT Jr, Ward HB. A fifteen years wound surveillance study after coronary artery bypass. *Ann Thorac Surg*. 1993; 56: 1063-8.
5. Silva E, Fernandes Jr CJ, Akamine N, Sogayar AMCB, Knobel E. Sepsis e choque séptico. In: Knobel E. *Conduitas no paciente grave*. 3ª ed. São Paulo: Editora Atheneu; 2006. p. 61-78.
6. Dellinger RF, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med*. 2008; 36: 297-327.
7. Friedman G, Victorino JA. Sepsis. In: Barreto SSM, Vieira SRR, Pinheiro CTS. *Rotinas em terapia intensiva*. 3ª ed. Porto Alegre: Editora Artmed; 2001. p. 287-95.
8. Fowler VG Jr, Kaye KS, Simel DL, Cabell CH, McClachlan D, Smith PK, et al. Staphylococcus aureus bacteremia after median sternotomy: clinical utility of blood culture: results in the identification of postoperative mediastinitis. *Circulation*. 2003; 108: 73-8.
9. Wang FD, Chang CH. Risk factors of deep sternal wound infections in coronary artery bypass graft surgery. *J Cardiovasc Surg*. 2008; 41: 709-13.
10. Ferguson TB Jr, Dziuban SW Jr, Edwards FH, Eiken MC, Shroyer AL, Pairolero PC, et al. The STS National Database: current changes and challenges for the new millennium. *Ann Thorac Surg*. 2000; 69: 680-91.
11. Edwards FK, Clark RE, Schwartz M. Practical considerations in the management of large multiinstitutional databases. *Ann Thorac Surg*. 1994; 58 (6): 1841-4.
12. Welke FK, Ferguson TB Jr, Coombs LP, Dokholyan RS, Murray CI, Schrader MA, et al. Validity of the Society of Thoracic Surgeons National Adult Cardiac Surgery Database. *Ann Thorac Surg*. 2004; 77: 1137-9.
13. Athanasiou T, Aziz O, Shapinkas P, Penunovic B, Hart J, Crossman MC, et al. Leg wound infection after coronary artery bypass grafting: a meta-analysis comparing minimally invasive versus conventional vein harvesting. *Ann Thorac Surg*. 2003; 76: 2141-6.
14. Kollef MH, Sharpless L, Vlasnik J, Pasque C, Murphy D, Fraser VJ. The impact of nosocomial infections on patient outcomes following cardiac surgery. *Chest*. 1997; 112: 666-75.
15. Abboud CS, Wey SB, Baltar VT. Risk factors for mediastinitis after cardiac surgery. *Ann Thorac Surg*. 2004; 77: 676-83.

16. Gummer JF, Barten MI, Hans C, Kluge M, Doll N, Walther T, et al. Mediastinitis and cardiac surgery: an updated risk factor analysis in 10.373 consecutive adult patients. *Thorac Cardiovasc Surg.* 2002; 50: 87-91.
17. Milano CA, Kesler K, Archibald N, Sexton DJ, Jones RH. Mediastinitis after coronary artery bypassgraft surgery: risk factors and long-term survival. *Circulation.* 1995; 92 (8): 2245-51.
18. Prabhakar G, Haan CK, Peterson ED, Coombs LP, Cruzzavala JL, Murray GF. The risks of moderate and extreme obesity for coronary artery bypass grafting outcomes: a study from the Society of Thoracic Surgeons' database. *Ann Thorac Surg.* 2002; 74 (4): 1125-30.
19. Estrada CA, Young JA, Nifong LW, Chitwood WR Jr. Outcomes and perioperative hyperglycemia in patients with or without diabetes mellitus undergoing coronary artery bypass grafting. *Ann Thorac Surg.* 2003; 75: 1392-9.
20. Furnary AP, Wu Y, Bookin SO. Effect of hyperglycemia and continuous intravenous insulin infusions on outcomes of cardiac surgical procedures: the Portland Diabetic Project. *Endocr Pract.* 2004; 10 (Suppl 2): 21-3.
21. Ford EG, Baisden CE, Matteson ML, Picone AL. Sepsis after coronary bypass grafting evidence for loss of the gut mucosal barrier. *Ann Thorac Surg.* 1991; 52: 514-7.
22. Michalopoulos A, Stavridis G, Geroulanos S. Severe sepsis in cardiac surgical patients. *Eur J Surg.* 1998; 164: 217-22.
23. Eidelman LA, Sprung CL. Why have new effective therapies for sepsis not been developed? *Crit Care Med.* 1994; 22: 1330-4.
24. Pilz G, Kaab S, Kreuzer E, Werdan K. Evaluation of definitions and parameters for sepsis assessment in patients after cardiac surgery. *Infection.* 1994; 22: 8-17.
25. Toumpoulis IK, Anagnostopoulos CE, Toumpoulis SK, De Rose Jr JJ, Swistel DC. Risk factors for sepsis and endocarditis and long-term survival following coronary artery bypass grafting. *World J Surg.* 2005; 29: 621-8.
26. Fowler VG, O'Brain SJ, Muhlbaier LH, Corey GH, Ferguson BT, Peterson ER. Clinical predictors of major infections after cardiac surgery. *Circulation.* 2005; 112: 1358-65.