Frequency, characteristics, and predictors of microbiologically documented nosocomial infections after cardiac surgery

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Abstract

Objective: Nosocomial infections still remain a serious problem in patients undergoing open heart surgery. The objective of this study was to evaluate frequency, characteristics, and predictors of nosocomial infections after cardiac surgery. Methods: This prospective case–control study was conducted in adult patients who underwent open heart surgery with use of extracorporeal circulation over a period of 16 months. Cases were patients who developed microbiologically documented nosocomial infection. Controls were patients who had open heart surgery within a randomly selected two-month period of the study (defined before the start of the study) and did not develop nosocomial infection. Various variables, available before, during or within the first two days after operation, were examined as possible risk factors of nosocomial infections in bivariable analysis. Then, variables that were found to be statistically associated with nosocomial infections in the bivariable analysis were included in a multivariable logistic regression model to identify independent risk factors associated with nosocomial infections after open heart surgery. Results: One hundred and seven of 2122 (5.0%) patients developed microbiologically documented nosocomial infection after open cardiac surgery. The majority of nosocomial infections were respiratory tract infections (45.7%) and central venous catheter-related infections (25.2%). All cause hospital mortality was 16.8% in patients with nosocomial infection and 3.5% in the control group (p = 0.005). Out of 20 variables studied as possible risk factors, 12 had a statistically significant association with postoperative infection. History of immunosuppression (OR = 3.6, 95% CI 1.2—11.0%), transfusion of more than five red blood cell units in both the operating room and during the first ICU postoperative day (OR = 21.2, 95% CI 11.9—37.8%), and development of acute renal failure within the first two days after operation (OR = 49.9, 95% CI 22.4—111.0%), were found to be independent predictors of nosocomial infections after cardiac surgery in a multivariable logistic regression model. Conclusions: Postoperative nosocomial infections are a considerable problem in cardiac surgery patients. The identified independent predictors of nosocomial infection may be useful in identifying those at high risk for development of such infection in cardiac surgery patients.

Keywords: Cardiac surgery; Open heart surgery; Postoperative complications; Nosocomial infection; Risk factors

1. Introduction

Nosocomial infections still represent a serious problem. They are associated with substantial morbidity, prolonged hospitalization and maybe higher mortality [1]. Hospital-acquired infections are more common in ICU patients, including patients undergoing cardiac surgery. Several studies have examined the incidence and risk factors of nosocomial infections after open heart surgery. Postoperative infection has been reported to occur in 5—21% of cardiac surgery patients in various institutions [2]. In this group of patients, infections are serious and often life-threatening complications [2]. We designed the present study in order to identify frequency, characteristics, and risk factors (determinants) of postoperative infection in our cohort of patients undergoing open heart surgery in a Cardiac Surgery Center in Greece.

2. Patients and methods

2.1. Study design-setting

This is a prospective case–control study which was conducted at the Onassis Cardiac Surgery Center, Athens,
Greece that is a referral Center for patients with cardiovascular diseases. Approval was obtained from the Ethics and Research Committee of the Center.

2.2. Patient population

We studied all adult patients (aged above 16 years) who underwent open heart surgery with the use of extracorporeal circulation over a period of 16 months (June 1996—September 1997). Cases were patients who developed microbiologically documented nosocomial infection. Controls were patients who had open heart surgery during two consecutive months of the study period and did not develop nosocomial infection (n = 314). The selection of this two-month period was done randomly at the beginning of the study (out of eight candidates two-month periods of the whole 16-month study period and it was January and February 1997).

All patients were admitted to the Cardiothoracic ICU (16 beds) immediately following open heart surgery and subsequently transferred to the ward according to the improvement of their medical condition. Patients with pre-existing infection or receipt of antibiotics during the last two days before surgery or pre-existing intra-aortic balloon pump were excluded from the study. Heart transplant recipients, as well as all patients who died in the operating room and in the ICU during the first two postoperative days, were also excluded.

2.3. Data collection

We recorded all the infectious complications that occurred in patients during their ICU and regular ward, regardless of the total length of hospital stay. For each patient we entered data for 20 variables that were considered risk factors for development of nosocomial infection into a database. These were patient-related factors, surgery-related factors, and ICU-related factors.

Patient-related factors included gender, age, preoperative left ventricular ejection fraction assessed by angiography, and New York Heart Association class. We also recorded history of immunosuppression, diabetes mellitus, use of insulin, arterial hypertension, smoking history, pulmonary hypertension, and chronic obstructive pulmonary disease requiring medical therapy with bronchodilators.

Surgery-related factors included the surgical team, type of surgical procedure, combined use of left and right internal mammary artery (LIMA, RIMA) and bypass time. The number of red blood cell units transfused in the operating room or during the first ICU postoperative day, the number of inotropic agents administered during the first postoperative day (for at least 6 h), and the use of intra-aortic balloon counterpulsation and Swan–Ganz catheter during the first postoperative day. Inotropic drugs were used to treat low cardiac output syndrome, defined as a cardiac index <2 l/min and square body surface meter, despite optimal filling pressures (wedge pressure 12 mmHg). In this situation, dobutamine, adrenaline, dopamine, milrinone, or noradrenaline were given up to their maximum doses. Dopamine at renal doses was not taken into consideration. Red blood cell transfusion was given when the patient’s hematocrit was less than 27%.

We also recorded complications that occurred during the early postoperative period in the ICU which theoretically may increase the possibility of nosocomial infection such as low cardiac output syndrome and acute renal failure. Patient outcome evaluated on the day of hospital discharge and the cause(s) of death that occurred during hospitalization were recorded in all patients.

2.4. Management—clinical assessment

Cardiac surgical procedures were performed by three surgical teams. Anesthesia was provided by three teams according to a set protocol. The myocardial protection protocol included the use of antegrade cold crystalloid cardioplegia and antegrade/retrograde cold blood cardioplegia. All patients had at least one central venous catheter. Swan–Ganz catheter was used only in high risk cardiac surgical patients.

Antibiotic prophylaxis was administered in all patients according to a set protocol. In the patients undergoing coronary artery bypass grafting surgery, cefuroxime was given intravenously as single dose (3 g) at the induction of anesthesia. No additional dose was given in the pump priming solution. In patients who underwent valve replacement surgery or combined coronary artery bypass grafting and valve replacement surgery, a combination of intravenous vancomycin (1 g every 12 h) and netilmicin (150 mg every 12 h) was administered for 2–4 days. The first doses were given at the induction of anesthesia.

Hematological and biochemical tests, and chest X-rays were performed preoperatively and every day during ICU stay and before discharge. In addition, laboratory tests and X-rays were performed when clinically indicated. All patients were daily examined by the intensivists of the Center in order to detect any nosocomial infection. Body temperature was recorded every 1 h in the ICU, every 3 h for the next two days and at least twice daily thereafter. The wounds were examined daily. Bacteriological examinations of blood, tracheal secretions, urine, central venous catheter tips, and of wound swabs were performed in case of a suspected infection.

2.5. Classification of infection

An infection was classified as nosocomial when developed within the hospital and became clinically apparent while the patient was still hospitalized. The infection should not be present or incubating prior to admission to the surgical ICU, occurring after 48 h following admission to the ICU [3,4].

Nosocomial pneumonia was diagnosed based on the presence of the following criteria: fever >38 °C, rales, leukocytosis, detection of new or progressive lung infiltrate(s) not explained otherwise, and purulent respiratory secretion yielding growth of relevant pathogen. A positive culture of blood, pleural fluid, or bronchoalveolar lavage was regarded as additional proof of nosocomial pneumonia [4]. Urinary tract infection was diagnosed in the presence of clinical manifestations such as fever >38 °C, dysuria, or...
suprapubic tenderness and a positive urine culture, that is, >100,000 microorganisms per cubic centimeter of urine [4].

Infective endocarditis was diagnosed by echocardiography (presence of valve vegetations) combined with compatible clinical signs of infection and positive blood cultures. Central venous catheter-related infection was diagnosed in the presence of bacteremia (with or without the signs of sepsis) that was exclusively attributable to a central venous catheter associated with a count of more than 15 colonies in a semi-quantitative culture of catheter tip (Maki's technique). Primary bloodstream infection was diagnosed in the presence of clinical signs of sepsis plus at least one positive blood culture drawn through a peripheral line in response to unexplained fever of 38.5 °C after the second postoperative day, associated with leukocytosis of >11,000 cm⁻³ or leucopenia of <4000 cm⁻³. The absence of a known focus of infection in another site was necessary for this diagnosis. Diagnosis of sepsis was based on the ACCP/SCCM criteria [5].

Poststernotomy wound infection was defined by clinical evidence of infected pre sternal tissue and/or sternal osteomyelitis, with or without mediastinal sepsis and with or without unstable sternum. Subtypes included (1) superficial wound infection defined as wound infection confined to the subcutaneous tissue and (2) deep wound infection defined as wound infection associated with sternal osteomyelitis with or without infected retrosternal space. Incisional or deep surgical wound infection was diagnosed based on the following criteria: purulent drainage from the incisional or the drain site, pathogen(s) isolated from wound drainage cultures and signs or symptoms of infection.

Acute renal insufficiency was defined as an absolute abrupt postoperative rise in peak serum creatinine level by 2 mg/dl in a previously normal renal function or a doubling in the admission creatinine level in patients with chronic renal failure [6]. Patients were classified as immunocompromised if they had HIV infection or solid organ transplantation or malignancy or neutropenia (absolute neutrophil count of <1000 mm⁻³) and those receiving corticosteroids (at least 10 mg of prednisone or its equivalent, per day for >14 days prior to surgery) or those received chemotherapy within the past 45 days before surgery.

2.6. Statistical analysis

Data were analyzed using the BMDB Statistical Software (Los Angeles, CA, USA). Tests on categorical variables were based on Pearson chi-square statistics in the case of 2 × 2 tables. Continuous variables were subjected to t-tests with statistical significance confirmed using Welch’s method, if appropriate. The variables found to be predictors of nosocomial infection based on univariate analysis were subjected to logistic regression analysis in order to identify a subset of variables for predicting infection. A p-value <0.05 was considered statistically significant.

3. Results

One hundred and seven of the 2122 (5.0%) patients developed microbiologically documented nosocomial infection after open cardiac surgery. The sites of nosocomial infection are presented in Table 1. The majority of nosocomial infections were respiratory tract infection (45.7%), central venous catheter-related infection (25.2%), and wound infection (17.7%). Infection in 105 out of 107 patients was monomicrobial. Two patients developed polymicrobial infection. Thus, the total number of pathogens was 109. From them, 74 isolates were Gram-positive cocci (74/109, 67.9%) and 33 were Gram-negative bacteria (33/109, 30.7%). The predominant pathogens isolated were Staphylococcus species (66/109, 60.6%), mainly Staphylococcus epidermidis (35/109, 32.1%) and Staphylococcus aureus (31/109, 28.4%). Gram-positive cocci were responsible for the majority of central venous catheter-related infections, wound infections, bacteremias, and endocarditis. The Gram-negative isolates were Enterobacter species (11/109, 10.1%), Escherichia coli (7/109, 6.4%), Serratia species (5/109, 4.6%), Pseudomonas aeruginosa (5/109, 4.6%), and Klebsiella pneumoniae (5/109, 4.6%). Gram-negative microbes caused mostly respiratory tract infections. Two patients had candidemia. The majority of respiratory tract infections developed in patients with prolonged (>5 days) mechanical ventilatory support which usually occurred in patients with low cardiac output syndrome and CNS disturbances. Endocarditis occurred in 2.1% of patients who underwent valve replacement surgery or combined (CABG and valve replacement) surgery.

All cause mortality rate was 18/107 (16.8%) in patients with nosocomial infection, 11/314 (3.5%) in the studied control group and 77/2122 (3.6%) in the whole cohort of cardiac surgery patients during the study period. Mortality was not different between control patients (3.5%) and the rest of the patients of the cohort who did not develop nosocomial infection 48/1701 (2.8%), p = 0.51.

Table 2 shows the results of the bivariable analysis of the association of various variables with development of nosocomial infection. Twelve of the original 20 potentially predictive variables had a statistically significant relationship to nosocomial infection. Multivariable logistic regression analysis showed that among all these variables examined, three were independent predictors of nosocomial infection in this group of patients. These were history of immunosuppression (OR = 3.6), transfusion of more than five red blood cell units during the first postoperative day in both the operating room and ICU (OR = 21.2), and development of acute renal failure within the first two days after operation (OR = 49.9) (Table 3).
Table 2
Patient characteristics and several preoperative, operative, and postoperative risk factors in cardiac surgery patients developing nosocomial infection and in the control group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Infection group (% (n = 107)</th>
<th>Non-infection group (% (n = 314)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (males/females)</td>
<td>80/27 (74.8/25.2)</td>
<td>267/47 (85/15)</td>
<td>0.02</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.0 ± 10.2</td>
<td>61.5 ± 9.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Preoperative LVEF (%)</td>
<td>0.43 ± 0.11</td>
<td>0.47 ± 0.09</td>
<td>0.0001</td>
</tr>
<tr>
<td>New York Heart Association class III or IV</td>
<td>56 (52.3)</td>
<td>134 (42.7)</td>
<td>0.2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>35 (32.7)</td>
<td>100 (31.8)</td>
<td>0.9</td>
</tr>
<tr>
<td>Use of insulin</td>
<td>10 (9.3)</td>
<td>21 (6.7)</td>
<td>0.5</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>45 (42.1)</td>
<td>158 (50.3)</td>
<td>0.2</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>24 (22.4)</td>
<td>30 (9.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>51 (47.7)</td>
<td>136 (43.3)</td>
<td>0.5</td>
</tr>
<tr>
<td>COPD</td>
<td>23 (21.5)</td>
<td>39 (12.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>7 (6.5)</td>
<td>6 (1.9)</td>
<td>0.04</td>
</tr>
<tr>
<td>Two arterial grafts</td>
<td>7 (6.5)</td>
<td>42 (13.2)</td>
<td>0.07</td>
</tr>
<tr>
<td>Surgical team (A/B/C)</td>
<td>42/35/30</td>
<td>102/111/101</td>
<td>0.4</td>
</tr>
<tr>
<td>Bypass time (min)</td>
<td>141 ± 39</td>
<td>98 ± 36</td>
<td>0.0001</td>
</tr>
<tr>
<td>Swan–Ganz catheter</td>
<td>71 (66.3)</td>
<td>187 (59.5)</td>
<td>0.2</td>
</tr>
<tr>
<td>Blood units transfused (n)</td>
<td>8.9 ± 8.4</td>
<td>1.9 ± 2.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Inotropes (n)</td>
<td>1.4 ± 1.2</td>
<td>0.4 ± 0.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Low cardiac output syndrome</td>
<td>43 (40.2)</td>
<td>13 (4.1)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>60 (56.1)</td>
<td>8 (2.5)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Intra-aortic balloon pump (IABP)</td>
<td>26 (24.3)</td>
<td>9 (2.9)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or n (%). LVEF: left ventricular ejection fraction; COPD: chronic obstructive pulmonary disease.

Table 3
Summary of results of the multivariable logistic regression stepwise analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of immunosuppression</td>
<td>3.6 (1.2, 11.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>More than five red blood cell units transfused during the first postoperative day</td>
<td>21.2 (11.9, 37.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Acute renal failure the first two postoperative days</td>
<td>49.9 (22.4, 111.0)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

4. Discussion

Microbiologically documented nosocomial infection occurred in 107 of the 2122 (5.0%) patients undergoing open heart surgery. Our data demonstrated that multiple risk factors are associated with the development of nosocomial infection in this group of patients. However, only three risk factors were found to be independently associated with nosocomial infection after open heart surgery, namely: history of immunosuppression, transfusion of more than five red blood cell units during the first postoperative day in both operating room and ICU, and development of acute renal failure during the first two postoperative days.

Nosocomial infection still remains a diagnostic and therapeutic challenge in the care of cardiac surgery patients. The diagnosis of nosocomial infection in this patient population is sometimes difficult, since clinical and laboratory signs of inflammation may be caused not only by infection, but also by tissue injury and mainly by the systemic inflammatory response syndrome (SIRS) associated with cardiopulmonary bypass. Measurement of CRP could not be demonstrated to clearly help in differentiating between presence and absence of infection in ICU patients [7]. In addition, surgical patients usually receive systemic antibiotics, especially in the ICU, thus negatively influencing blood culture yield [8]. Furthermore, clinical diagnostic criteria for nosocomial pneumonia, central venous catheter-related infection, or bacteremia are non-specific.

Immunosuppression is a documented predisposing factor for development of nosocomial infection [9]. In addition, acute renal failure developed in approximately 4% of patients undergoing cardiac surgery and it is associated with high morbidity and mortality rates [10]. Stallwood et al. [11] recently reported that the use of cardiopulmonary bypass is associated with significantly increased risk of acute renal failure following isolated coronary artery bypass surgery compared to off-pump myocardial revascularization. All efforts are targeting to prevent the development of acute renal failure by better protection of renal function perioperatively.

In addition, any strategy targeting the avoidance of bleeding, and subsequently, of blood transfusion may reduce significantly the incidence of postoperative infection in this group of patients. Regarding the effect of allogeneic blood transfusion on immune function and its association with increased rates of postoperative infections, there are controversial data [12–16]. The significance of multiple transfusions on the outcome of patients undergoing myocardial revascularization has been demonstrated [17]. On the other hand, our transfusion trigger (hct below 27) seems to be high. This transfusion trigger was the subject of a recent randomized prospective study suggesting no benefit and possible harm for transfusing at that level [18]. It has been supported that apart from blood transfusion other related factors, such as general anesthesia, hemorrhage, surgical stress, low cardiac output syndrome and/or temporary shock, and possibly systemic inflammatory response syndrome may predispose to immunosuppression and infection [19].

Niederhauser et al. tried to lower infectious complications by administration of prolonged antibiotic prophylaxis in high-risk cardiac surgery patients. They concluded that an additional postoperative prophylaxis regimen with vanco-
mycin and ticarcillin/clavulanate did not reduce the rate of nosocomial infections [20]. For this reason, prolongation of antibiotic prophylaxis is not necessary and sometimes is associated with development of resistant pathogens especially in the ICU setting [21]. On the contrary, the early diagnosis and treatment of postoperative infections is considered very important for the patient’s outcome.

Our study has several limitations. First, it is not a matched case—control study. Specifically, we used as control patients those who had cardiac operation at the same center during a randomly defined two-month period and did not develop nosocomial infection. However, there are several factors that may influence the development of nosocomial infections in different time periods such as changes in patient population, in staff (especially among doctors and nurses), in hospital and its infection control measures, and changes of the season. Furthermore, potential nosocomial outbreaks of pathogens could also increase the number of nosocomial infections in the studied period of 16 months. Also, we used an old data set in order to identify risk factors of postoperative infection in patients that underwent open heart surgery with use of extracorporeal circulation several years ago, without taking into account the development in the surgical techniques of open heart surgery. For example, several studies have shown that off-pump bypass is associated with a significant reduction in transfusions, inflammatory response, and post-operative infections, especially respiratory tract infections that were the majority of nosocomial infections in our group of patients [22].

In conclusion, we evaluated the frequency and the characteristics of nosocomial infections and we found that a relatively low proportion of these patients developed a microbiologically documented nosocomial infection associated with a notable mortality rate (16.8%). In addition, we found three variables with a statistically significant association with the development of nosocomial-acquired infection during hospitalization in adult patients undergoing open heart surgery by means of cardiopulmonary bypass that could help clinicians to identify uncertain cases of infection.

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References


