SURGERY FOR ACQUIRED HEART DISEASE

NOSOCOMIAL INFECTIONS IN PATIENTS HAVING CARDIOVASCULAR OPERATIONS: A MULTIVARIATE ANALYSIS OF RISK FACTORS

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A total of 970 adult patients undergoing cardiovascular operations during a 1-year period were eligible for a case-control study on the risk factors for nosocomial infection. Cases were defined as patients in whom a postoperative infection developed. Every case was paired with one uninfected subject. Nosocomial infection occurred in 89 (9.2%) patients. A total of 120 episodes of infection were diagnosed (1.3 episodes per patient). The infection ratio was 12.4%. Surgical site infection was the most common (5.6%), followed by pneumonia (3.2%), urinary tract infection requiring the use of intravenous antibiotics (1.8%), deep surgical site (0.9%), and bacteremia (0.7%). Advanced age, urgent intervention, duration of surgical procedure, blood transfusion, and use of invasive procedures (urinary catheter, chest tubes, nasogastric tube passage) were significantly associated with infection in the bivariate analysis. Nosocomial infection resulted in a significant increase in the length of hospital stay. Cases showed an almost fivefold greater risk of death than controls (odds ratio, 4.73; 95% confidence interval, 1.11 to 6.83; $p = 0.009$). Age older than 65 years, female sex, and mode of surgical intervention were selected in the multivariate analysis for patients undergoing cardiac operations, whereas general anesthesia or assisted ventilation, central venous catheter, and blood transfusion were the variables selected for patients undergoing operation for vascular disorders. In summary, the recognition of risk factors for postoperative infection in patients undergoing cardiovascular surgical procedures may contribute to improve their prognosis and to more organized surveillance and control activities in the hospital environment. (J Thorac Cardiovasc Surg 1996;112:908-13)

Nosocomial infections after cardiovascular operations represent serious complications associated with substantial morbidity, mortality, and economic burden.¹⁻³ Patients undergoing cardiac operations are particularly susceptible to infection owing to

numerous predisposing factors, such as prolonged operating time, multiplicity of invasive procedures, postoperative intensive manipulation, and high dependency on hospital staff, and the infections are often severe.⁴ Although wide experience has been achieved in dealing with these complications, the actual influence of different risk factors has rarely been evaluated by comparing patients who had infections and control patients who did not. We report a case-control study on the risk factors for nosocomial infection in cardiovascular surgery.

Patients and methods

All consecutive adult patients undergoing cardiovascular surgery at our institution between July 1993 and June 1994 were eligible for a case-control study with one-to-one

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matching of patients recognized as having postoperative infection with other patients not recognized as having postoperative infection. Data were recorded on special forms. Hospital Universitario Valdecilla is a 1200-bed teaching hospital serving a population of 2,000,000, in which approximately 20,000 surgical procedures are performed each year. The definitions of nosocomial infection were based on those proposed by the Centers for Disease Control.⁵ The method of surveillance was active searching daily for nosocomial infection and identification of the infection in the laboratory. Cases were defined as those patients in whom at least one episode of nosocomial infection developed in the postoperative period. Nosocomial infection in patients already discharged from the hospital were diagnosed only in case of readmission. The only criterion for matching was that cases and controls underwent exactly the same cardiovascular procedure, that is, coronary artery bypass grafting, valvular surgery, and vascular surgery (mostly bypass grafting for occlusive disease of the lower extremities). Every case was paired with one control subject who did not have an infection. All patients undergoing cardiovascular operations during the study period were eligible to serve as controls. Controls were retrospectively selected among recently discharged patients by means of a table of random numbers. The study protocol was approved by the institutional review board.

Patients were divided into four groups according to the indications for cardiovascular procedures—operations for ischemic heart disease, operations for valvular heart disease, valve operations plus coronary artery bypass grafting, and operations for vascular disorders. Information about each patient included age, sex, date of admission, date of surgical operation, date of hospital discharge, stage at discharge (alive, dead), type of surgical procedure, mode of surgical intervention (elective, urgent), type of anesthesia, need for assisted mechanical ventilation, duration of surgical procedure (skin-to-skin), use of invasive procedures, blood transfusions, site of infection, and causative organisms. The use of invasive procedures (nasogastric tube passage, central intravascular lines, arterial lines, and urinary catheters), blood transfusion, and type of anesthesia were assessed only in patients undergoing operations for vascular disorders. Vascular surgery was performed with the patient under general anesthesia in 57.7% of the patients who had infections and in 34.6% of those who did not. During the study period, all patients received a single intravenous dose of cefazolin (2 gm) at the time of anesthesia as antibiotic prophylaxis.

Statistical analysis

Computations were done by means of the EPIINFO and PRESTA 2.0 programs (EPIINFO, Centers for Disease Control and Prevention, Atlanta, Georgia, PRESTA 2.0, V. Abaira and J. Zapalana, Fondo de Investigacion Sanitaria, Madrid, Spain). Basic methods of bivariate analysis with stratification for case-control studies⁶ included the χ^2 test, the Mantel-Haenszel test for estimation of odds ratio and 95% confidence intervals, and Fisher's exact test for qualitative variables. Quantitative variables were analyzed by means of Bartlett's test for homogeneity of variance; in cases of homogeneity of

variances, an analysis of variances was used. In cases of nonhomogeneity of variances or when it was not possible to affirm that distributions were normal, means were compared by use of the Kruskal-Wallis test. A multiple stepwise logistic regression analysis in which the probability of a nosocomial infection developing was considered the dependent variable was then carried out.

Results

Description of cases. A total of 970 adult patients underwent cardiovascular operations during the study period, and nosocomial infection occurred in 89 (9.2%). There were 52 men and 37 women with a mean ($\pm$ standard deviation) age of 62.1 ± 12.5 years. Operations for ischemic heart disease were performed in 16.8% of cases (15 patients aged 59.9 ± 15.6 years), for valvular heart disease in 48.3% (43 patients aged 61.9 ± 11.7 years), combined operations for coronary artery disease and valvular heart disease in 5.6% (5 patients aged 70.6 ± 3.3 years), and for vascular disorders in 29.2% (26 patients aged 65.5 ± 10.6 years). Mode of surgical intervention was elective in 67 patients and urgent in 22. Invasive procedures included intravascular lines (peripheral in 100% of the cases, central in 78.6%), assisted mechanical ventilation (87.6%), urinary catheter (82%), blood transfusion (79.8%), chest tubes (77.5%), and nasogastric tube passage (71.9%).

A total of 120 episodes of nosocomial infection were diagnosed, an average of 1.3 episodes per patient having an infection. The infection ratio was 12.4% (120/970). Frequency distribution of complications according to indications for cardiovascular surgery and sites of infection are shown in Table I. Surgical site infection was the most common complication (infection ratio of 5.6%, 54/970). Patients undergoing combined coronary artery bypass grafting and valve operation accounted for the highest rate of infections of the surgical site (27.3%), respiratory tract (18.2%), and urinary tract (9.1%). *Staphylococcus aureus* was the most frequent bacterial species isolated in patients with postoperative surgical site infection (31.4%), bacteremia (66.7%), and deep site infection (66.7%), whereas *Pseudomonas aeruginosa* and *Escherichia coli* were the most common in those with pneumonia (30.8%) and urinary tract infection (33.3%), respectively. The mean length of stay in the hospital was 25.2 ± 18.1 days. Seventy-three patients were discharged (82%) and 16 died (18%).

Case-control study. The results of this study are shown in Tables IIA and IIB. The 11 patients with

Table I. Frequency distribution of 120 episodes of nosocomial infections among 970 patients undergoing cardiovascular operations

Data	Total	Ischemic heart disease	Heart valve disease	Ischemic and heart valve disease	Vascular disorders
No. of patients	970	149	353	11	457
No. of patients infected (%)*	89 (9.2)	15 (10.1)	43 (12.2)	5 (45.4)	26 (5.7)
Infection rate (%)	120 (12.4)	21 (14.1)	59 (16.7)	6 (54.5)	34 (7.4)
Site of infection (%)					
Surgical site	54 (5.6)	7 (4.7)	19 (5.4)	3 (27.3)	25 (5.5)
Respiratory tract	31 (3.2)	5 (3.4)	21 (5.9)	2 (18.2)	3 (0.7)
Urinary tract	19 (1.8)	3 (2.0)	10 (2.8)	1 (9.1)	5 (1.1)
Deep site	9 (0.9)	4 (2.7)	5 (1.4)	—	—
Bacteremia	7 (0.7)	2 (1.3)	4 (1.1)	—	1 (0.2)
Duration of operation (min)	230.7 ± 98.1	270.7 ± 49.9	261.5 ± 82.9	312 ± 61.4	141.1 ± 9.6

*Figures in parentheses are percentages.

Table IIA. Case-control study: Quantitative variables

	Cases	Controls	Statistical comparison
Age (yr)	62.1 ± 12.5	58.2 ± 13.4	$p = 0.04$ (ANOVA)
Duration of operation (min)	230.7 ± 98.5	203.1 ± 88.8	$p = 0.04$ (ANOVA)
Hospital stay (days)	25 ± 18.1	14.1 ± 14.4	$p < 0.0001$ (Kruskal-Wallis)

Values are mean ± standard deviation.

Table IIB. Case-control study: Qualitative variables

	Odds ratio	p Value
Age > 65 years	1.96	0.05
Transfusion	11.11	0.012
Chest tubes	7.50	0.049
Urinary catheter	4.71	0.016
Nasogastric tube	8.28	0.001
Urgent operation	2.47	0.045
Death	4.73	0.009

Table III. Risk of death after cardiovascular operations in relation to site of infection

Site of infection	Odds ratio	95% CI	p Value
All sites	4.73	1.39to17.90	0.009
Respiratory tract	14.33	3.05to67.31	0.0004
Urinary tract	5.65	1.26to25.36	0.047
Surgical site	4.22	1.29to13.79	0.017

CI, Confidence interval.

ischemic and valvular heart disease were excluded from the case-control portion of the analysis because of the low number of cases. Patients with nosocomial infection were significantly older, had longer operations, and stayed in the hospital for more days than controls. Postoperative infection risk increased as age increased (χ^2 for linear trend = 4.34, $p = 0.004$) and as duration of the intervention

increased (χ^2 for linear trend = 7.33, $p = 0.007$). On the other hand, as infection risk after the operation increased, corresponding length of hospital stay increased (χ^2 for linear trend = 21.95, $p = 0.00001$). The risk of nosocomial infection in association with the need for blood transfusion, chest tubes, urinary catheters, nasogastric tube passage, and urgent operation was significantly higher in cases than in controls (Table IIB).

The risk of death in the postoperative period was almost fivefold greater in patients who had infections than in those who did not (Table III). Differences in the length of hospital stay between cases and controls were 13.7 extra days for infection of the surgical site ($p < 0.0001$), 13.2 extra days for urinary tract infections necessitating the use of intravenous antibiotics ($p < 0.0001$), and 12.5 extra days for infections of the respiratory tract ($p = 0.0003$).

Multivariate analysis. Results of multivariate analysis are shown in Table IV. For cardiac surgery, age, sex, and mode of surgical intervention were the three variables that entered into the final model of the multiple logistic regression analysis according to the following equation:

$$p(y = 1) = 1/(1 + \exp[-(0.089 + 0.040x_1 - 0.809x_2 - 2.162x_3)])$$

Table IV. Risk factors for postoperative nosocomial infection in cardiovascular operations

Variable	β	95% CI	χ^2	p Value
Cardiac surgery				
Age, years	0.040	0.007 to 0.073	5.312	0.020
Female sex	-0.809	-1.577 to -0.041	4.261	0.037
Elective surgery	-2.162	-3.759 to -0.565	7.039	0.008
Vascular surgery				
General anesthesia*	2.180	0.385 to 3.975	5.671	0.016
Central line	-3.074	-5.253 to -0.895	7.634	0.005
Blood transfusion	3.676	2.918 to 4.434	7.018	0.008

*Or assisted mechanical ventilation.

where $y = 1$ (cases) and $y = 0$ (controls); x_1 (age in years); $x_2 = 1$ (male sex) and $x_2 = 0$ (female sex); $x_3 = 1$ (elective surgery) and $x_3 = 0$ (urgent surgery).

The probability of infection is multiplied by 1.04 for each year of age, by 2.25 for female sex, and by 8.69 for urgent surgery. The overall efficiency of the model was 71% with a sensitivity of 67% and a specificity of 75%.

In the case of operations indicated for vascular disorders, the use of general anesthesia or assisted mechanical ventilation, a central venous catheter, and blood transfusion were the three variables that entered into the final model of multiple logistic regression analysis according to the equation:

$$p(y = 1) = 1 / (1 + \exp[-(0.470 + 2.180x_1 - 3.074x_2 + 3.676x_3)])$$

where $y = 1$ (cases) and $y = 0$ (controls); $x_1 = 1$ (general anesthesia or assisted mechanical ventilation) and $x_1 = 0$ (local/epidural anesthesia); $x_2 = 1$ (exposed to central venous catheter) and $x_2 = 0$ (unexposed); $x_3 = 1$ (exposed to blood transfusion) and $x_3 = 0$ (unexposed).

The probability of infection is multiplied by 8.85 for use of general anesthesia or assisted mechanical ventilation, by 21.63 for exposure to a central venous catheter, and by 39.49 for exposure to blood transfusion. The overall efficiency of the model was 73% with a sensitivity of 78% and a specificity of 88%.

Comment

Epidemiologic features of postoperative nosocomial infections in cardiovascular surgery found in this study are similar to those described by other authors.^{1,7} Rate (9.2%) and ratio (12.4%) of infections were somewhat lower than figures reported in the literature,^{2,4,7-11} particularly in the subset of patients having operations for ischemic heart disease, but the infection rate for vascular surgery was higher (7.4% vs 2.0% to

5.6%).¹¹ The frequency distribution of sites of infection was also similar to that reported in several studies.^{2,4,7,8,12} However, the systematic use of a closed drainage system at our institution may explain the lower rate of urinary tract infections found in this study as compared with others.¹³ On the other hand, the relevance of *S. aureus* as an important pathogen in surgical site infection^{7,10} and *P. aeruginosa* in respiratory tract infection^{14,15} is reiterated here. Thoracic surgical procedures and the use of respiratory care devices are widely noted predisposing factors for nosocomial pneumonia.^{14,16,17} The following variables were significantly associated with nosocomial infection in the bivariate analysis: age, length of postoperative hospital stay, death category at discharge, duration of surgical procedure, urgent operation, urinary catheters, chest tubes, blood transfusion, and nasogastric tube passage. Our study, like others,^{18,19} has shown an increased risk for hospital infections in elder patients. The relative risk of infection for patients older than 65 years was twofold greater than that for those who were younger. It is important to realize that elderly patients who do get an infection have major implications for the economic costs of health care. The length of the operation also had a significant effect on the occurrence of postoperative infection. Carefully but expeditiously performing surgical procedures can protect from many complications including infections. Contamination of the surgical field is likely to be time related,²⁰⁻²² and prolonged operations can also be the most complicated. Urgent operations carried a higher risk of infection. Urgent procedures are usually performed on more critically ill patients, more frequently lead to bleeding, and account for more reoperations. All of these conditions are contributing factors to a higher risk of infection. Excessive blood transfusions have been considered a predisposing factor for surgical site infection. In the study of Ottino and colleagues,⁴ amount of blood transfused emerged as a significant variable in the logistic model. In our subset of patients

undergoing operations for vascular disorders, blood transfusion (categorized as present/absent) was significantly associated with infection in both univariate and multivariate analyses.

Other significant variables, such as excess hospital stay and higher postoperative mortality, are early measurable consequences of the infectious process. The postoperative stay was longer in all types of infection, but particularly in surgical site infection, which is in agreement with results of several studies.^{3,11} Our figure of 12.5 extra days in cases of nosocomial pneumonia is comparable with those reported by others.^{19,23} However, our finding of 13.2 extra days for urinary tract infections is higher than additional lengths of stay of a few days usually associated with urinary tract infections. In a review of excess hospital stay attributable to nosocomial infection in case-control studies, Wenzel¹⁹ showed an increase by 2 to 10 days for urinary tract infections. Monge and associates²³ found 11 extra days for patients with hospital-acquired urinary infections as compared with those not having infections. In addition to a result of nosocomial infection, length of hospital stay might also be a risk factor for urinary tract infection. Our data add evidence to the effect of nosocomial infection on mortality. We identified an almost fivefold increase in hospital mortality among patients with nosocomial infection and a fourteenfold increase among those with respiratory tract infection. These findings are of special concern.

The stepwise multiple logistic regression model demonstrated that age and female sex were significant independent factors for postoperative infection in patients undergoing cardiac operations, whereas general anesthesia or assisted mechanical ventilation and blood transfusion were those found in patients undergoing vascular operations. Other significant factors, such as elective operation for cardiac surgery and central venous catheter for vascular surgery, would exert a favorable influence decreasing the risk of infection. Efficiency of the models was 71% and 73%, respectively.

In summary, recognition of risk factors for postoperative infection in patients undergoing cardiovascular surgical procedures may help to improve their prognosis and may allow more organized surveillance and control of activities in the hospital environment.

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