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Morbidity and Mortality of Nosocomial Infection after Cardiovascular Surgery: A Report of 1606 Cases

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Summary: Nosocomial infection (NI) is one of the most significant complications arising after open heart surgery, and leads to increased mortality, hospitalization time and health resource allocation. This study investigated the morbidity, mortality, and independent risk factors associated with NI following open heart surgery. We retrospectively surveyed the records of 1606 consecutive cardiovascular surgical patients to identify those that developed NI. The NI selection criteria were based on the Centers for Disease Control and Prevention (CDC) guidelines. The term NI encompasses surgical site infection (SSI), central venous catheter-related infection (CVCRI), urinary tract infection (UTI), respiratory tract infection and pneumonia (RTIP), as well as other types of infections. Of 1606 cardiovascular surgery patients, 125 developed NI (7.8%, 125/1606). The rates of NI following surgery for congenital malformation, valve replacement, and coronary artery bypass graft were 2.6% (15/587), 5.5% (26/473) and 13.6% (32/236), respectively. The NI rate following surgical repair of aortic aneurysm or dissection was 16.8% (52/310). Increased risk of NI was detected for patients with a prior preoperative stay ≥3 days (OR=2.11, 95% CI=1.39–3.20), diabetes (OR=2.00, 95%=CI 1.26–3.20), length of surgery ≥6 h (OR=2.26, 95% CI=1.47–3.47), or postoperative cerebrovascular accident (OR=4.08, 95% CI=1.79–9.29). Greater attention should be paid toward compliance with ventilator and catheter regulations in order to decrease NI morbidity and mortality following cardiovascular procedures.

Key words: nosocomial infection; cardiovascular surgery; morbidity; mortality

Thoracotomy is the primary means of surgically operating on a range of cardiovascular conditions, but complications can arise as a result of this procedure. Nosocomial infection (NI) is one of the more common postoperative complications, and is sometimes fatal[1]. Therefore, it is important to identify risk factors that are associated with NI in order to prevent and reduce complications.

Rapid recovery and return to daily activity are becoming increasingly important in postoperative prognosis. Despite advances in anesthesia, surgical techniques and biological materials, NI is still one of the most troublesome complications following open heart surgery, resulting in increased mortality, hospitalization time, and health resource allocation[2, 3].

The term NI includes surgical site infection (SSI), central venous catheter-related infection (CVCRI), urinary tract infection (UTI), respiratory tract infection and pneumonia (RTIP), and other infections.

Renmin Hospital of Wuhan University is a tertiary care teaching hospital in Wuhan, China. The Department of Cardiovascular Surgery with 50-bed ward that includes a 9-bed intensive care unit (ICU), employs 6 surgeons and performs nearly 800 open heart surgical procedures each year. The aim of the present study was to investigate the incidence of NI after cardiovascular surgery and outcomes following

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NI.

1 PATIENTS AND METHODS

1.1 Patient Population

We surveyed the records of 1606 patients who had undergone open heart surgery in Renmin Hospital of Wuhan University between 2010 and 2015. Of these cases, 587 surgeries were for congenital malformations, 473 for valve replacement, 236 for coronary artery bypass graft (CABG), and 310 for repair of aortic aneurysm (AA) or aortic dissection (AD). In the retrospective analysis, 27 cases were excluded due to valve vegetation or infective endocarditis, as well as 9 cases of heart transplantation. We excluded patients who had mixed cardiovascular procedures; for example, valve replacement combined with CABG, or aortic artery disease repair combined with another cardiac procedure. Cases involving tumors, HIV, tuberculosis, liver or renal failure, severe lung infection and serious neurological conditions were also excluded[4]. This study was approved by the Institutional Review Board and the Medical Ethics Committee of Renmin Hospital of Wuhan University. All patients enrolled in the study provided informed consent.

The NI selection criteria were based on Centers for Disease Control and Prevention (CDC) guidelines[5]. A CVCRI was identified in patients who had had an intravascular device fitted and had a single positive blood culture afterwards. These patients had resolution of clinical signs and symptoms after removal of the device or appropriate therapy. A UTI was identified in patients who returned a positive urine culture and had appropriate clinical symptoms that were able to be treated according to the causative agent. An SSI was identified in patients who had an infection involving the skin and superficial or deep soft tissues together with a positive wound culture. An RTIP was identified in patients with a chest radiograph or computed tomography scan that showed new infiltrates, consolidation or cavitations. These patients also had a fever exceeding 38°C, together with positive sputum and tracheal fluid cultures and had no pneumonia or a respiratory tract infection in the 15 days before cardiac surgery. To reduce the likelihood of culturing oral contaminants we collected the samples by a bronchoscope, and several sputum samples were collected from each patient. Microbiology samples were processed and diagnosed using VITEK bioMerieux products.

Cefazolin or cefuroxime was given as preoperative antibiotic prophylaxis; 1 g of cefazolin was administered 30 min before surgery followed by 1 g per 6 h after surgery, or 1.5 g of cefuroxime was administered 30 min before surgery followed by 1.5 g per 12 h after surgery. Antibiotics were given for a maximum of 48 h, until all chest and mediastinal drain tubes were removed[6].

The NI rate was calculated as follows: number of patients with NI following cardiovascular surgery/ total number of patients who underwent cardiovascular surgery. The crude mortality rate was calculated as the ratio of the number of cardiovascular surgery NI patients who died during hospitalization to the total number of cardiovascular surgery NI patients.

1.2 Statistical Analysis

Statistical analysis was performed using SPSS 19.0 for Windows. A Kolmogorov–Smirnov test of normality was used to verify whether the variables followed a Gaussian distribution. Data were presented as $\bar{x}\pm s$ or as percentages. The means of different groups were compared using Student's *t*-test. Correlations between variables were analyzed using Pearson's coefficient. Logistic regression analysis was used to determine the association between the severity of the thoracic aortic dissection (TAD) and all other variables considered in the present study.

2 RESULTS

Among the 125 cardiovascular surgery patients who developed NI, the durations of the operation (8.3±3.5 h), cardiopulmonary bypass (196.3±36.1 min), central venous catheterization (76.6±7.8 h), and mechanical ventilation (80.4±22.3 h) were longer than those of the 1481 patients who did not develop NI. The NI patients required more blood transfusions (9.7±3.6 units) to compensate for bleeding, and their average length of hospital stay was significantly longer than that of the 1481 cardiovascular surgery patients without NI. The NI patients required almost two-week longer hospitalization than the other patients. Moreover, patients with hypertension or congestive heart failure co-morbidities were more susceptible to NI. This effect was irrespective of the EuroSCORE, alcohol consumption, smoking, hyperlipidemia and body mass index (table 1).

Among the 1606 cardiovascular surgery patients in our study, 125 developed NI (7.8%, 125/1606). The NI rates following surgeries for congenital malformation, valve replacement, and CABG were 2.6% (15/587), 5.5% (26/473) and 13.6% (32/236), respectively. The NI rate following surgical repair of AA or AD was 16.8% (52/310). The rates of the different main types of NI were 0.7% for SSI (11/1606), 0.8% for CVCRI (13/1606), 1.1% for UTI (17/1606) and 5.2% for RTIP (84/1606, table 2).

Of the 125 cardiovascular surgery patients who developed NI, 21 died. The cardiovascular surgery crude mortality rate for patients with NI was significantly higher than that of patients without NI (16.8%, 21/125 *vs*. 2.7%, 40/1481, $P<0.01$). The

Table 1 Preoperative, operative demographic data and outcome of patients with NI and without NI in cardiovascular surgery

Variables	Non-infection (n=1481)	Infection (n=125)	P value
Cardiovascular surgery, n	1481	125	<0.001*
Congenital malformation, n	572 (38.6%)	15 (12.0%)	<0.001*
Valve replacement, n	447 (30.2%)	26 (20.8%)	0.03
CABG, n	204 (13.8%)	32 (25.6%)	<0.001*
AA or AD, n	258 (17.4%)	52 (41.6%)	<0.001*
Age (years)	54.8±10.3	57.6±8.9	0.080
Body mass index (kg/m²)	26.5±4.7	27.9±5.1	0.063
EuroSCORE	13.3±0.9	13.7±1.4	0.247
Congestive heart failure, n	515	70	0.033*
Hypertension, n	678	87	0.035*
Smoking, n	681	60	0.067
Alcohol, n	662	54	0.161
Hyperlipidemia, n	286	26	0.361
Mechanical ventilation time (h)	45.6±0.8	80.4±22.3	0.003*
Duration of central venous catheter (h)	24.6±.8	76.6±7.8	0.002*
Transfusion, n	2.6±1.2	9.7±3.6	<0.001*
Operation time (h)	5.6±1.7	8.3±3.5	0.016*
Cardiopulmonary bypass time (min)	110.0±62.1	196.3±36.1	0.003*
Died cases, n	40	21	<0.001*
Length of stay (days)	19.1±9.7	33.5±11.5	<0.001*

CABG: coronary artery bypass graft; AA: aortic aneurysms; AD: aortic dissection; NI: nosocomial infection. Data are expressed as either $\bar{x}$±s or n (%). *P<0.05

Table 2 Analysis of 125 cases of NI and 21 deaths due to NI among 1606 patients following cardiovascular surgery

Type of procedures	No. of procedures	No. of infection cases	Death due to NI	SSI	CVCRI	UTI	RTIP
Congenital malformation	587	15	2	2	1	1	11
Valve replacement	473	26	3	2	4	3	17
CABG	236	32	7	2	3	5	22
AA or AD	310	52	9	5	5	8	34
Total	1606	125	21	11	13	17	84

CABG: coronary artery bypass graft; AA: aortic aneurysms; AD: aortic dissection; NI: nosocomial infection; SSI: surgical site infection; CVCRI: central venous catheter-related infection; UTI: urinary tract infection; RTIP: respiratory tract infection and pneumonia

crude mortality rates for patients who developed NI following surgery for congenital malformation, valve replacement, and CABG were 13.3% (2/15), 11.5% (3/26) and 21.9% (7/32), respectively. The crude mortality rate for patients who developed NI following surgical repair of AA or AD was 17.3% (9/52).

A total of 125 different species of microorganisms were cultured from the 125 NI patients. Of these, 42.4% (n=53) were gram negative bacteria, 29.6% (n=37) were gram positive cocci and 28.0% (n=35) were fungi. The most abundant species were *Pseudomona-saeruginosa* (8.0%, n=10), *Acinetobacter baumannii* (8.8%, n=11), *Staphylococcus aureus* (8.0%, n=10), *Staphylococcus epidermidis* (7.2%, n=9), *Candida albicans* (13.6%, n=17) and *Candida tropicalis* (6.4%, n=8; table 3).

We next examined the main risk factors for developing NI. Preoperative factors that increased the risk of NI included a preoperative stay ≥3 days (OR=2.11, 95% CI=1.39–3.20, with an increased risk for each additional day in hospital) and diabetes (OR=2.00, 95% CI=1.26–3.20). In relation to intraoperative events, a length of surgery ≥6 h (OR=2.26, 95% CI=1.47–3.47) was a risk factor for NI. The analysis of postoperative therapy variables identified cerebrovascular accident (OR=4.08, 95% CI=1.79–9.29) as an independent risk factor for the development of NI. Other factors that increased NI risk were ventilation time, placement of a central venous catheter, urinary catheter or chest tube, and blood transfusion. Among preoperative variables (table 4), age, sex, alcohol consumption and hyperlipidemia were not identified as risk factors for the development of NI. Following congenital heart disease surgery there was a low probability of developing NI, although these results were not statistically significant (table 5).

Table 3 Relative proportion of microorganisms causing 125 patients with NI following cardiovascular surgery

Species	Cases	% of all microorganisms
Gram negative bacteria	53	42.4
Pseudomonas aeruginosa	10	8.0
Acinetobacter baumannii	11	8.8
Escherichia coli	7	5.6
Klebsiella pneumoniae	6	4.8
Burkholderia cepacia	4	3.2
Stenotrophomonas maltophilia	4	3.2
Citrobacter freundii	3	2.4
Haemophilus influenzae	4	3.2
Enterobacter aetogenes	1	0.8
Enterobacer cloacae	2	1.6
Pro Staphylococcus aureus teus Vulgaris	1	0.8
Gram positive cocci	37	29.6
Staphylococcus aureus	10	8.0
Staphylococcus epidermidis	9	7.2
Staphylococcus saprophyticus	2	1.6
Staphylococcus citreus	2	1.6
Streptococcus pneumonia	5	4.0
Streptococcus viridans	2	1.6
Enterococcus faecium	4	3.2
Enterococcus faecalis	2	1.6
Enterococcus mundtii	1	0.8
Fungi	35	28.0
Candida albicans	17	13.6
Candida tropicalis	8	6.4
Candida parapsilosis	6	4.8
Candida krusei	2	1.6
Candida glabrata	1	0.8
Aspergillns spp	1	0.8

Table 5 The risk factors analyzed for congenital malformation

Variables	No. of infections/ no. of procedures	OR (95% CI)
Surgical site infection	2/9	1
Renal failure	1/7	0.58 (0–5.99)
Previous infection	6/21	1.4 (0.25–7.53)
Second operation	2/12	0.70 (0.10-5.05)
Ventilator	3/15	0.88 (0.13-5.50)
Central venous catheter	1/11	0.35 (0–3.36)
Ventilator time ≥24 h	8/75	8.61 (3.14–23.63)
Central venous catheter ≥24 h	6/102	3.31 (1.20–9.14)
Catheter ≥2 days	4/101	1.78 (0.59-5.42)
Chest tube ≥3 days	5/167	1.27 (0.45-3.60)

Table 4 The adult (excluding congenital malformation) risk factors analyzed

Variables	No. of infections/No. of procedures	OR (95% CI)
Age >65 years	78/872	0.35 (0.22–0.56)
Sex gender (made)	77/662	1.29 (0.84–1.98)
Smoking status		
Never-smoker	48/367	1
Ex-smoker	21/197	0.79 (0.46–1.36)
Smoker	38/455	0.61 (0.39–0.95)
Alcohol status		
Never-drink	52/418	1
Ex-drink	31/323	0.75 (0.47–1.19)
Drinker	27 /278	0.76 (0.46–1.23)
Hyperlipidemia	26/286	0.77 (0.49–1.22)
Diabetes	28/160	2.00 (1.26–3.20)
Preoperative length of stay (days)		
1–2 days	70/785	1
≥3 days	40/234	2.11 (1.39–3.20)
Priority of surgery		
Acute	62/385	1
Elective	48/634	0.43 (0.29-0.64)
Type of operation		
Valve replacement	26/473	1
CABG	32/236	2.70 (1.57–4.62)
Aortic aneurysm and dissection	52/310	3.47 (2.12–5.66)
Length of surgery		
0–6 h	32/469	1
≥6 h	78/550	2.26 (1.47–3.47)
Surgical site infection	9/121	1
Renal failure	16/163	1.35 (0.59–3.11)
Previous infection	5/39	1.83 (0.60–5.60)
Second operation	13/158	1.12 (0.47–2.64)
Cerebrovascular accident	21/85	4.08 (1.79–9.29)
Central venous catheter	13/112	1.63 (0.68–3.90)
Ventilation	33/213	2.28 (1.07–4.87)
Ventilation time		
0–12 h	9/516	1
12–24 h	28/321	5.38 (2.55–11.37)
≥24 h	73/182	37.73 (18.54–76.66)
Central venous catheter		
0–24 h	34/407	1
≥24 h	76/612	1.56 (1.02–2.37)
Chest catheter		
<2 days	59/785	1
≥2 days	51/234	3.43 (2.28–5.15)
Urinary catheter		
<3 days	53/641	1
≥3 days	47/378	1.30 (0.87–1.94)
Blood transfusion >800 mL	41/132	5.34 (3.44–8.30)

3 DISCUSSION

The NI rate among cardiovascular surgery patients in this study was 7.8% (125/1606), which was lower than that of previous studies[7, 8], but higher than that reported by Riera *et al*[9]. These differences may be partly attributed to the exclusion of patients with device-associated infections, such as infective endocarditis, in this study. Historically, severe damage to the heart has been considered to be a death sentence. However, as medical technology has advanced, cardiac surgeries for pacemakers and ventricular devices have become commonplace. Therapeutic modalities help the damaged heart to continue functioning and thereby prolong life. Nevertheless, the invasive nature of these procedures predisposes patients to a broad range of infections[10], particularly problematic cardiovascular infections like endocarditis. One study found that the NI rate following pediatric cardiovascular surgery was 38.3%, while the prevalence of pediatric ICU infection was 25.6%[11]. Therefore, another possible explanation for the differences in the NI rates between studies may be differences in the complexities of the cardiac procedures that are performed in different centers. We also excluded mixed surgical procedures from our study and we did not take into account repeated occurrence of NI within the same patient.

The NI rates following surgery for congenital malformation, valve replacement, and CABG were 2.6% (15/587), 5.5% (26/473) and 13.6% (32/236), respectively. The NI rate following surgical repair of AA or AD was 16.8% (52/310). The NI rate for AA or AD surgeries was highest, presumably because these are usually emergency procedures carried out on seriously ill patients. Such patients frequently have unstable hemodynamics, increased operative bleeding and require reoperation. Consequently, these surgeries often necessitate prolonged placement of central venous catheters, which are an important portal of entry for microorganisms[12].

The average duration of central venous catheter placement in the 125 patients with NI was 76.6 h, which was three times longer than that of patients without NI. Preoperative blood transfusions[9] has been identified as a risk factor for sternal infection. Transfusion may be more common in patients who undergo reoperation for bleeding, and excessive blood transfusions are considered as a predisposing factor for surgical site infection. Furthermore, the association between blood transfusion and infection is dose-dependent. The average transfusion quantity among the 125 patients with NI was 9.7 units, and only 2.6 units for patients without NI.

In contrast, elective surgery for congenital malformation, valve replacement, or CABG is associated with earlier tracheal extubation, shorter ICU stays, shorter hospitalization and fewer complications of postoperative infections. The average mechanical ventilation time among the 1481 patients who did not develop NI was 45.6 h, whereas 80.4 h for the NI patients. Surgery for CABG has previously been identified as a risk factor in SSI, in particular, bilateral internal mammary artery grafting[11, 13].

History of neurological disorders was remarkably frequent among patients with NI, as was history of arterial hypertension[14]. Heart failure and prolonged use of central venous catheters were also associated with the development of NI[15].

The operation time also had a significant effect on the occurrence of NI. Careful and expeditious performance of surgical procedures is likely to provide protection from many complications, including infections. The average operation time of the 125 patients with NI was 8.3 h, while 5.6 h for patients without NI. Contamination of the surgical field is likely to be time related, and prolonged operation time is associated with more complicated procedures. Prolonged postoperative hospitalization and increased postoperative mortality are early measurable consequences of the infection process. The postoperative hospitalization period is longer for all types of infection, particularly SSI[8].

In the present study, the rates of SSI, CVCRI, UTI and RTIP were 0.7%, 0.8%, 1.1% and 5.2%, respectively. Twenty-one patients with NI died, and the crude mortality rate was 16.8% (21/125). The crude mortality rates following surgery for congenital malformation, valve replacement, CABG, and AA and AD were 13.3% (2/15), 11.5% (3/26), 21.9% (7/32) and 17.3% (9/52), respectively. The rates were significantly higher than 2.7% (40/1481) in non-infection group. The crude mortality rate for CABG patients that developed NI was the highest. This may be partly attributed to an extreme age (very old or in infancy), a cerebrovascular accident, respiratory failure or myocardial infarction, or multiple organs dysfunction syndrome in these patients.

Nosocomial pneumonia (NP) is a significant contributor to patient morbidity, the most common infection in ICU, and associated with the greatest mortality among NIs. In 1992, the CDC estimated that each case of NP added an average of 5.9 days to hospitalization time and increased costs[2]. In our study, NI prolonged hospitalization by nearly two weeks, with the extra medical costs increasing by 60%.

A total of 125 microorganisms were isolated from the 125 patients that developed NI. The main causative organisms were gram negative bacteria (42.4%, 53/125), gram positive cocci (29.6%, 37/125) and fungi (28.0%, 35/125). The most common species were *P. aeruginosa* (8%, 10), *A. baumannii* (8.8%, 11), *S. aureus* (8%, 10), *S. epidermidis* (7.2%, 9), *C. albicans* (13.6%,

17) and *C. tropicalis* (6.4%, 8). These results were different from those obtained by the Duke Registry[2]. Started in 1994, the Duke Registry contains data from approximately 1000 consecutive patients that have been observed to date, and indicates a changing nature of *S. aureus* infections. *S. aureus* infection is primarily acquired among patients with intensive contact with the health care system. Moreover, the proportion of infective endocarditics cases caused by *S. aureus* has increased significantly. *S. aureus*[2] is associated with a high prevalence of staff carriage and NI may arise as a result of incomplete compliance with recommended standard preoperative infection control measures[16]. In our study, we excluded 27 patients with infective endocarditis that had valve vegetations. Supporting our results, Poncelet *et al*[2] found that *P. aeruginosa* in respiratory tract infections following thoracic surgical procedures and following the use of respiratory care devices is the predisposing factor for NP. Pneumonia was associated with increased mortality, duration of mechanical ventilation, length of stay in ICU and hospitalization time. Moreover, it is well-established that mechanical ventilation prolongs the length of ICU stay and may increase the risk of death[9].

Up to one-third of NI cases are caused by fungi, particularly candida species. Consequently, prophylactic fluconazole has been recommended. Multiple studies have shown that there is no ongoing benefit in continuing prophylactic antibiotics for longer than 48 h. Therefore, prolonged antibiotic prophylaxis is unlikely to have any benefit in reducing the likelihood of wound infections, and might in fact increase the risk of acquired antibiotic resistance and fungal infections[12]. Indeed, CABG with extracorporeal circulation procedures is associated with an increased use of antibiotics, but also results in a higher risk of candida colonization. Given that there is such a high crude mortality rate among the cardiovascular surgery patients that developed NI in our study, it is important that attention is paid to compliance with NI regulations. Moreover, there are a number of risk factors that could be targeted to reduce NI morbidity and mortality of cardiovascular procedures. Examples include reducing central venous catheterization, shortening operative and mechanical ventilation time, reducing bleeding, improving operation skills, eliminating cardiopulmonary bypass[17, 18], and achieving early tracheal extubation.

In our study, age, gender and EuroSCORE were not risk factors for postoperative infection, but the result showed: longer mechanical ventilation time, operation time and cardiopulmonary bypass time, and more transfusion requirements would increase the risk of infection. We also found a correlation between infectious complications and the site infection,which is the same as that reported by Guo[19].

Multivariate analysis identified length of preoperative hospitalization as a predictor of NI. A large number of studies have shown that increased infection rates are associated with long periods of hospitalization prior to surgery[20, 21], as well as urinary catheter use[22]. The results from these studies are consistent with those reported in our study. The increased infection rates are probably attributable to ongoing invasive therapeutic procedures while the patient waits until they are suitable for surgery.

Conflict of Interest Statement

All the authors do not have any possible conficts of interest.

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