

# Clinical investigation of nosocomial infections in adult patients after cardiac surgery

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## Abstract

Background: Nosocomial infections (NI) are common complications after cardiac surgery. Till now, there are rare manuscripts investigating NI in intensive care unit (ICU) after cardiac surgery. Our article was designed to investigate the characteristics of distribution of pathogenic bacteria and antibiotics resistance of NI. Methods: 1360 patients received standard postoperative care including antibiotic prophylaxis. Microbiological examinations of the sputum, blood, catheter tips and excretion were performed as clinically indicated to isolate pathogens. Results: 89 patients (6.54%) acquired microbiological documented NI. There was a statistical difference in mortality between two groups with or without postoperative NI (23.60% vs 2.28%,  $p < 0.00$ ). 98 (73.13%) were isolated from sputum and 32 (23.88%) from blood. 3 (2.24%) SSI were detected (2 superficial SSI, 1 mediastinitis) and only 1 (0.75%) from urine. The most common pathogens were Gram-negative bacteria (78.36%), followed by Gram-positive bacteria (14.93%) and fungi (6.71%). The major species of pathogens had different levels of drug resistance and most of them exhibited multidrug-resistance (MDR). Conclusions: We analyzed the characteristics of distribution of pathogens and antibiotics resistance of NI in our center and provided some suggestions for clinical practice. Except for antibiotic treatment, aggressive infection control measures may be crucial to stop or prevent outbreaks.

## Introduction

Nosocomial infections (NI) include all infections acquired between 48 hours after hospital admission and 2 days of hospital discharge. As everyone knows, cardiac surgical intensive care unit (ICU) is a special ward with higher incidence of NI and usage rate of antibiotics owing to severity of illness, complexity of surgery and common use of invasive devices (endotracheal tubes, central venous catheters, peripheral arterial catheters and urinary catheters) [1]. NI are associated with increased morbidity and mortality, as well as length of ICU stay and healthcare costs [2,3]. Furthermore, the burden of antimicrobial resistance in ICU is growing high, which has been attributed to the increased difficulty of clinical treatment and hospital control of NI. So treatment should be converted into organism-specific treatment from experiential use of antibiotics as soon as possible. The aims of our study were to investigate the characteristics of distribution of pathogenic bacteria and antibiotics resistance of NI.

## Materials and Methods

### Study population and design

From January 2018 to December 2018, 1381 patients ([?]18) undergoing cardiac surgery were transferred to our cardiac surgical ICU. All of them were eligible for the investigation except for those who died within 24 hours postoperatively ( $n=21$ ). All patients received standard postoperative care complied with published guidelines [4,5]. Antibiotic prophylaxis was a single second generation cephalosporin. Body temperature was recorded every 6 hours routinely and anytime when necessary. Haematologic tests and chest radiographs were performed regularly. Microbiological examinations of the sputum, blood, catheter tips and excretion

of these patients were performed as clinically indicated to isolate pathogens according to the criteria of Clinical and Laboratory Standards Institute (CLSI). One pathogen cultured positively more times in the same patient within one week was regarded as one.

## Definition

All definitions were defined according to criteria established by the Centers for Disease Control and Prevention. The most common types of NI are hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), blood stream infection (BSI), catheter-related blood stream infection (CRBSI), catheter-associated urinary tract infection (CAUTI) and surgical site infection (SSI) [6-8]. VAP is a subset of HAP which occurs over 48 hours after endotracheal intubation. In our study, both HAP and VAP were included into the type of pneumonia. CRBSI is a subset of BSI with the presence of central venous catheters and signs of catheter insertion site infection. SSI can be divided into three types: superficial SSI, deep SSI and mediastinitis.

Antibiotics resistance means acquired resistance except for natural resistance. Multidrug-resistant (MDR) bacteria means the one that were antimicrobial resistant to three or more classes of antibiotics. And bacteria only sensitive to colistin and/or tigecycline was defined as extensively drug resistant (XDR) bacteria [9].

## Data analysis

Continuous variables are shown as means plus SD; categorical data are presented as proportions. A P value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS 21.

## Results

### Source of nosocomial infection and associated mortality

For 1360 patients admitted into our study, 89 patients (6.54%) acquired microbiological documented NI. Among the 89 patients, 21 patients died with the mortality rate of 23.60%. For the other 1271 patients without NI, the mortality rate was only 2.28% (29/1271,  $p < 0.00$ ). 56 patients (62.92%) developed a single infection while 33 patients (37.08%) experienced two or more different nosocomial infections. A total of 134 strains of pathogenic bacteria were detected. 98 (73.13%) of them were isolated from sputum and 32 (23.88%) were from blood. 3 (2.24%) SSI were detected in our study (2 superficial SSI, 1 mediastinitis). Only 1 (0.75%) were isolated from urine. The details of source of NI and associated mortality were demonstrated in Figure 1. The distribution of pathogens for each type of NI were different. Microorganisms causing pneumonia were Gram-negative bacilli while the main pathogens of BSI were Gram-positive cocci (Figure 2).

### Constituent ratio of pathogenic bacteria

A total of 134 strains of pathogenic bacteria were isolated in our study. The most common pathogens were Gram-negative bacteria (78.36%), followed by Gram-positive bacteria (14.93%). Table 1 presents the constituent ratio of predominant infectious pathogens.

### Antibiotics Resistance of main pathogens for NI in clinical practice

Along with the development and inappropriate use of antibiotics, especially wide-spectrum ones, drug resistance of bacteria remain changing. Timely and continuous determination of antibiotic susceptibility is required. The details of antibiotics resistance for common pathogens were as follows (Table 2-3):

There were total 9 strains of fungi isolated in our study. 8 of them were candidas, including 7 candida albicans and 1 candida tropicalis. All of the 7 candida albicans were susceptible to azoles, 5-fluorocytosine and amphotericin B. Aspergillosis was naturally resistant to fluconazole but sensitive to voriconazole and echinocandins.

## Discussion

In our retrospective study, HAP was the main cause of postoperative NI accounting for 73.13%. it was also a leading cause of mortality as high as 17.34%. The generation of HAP was associated with the operation of endotracheal intubation and mechanical ventilation. Intubation destroyed the normal barrier of epiglottis and weakened the cough reflex and movement of cilia, which led to the impairment of organism clearance of airway secretion. Sputum was a good culture medium for bacteria. Mechanical ventilation also contributed to the development of VAP and the risk peaked within the first week. The initial step of VAP was the colonization of potentially pathogenic bacteria in the upper respiratory tract. Aspiration of these microorganisms either through the endotracheal tube or a leak around the cuff allowed them to enter the lower respiratory tract. Accompanied with diminished host immunity, NI developed.

The predominant bacteria for HAP was *Acinetobacter baumannii*. *A. baumannii* is a conditional pathogen that may cause NI in critically ill patients. *A. baumannii* has simple growth requirements and may survive in desiccated environment for prolonged periods [10]. Contaminated environmental sources and transmission via medical personnel may cause outbreaks of NI [11,12]. *A. baumannii* has been associated with high mortality and morbidity [13,14]. Vincent JL and colleagues reported that infection with *A. baumannii* was independent associated with a greater risk for hospital death among 14414 ICU patients [15]. In recent years, the incidence of *A. baumannii* infection increased rapidly as well as its antibiotic resistance. Treatment of *A. baumannii* is difficult owing to its resistance to various antibiotics and remarkable ability to acquire new resistance via different mechanisms, such as plasmids, transposons, integrons and resistance islands. Antimicrobial resistance has posed a serious threat to the whole world. In early 1990, carbapenem-resistant (CPR) strains of *A. baumannii* emerged. CPR-*A. baumannii*s were often resistant to all classes of antibiotics except for colistin and tigecycline [16]. Furthermore, a large dose of sulbactam, fluoroquinolones, aminoglycosides and tetracyclines may also have bacterial activity against CPR-*A. baumannii*s [17-20]. In our study, we discovered that the carbapenem-resistance rate of *A. baumannii* had reached up to >50%. 90% of *A. baumannii* were sensitive to colistin and tigecycline. While the resistance rate of ceftazidime-sulbactam, levofloxacin and minocycline were 34.00%, 42.00% and 38.10% respectively. Instead of amikacin, we routinely analyzed the drug sensitivity of gentamicin as a representative of aminoglycosides but fortunately the resistance rate exceeded 80%.

The principles of treatment for *A. baumannii* were: antimicrobial susceptibility result ; combination therapy; enough dose; enough period; personal administration. Optimal therapy was established according to antimicrobial susceptibility result. But for MDR or XDR *A. baumannii*, the recommended therapy was colistin/tigecycline combined with other agents (i.e., carbapenem, sulbactams, fluoroquinolones or minocycline).

Except for *A. baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and other G- bacilli were also common pathogens for HAP. As proved in our study, all of them were clinically sensitive against carbapenem, extended-spectrum cephalosporins and fluoroquinolones.

BSI is also a serious and common type of NI. It more likely happened in patients with immunosuppression, malnutrition and various invasive devices. CRBSI is a subset of BSI with the presence of central venous catheters. Immediately after insertion, the catheter becomes coated with plasma protein. Bacteria could migrate from the skin along the surface of catheter. This may happen few hours or more than one week after insertion. Femoral venous catheter has the highest rate of infection, followed by internal jugular and subclavian ones [21]. For CRBSI, once infection is suspected, the central catheter should be removed as soon as possible. In our research, the most common pathogens for BSI were still G+ cocci (50%), for example *Staphylococcus* and *Enterococcus*. Within the past decades, resistance rate among G+ cocci escalated obviously. We reported that 78.13% of G+ bacteria were resistant to methicillin and only 6.25% were resistant to vancomycin. However, all of them were sensitive to linezolid.

Fungal infection is not unusual after cardiac operation. Risk factors for fungal infection include immunosuppression, malnutrition, diabetes mellitus and long period use of extended spectrum antibiotics[22,23]. In our research, *Candida* was the most common agent of fungal infection (88.89%; 8/9), which was concordant with previous studies [24-26]. Among 8 strains of *Candida*, 6 were *Candida albicans* and 2 were *Candida tropicalis*, with 7 strains isolated from bloodstream. Other than *Candida*, *Aspergillus* was also a common

agent of fungal infection . Lung was the most frequent site of aspergillosis infection[27]. Consistent with our result, most candidas were susceptible to fluconazole and voriconazole but not to candida glabrata. Aspergillosis was naturally resistant to fluconazole. Echinocandins was the best choice for definite and severe fungal infection, because it remained close to 100% effective.

Since the distribution of pathogenic bacteria and antibiotics resistance of NI after cardiac surgery vary distinctly worldwide, our research data only provide the epidemiological profiles and trends of our institution and play a certain guiding significance for the prevention and treatment of NI.

## Conclusion

NI is a common postoperative complication for cardiac surgery associated with increased morbidity and mortality. Nowadays, antimicrobial resistance, which differ in specific regions and/or population, has become a great challenge towards doctors for NI treatment. Therefore, we analyzed the characteristics of distribution of pathogens and antibiotics resistance of NI in patients after cardiac surgery and provided some suggestions for clinical practice. Except for antibiotic treatment, aggressive infection control measures, including identifying source of infection, environmental cleaning, contact precautions, isolation of infected patients and hand hygiene, may be crucial to stop or prevent outbreaks.

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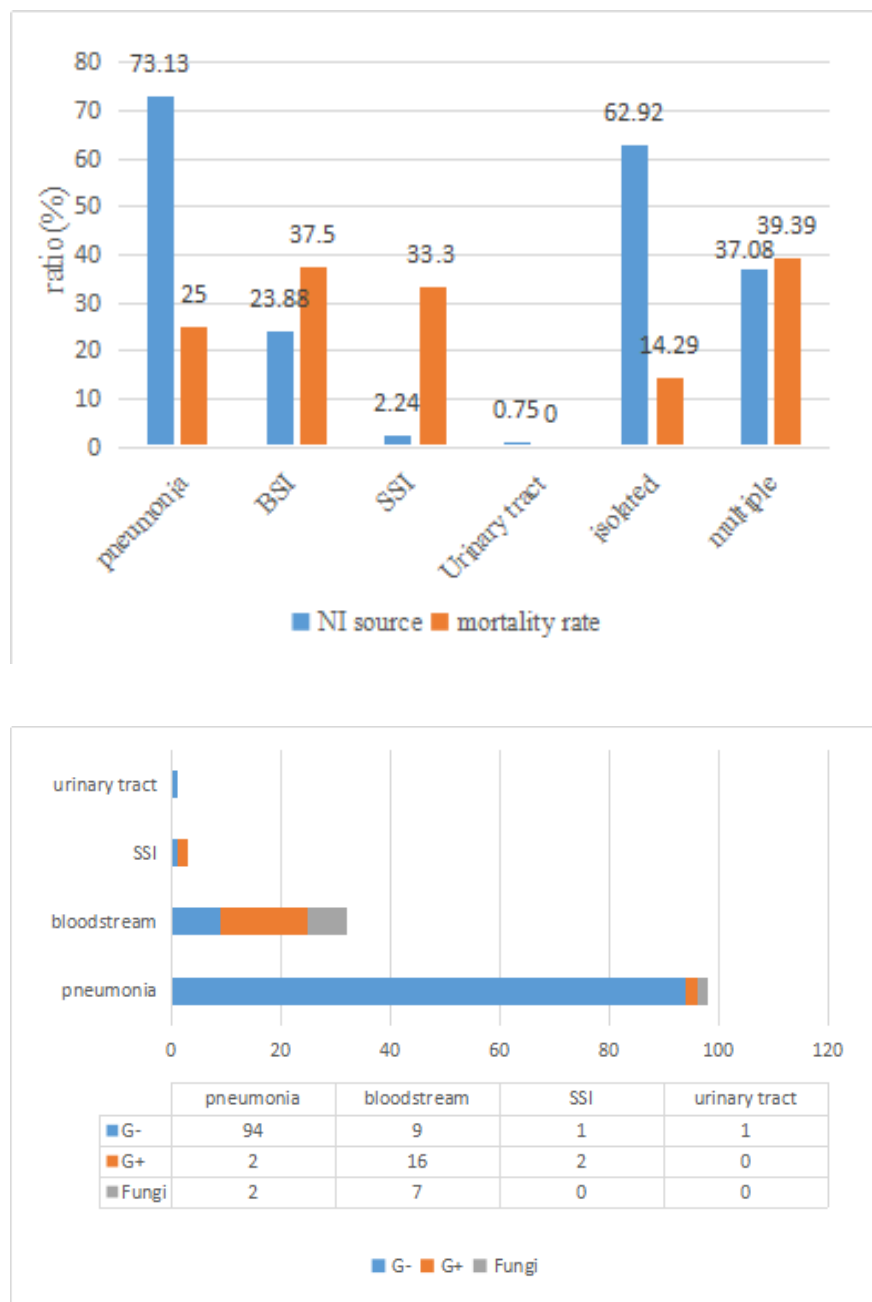
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## Figure Legends

Figure number: two

Figure 1. source of NI and associated mortality

Figure 2. distribution of pathogens in clinical specimens



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