ORIGINAL ARTICLE

Gram-negative rod bacteremia after cardiovascular surgery: Clinical features and prognostic factors☆

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Abstract *Background/Purpose:* Our aim was to describe the clinical features and prognostic factors of Gram-negative rod bacteremia (GNRB) after cardiovascular surgery (CVS).
Methods: This retrospective observational study included adults with GNRB onset within 100 days after CVS at a single institution from April 2004 to May 2013. Clinical data regarding episodes of GNRB were collected from patients' medical charts. Those having polymicrobial bacteremia with a bacterium other than a GNR were excluded.
Results: Among 2017 CVS patients, GNRB occurred in 78. *Klebsiella, Pseudomonas aeruginosa, Enterobacter,* and *Escherichia coli* were the most commonly isolated organisms. Graft replacement was the most common surgical procedure in patients with GNRB after CVS (44.9%). Prophylaxis antibiotics were ampicillin/sulbactam (76.9%), and vancomycin (12.8%). The crude 90-day mortality rate was 21.8%, and the mean Acute Physiology and Chronic Health Evaluation II score was 15.6 (range, 3—39). In 34.6% of patients, the same GNR species were isolated from other samples within 30 days of GNRB occurrence. Multivariate analysis indicated that *P. aeruginosa* bacteremia [odds ratio (OR), 175; confidence interval (CI), 2.40—1270; $p = 0.0182$], Acute Physiology and Chronic Health Evaluation II scores of ≥ 25 (OR 76.2; CI 1.04—5580; $p = 0.0479$), and vancomycin for prophylaxis (OR 45.4; CI 1.02—202; $p = 0.0488$) were significant independent prognostic factors associated with death due to GNRB after CVS.

Conclusion: Graft replacement was the most common surgical procedure in patients with GNRB after CVS. Empirical antibiotics covering Gram-negative rods including *P. aeruginosa* should be considered if bacteremia is suspected in unstable patients after CVS.

Introduction

Gram-negative rod bacteremia (GNRB) after cardiovascular surgery (CVS) is a serious complication associated with morbidity and mortality.[1,2] However, no studies have systematically studied GNRB after CVS. Infections after CVS, such as surgical site infection and mediastinitis, are often caused by *Staphylococcus* spp.[3–5] Fowler et al[5] reported that in patients with bacteremia that developed within 90 days after CVS, *Staphylococcus* spp. accounted for 75.8% of causative organisms of bacteremia episodes and Gram-negative rods (GNRs) accounted for 18.8%. GNRB may be a frequent cause of inappropriate treatment, because GNRs are underestimated in bacteremia after CVS.

We aimed to describe the demographical, clinical, microbiological, and prognostic factors of GNRB after CVS.

Methods

Study design

We conducted a retrospective observational study at Tokyo Women's Medical University Hospital in Tokyo, Japan, a 1423-bed university-affiliated hospital, with 200 beds in the cardiovascular department, which is one of the largest institutes for cardiovascular disease. Clinical data regarding episodes of GNRB were collected from patients' medical charts. All adult cases of GNRB after CVS from April 2004 to May 2013 were included. The Ethics Committee at Tokyo Women's Medical University Hospital approved the study protocol (approval number 3013).

Definitions

An episode of GNRB was defined as an adult patient with at least one positive blood culture yielding any GNRs. Blood samples were drawn under sterile conditions and processed using the BACTEC 9240 system (Becton Dickinson Diagnostic Instrument Systems, Towson, MD, USA) until March 11, 2011, and the BacT/ALERT 3D system (bioMérieux, Marcy l'Etoile, France) from April 2011 to May 2013. Blood samples were incubated for up to 7 days. GNRs were identified using GNR-Combo NC6.11J, NC6.12J, and NC3.12J (Siemens Healthcare Diagnostics, Deerfield, IL, USA). We defined the date of GNRB diagnosis as the day of sampling of positive blood culture. We enrolled patients for whom the number of days from CVS to GNRB diagnosis was within 100 days. If the patient had many episodes of GNRB, we included all episodes of GNRB and analyzed each episode separately. Basically ampicillin/sulbactam was used as prophylaxis antibiotics, and vancomycin was chosen for patients with β-lactam allergy or Methicillin-resistant *Staphylococcus aureus* colonization. The empiric antibiotic was considered "appropriate," if the treatment regimens included at least one antibiotic active *in vitro* against all identified pathogens. We considered antimicrobial therapy "inappropriate" if the drugs used did not have *in vitro* activity against the isolated strain, or if the patient did not receive any antibiotics empirically. If *in vitro* activity of the antibiotic was not tested, we defined it as "unknown." Bentall procedure was included in graft replacement (thoracic). We evaluated the species isolated from other sites within 30 days from when the blood culture was performed. If there was more than one sample from the same site, only the latest sample was enrolled.

Study population

Patients were observed from the day of GNRB diagnosis to the 90-day follow-up. The following data were obtained for all patients: age, sex, comorbidities, type of surgery, use of medical devices, source of bacteremia, empirical or definitive antibiotics, time period from surgery to bacteremia development, culture samples from any sites, Acute Physiology and Chronic Health Evaluation (APACHE) II score at the day blood cultures were performed, and crude mortality in 90 days. We determined the source of bacteremia after reviewing medical records written by the primary physicians and receiving agreement from the infectious disease physician. Exclusion criteria were patients younger than 20 years, being enrolled in another clinical trial, the presence of polymicrobial bacteremia with a bacterium other than a GNR, and the surgery type being catheter surgery.

Statistical analysis

Continuous data were compared using the Student t test and categorical data using Fisher's exact tests. Data were considered statistically correlated when $p < 0.05$. Multivariate analysis was used to determine the independent risk factors associated with mortality using forward stepwise logistic regression. All variables with $p < 0.1$ in univariate analysis were entered into the multivariate model. Statistical analyses were performed using R, version 3.0.2 (http://www.r-project.org/).

Results

Clinical features

Among 2017 CVS patients, 434 developed bacteremia. Gram-positive cocci were present in 267 (61.5%) patients