

# Incidence Rate, Pathogens and Economic Burden of Catheter-Related Bloodstream Infection: A Single-Center, Retrospective Case-Control Study

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**Purpose:** Indwelling central venous catheters (CVCs) can cause catheter related bloodstream infection (CRBSI). CRBSI occurring in intensive care unit (ICU) patients may lead to the worse outcomes and extra medical costs. The present study aimed to assess the incidence and incidence density, pathogens and economic burden of CRBSI in ICU patients.

**Patients and Methods:** A case-control study was retrospectively carried out in six ICUs of one hospital between July 2013 and June 2018. The Department of Infection Control performed routinely surveillance for CRBSI on these different ICUs. Data of the clinical and microbiological characteristics of patients with CRBSI, the incidence and incidence density of CRBSI in ICUs, the attributable length of stay (LOS), and the costs among patients with CRBSI in ICU were collected and assessed.

**Results:** A total of 82 ICU patients with CRBSI were included into the study. The CRBSI incidence density was 1.27 per 1000 CVC-days in all ICUs, in which the highest was 3.52 per 1000 CVC-days in hematology ICU and the lowest was 0.14 per 1000 CVC-days in Special Procurement ICU. The most common pathogen causing CRBSI was *Klebsiella pneumoniae* (15/82, 16.67%), in which 12 (80%) were carbapenem resistant. Fifty-one patients were successfully matched with control patients. The average costs in the CRBSI group were \$ 67,923, which were significantly higher ( $P < 0.001$ ) than the average costs in the control group. The total average costs attributable to CRBSI were \$33, 696.

**Conclusion:** The medical costs of ICU patients were closely related to the incidence of CRBSI. Imperative measures are needed to reduce CRBSI in ICU patients.

**Keywords:** CRBSI, prolonged length of stay, cost, CRKP, ICU

## Introduction

Central venous catheter (CVC), the intravenous catheter inserted into a large vein with the purpose of gaining direct access to the central venous system, including peripherally inserted central catheter (PICC), is commonly used in critically ill patients in intensive care unit (ICU). CVC offers several advantages for treatment of patients in ICU. However, indwelling CVC has the potential of causing several complications such as catheter related bloodstream infection (CRBSI), phlebitis, catheter blockage, catheter exfoliation, and venous thrombosis.<sup>1</sup> Several studies have

demonstrated that CRBSI is closely related with increased patient morbidity and mortality and prolonged length of stay (LOS).<sup>2-5</sup>

The average incidence of CRBSI in ICUs in China is 1.5/1000 catheter days,<sup>6</sup> similar to the rates in UK, Germany and Italy,<sup>7</sup> but lower than the rates reported in Oman.<sup>8</sup> This may be partly due to the different definitions of surveillance, diagnosis criteria, patient conditions, and catheterization of procedures in different countries and regions. CLABSI incidence showed regional differences in China. The lowest incidence area was in Northeast China and the highest incidence area was in Eastern China.<sup>6</sup>

Health care-associated bloodstream infections were reported as the most common site of health care-associated infection in different studies and increased costs.<sup>9</sup> Among them, CRBSI has a greater impact on the prognosis and cost burden of patients. In the USA, it was estimated that approximately 12.32% of CRBSI patients will die.<sup>10</sup> The cost of CRBSI has been estimated to be between \$69,332 and \$71,443 in the USA<sup>11-13</sup> and the ranges of €13,585 to €29,909 and in Europe.<sup>14,15</sup>

Previously, Gram-positive bacteria (GPB) such as *Staphylococcus aureus* is a common pathogen causing CRBSI. Nowadays, however, the pathogens causing CRBSI tend to change from Gram-positive bacteria to Gram-negative bacteria (GNB) such as *Klebsiella pneumoniae*.<sup>16,17</sup>

It is thus important to further investigate the present situation as well as the disease burden of CRBSI. Whereas limited data on CRBSI are available, we reported the findings of a single center, retrospective case-control study that assessed the incidence rate, the distribution of pathogens, attributable LOS, and costs of patients with CRBSI in ICU in a teaching hospital, Shanghai, China.

## Methods

### Setting

The study was carried out in six ICUs of a teaching hospital affiliated to Shanghai Jiao Tong University school of medicine, with a total of 2300 beds, between July 2013 and June 2018. These ICUs were Cardiology ICU (CICU), Surgical ICU (SICU), General ICU (GICU), Special Procurement ICU (SPICU), Respiratory ICU (RICU) and Hematology ICU (HICU). The department of infection control performed routinely surveillance for CRBSI on these six different ICUs.

### Definition

CRBSI is defined as an infection diagnosed in a patient with a CVC (including PICC) in place or removed within 48 hours prior to identification, who exhibits symptoms and has the same microorganism isolated from both peripheral blood sample culture and catheter tip culture. This is a modified definition developed by the CLABSI definition of the US Center for Disease Control (CDC). Such infections cannot be related to any other source for infection that the patient may have or be incubating when the patient was admitted.<sup>18-20</sup>

The incidence of CRBSI is defined as: CRBSI cases/ patients with CVC\*100%. The incidence density of CRBSI is defined as: CRBSI cases/ CVC-days\*1000. CVC-days is defined as the number of days a CVC has been accessed. When calculating the density, it is presented as the number of CRBSI per 1000 CVC-days.

### Study Design

The study was separated into two parts. In the first part, we collected descriptive statistics data about the characteristics of patients with CVC and CRBSI in ICU, including demographic characteristics, incidence and incidence density, prognosis and distribution of pathogens. In the second part, CRBSI patients were matched with other patients with CVC. We then analyzed the LOS and the costs attributable to CRBSI by conducting a pair matching case-control study (1:1).

Information for each patient was gathered from Hospital Infection Database. For all patients included in our study, the following demographic characteristics were collected: age, gender, date of ICU admission, LOS, Acute Physiology and Chronic Health Evaluation II (APACHE II) score,<sup>21</sup> and the ICU type. This study is approved by the Ethics Committee of

Ruijin Hospital, Jiaotong University School of Medicine with a waiver of informed consent for the following reasons: (1) the retrospective nature of the study, (2) all identifiable personal information was removed for privacy protection, (3) only medical records and charges were reviewed.

## Inclusion and Exclusion Criteria

The inclusion criteria were as follows: a) in ICU from July 2013 to June 2018; b) 18 years or older; c) with CVC;

The exclusion criteria were as follows: a) clinically diagnosed with BSI or who could be diagnosed with BSI according to the CDC definitions were excluded; b) more than one CRBSI during hospitalization.

## Matching Method

A matched (1:1) case-control study design was utilized. The total of five key variables were used to match in the procedure, including gender, ICU type, age ( $\pm 5$ yr.), APACHE II score ( $\pm 2$ pt), and date of ICU admission ( $\pm 1$ yr). If more than one control cases met the matching criteria, the priority of selection criteria was ordered as APACHE II score, age and date of ICU admission. The controls were defined as patients with CVC but without CRBSI. The matching method is nearest neighbor matching with replacement.

## Assessment of Medical Costs Attributable to CRBSI

The costs of patients with CRBSI were analyzed and compared between the matched groups. The difference in costs between the two groups during the hospitalization was calculated as the costs attributable to CRBSI. The costs consisted of eight specific categories: 1) antimicrobial agent, 2) non-antimicrobial agent, 3) bed costs, 4) health care technical service, 5) nursing care, 6) laboratory testing, 7) medical material, 8) others.

The analysis of the drug did not cover traditional Chinese medicine. Bed costs were defined as the payment of rent for bed during hospitalization. Health care technical service included physical examination, medical disposition, and group consultation. Nursing costs referred to costs of nursing service.

The exchange rate used for converting Chinese Yuan (CNY) to US Dollar (USD) was JD 1 = 0.155 USD on December 15, 2015.

## Statistics Method

All the calculations were done using SPSS version 20.0 (IBM, Armonk, NY, USA). The differences of the prognosis of CRBSI at different intubation sites were evaluated by Chi-square test. The difference in age, APACHE II score, LOS and costs between matched groups were tested by paired *t*-test and the LOS was tested by the Wilcoxon signed-rank test.

## Results

### Evaluation of the Incidence and Incidence Density

During the study period, there were 8019 ICU patients with CVC, of which a total of 82 (1.02%) patients were with CRBSI, and the demographic characteristics and the distribution of patients with CRBSI were shown in [Table 1](#). Nearly 1/4 patients with CRBSI were in Cardiac ICU, which involved more than half of patients with CVC. The CVC-days of patients in ICU was 64,477.8 ([Table 2](#)). CRBSI was occurred on average 22.96 days after intubation. The incidence density of CRBSI was 1.27 per 1000 CVC-days, and it was the highest in hematology ICU, which was 4.43 per 1000 CVC-days ([Table 2](#)).

There were 90 isolates collected from all of the 82 patients with CRBSI as shown in [Table 3](#). The proportion of GPB, GNB, and fungus was 31.11% (n=28), 44.44% (n=40) and 24.44% (n=22), respectively. Of the 28 GPB, *Enterococcus faecium* (n=9, 10.00%) and *S. epidermidis* (n=7, 7.78%) were the two most common. Among the *S. epidermidis*, 85.71% (n=6) were oxacillin-resistant. Of the 40 GNB, the most common was *K. pneumoniae* strains (n=15, 16.67%), followed by *E. coli* (n=7, 7.78%) and *A. baumannii* (n=6, 6.67%). Of note, 80.00% (n=12) *K. pneumoniae* were carbapenem-resistant. The mortality rate of patients with *K. pneumoniae* CRBSI was 66.67%, higher than that of patients with *A. baumannii* (16.67%) and *E. coli* (28.57%) CRBSI as shown in [Table 4](#).

**Table 1** Demographic Characteristics and Distribution of Patients with CVC and Those with CRBSI in ICU

	Patients with CVC (n=8019)	No. CRBSI (n=82)
Age	59.80(±16.9)	53.30(±18.1)
Female	2902(36.2%)	22(26.8%)
APACHE II	12.47(±5.5)	12.54(±4.4)
<b>ICU distribution</b>		
Cardiac ICU	4362(54.40%)	20(24.39%)
Respiratory ICU	149(1.86%)	1(1.22%)
Surgical ICU	1868(23.29%)	16(19.51%)
General ICU	869(10.84%)	11(13.41%)
Hematology ICU	498(6.21%)	33(40.24%)
Special Procurement ICU	273(3.40%)	1(1.22%)

**Notes:** Continuous variables are represented by  $\bar{x}$  (±s) and categorical variables are represented by n (%).

**Abbreviations:** CVC, central venous catheters; CRBSI, catheter related bloodstream infection; ICU, intensive care unit; APACHE II, Acute Physiology and Chronic Health Evaluation II score.

**Table 2** Incidence Density and Incidence of CRBSI in the Six ICUs

	No. CRBSI	Patients with CVC	CVC-Days	Incidence Density (Per 1000 CVC-Days)	Incidence (%)
Cardiac ICU	20	4362	14,785.8	1.35	0.46%
Respiratory ICU	1	149	1986.3	0.50	0.67%
Surgical ICU	16	1868	19,190.5	0.83	0.86%
General ICU	11	869	11,798.2	0.93	1.27%
Hematology ICU	33	498	9383.8	3.52	6.63%
Special Procurement ICU	1	273	7333.2	0.14	0.37%
Overall	82	8019	64,477.8	1.27	1.02%

**Abbreviations:** CVC, central venous catheters; CRBSI, catheter related bloodstream infection; ICU, intensive care unit.

## Fundamental Results of Matching

The demographic characteristics and department distribution of the patients in matched group were shown in [Table 5](#). According to the matching criteria, 51 pairs of patients were successfully matched. (Other 31 patients with CRBSI could not be matched properly for lack of data or suitable control). The average age of the case group was 50.0± 19.0 years old, and that of the control group was 50.3 ± 18.7 years old ( $P=0.18$ ). The average APACHE II score of the case group was 12.6± 4.6 point, and that of the control group was 12.4 ± 4.6 point ( $P=0.07$ ). Five ICUs were involved, including Cardiac ICU (11 pairs), Hematology ICU (25 pairs), General ICU (7 pairs), Surgical ICU (7 pairs), and Respiratory ICU (1 pair).

## Evaluation of the LOS

The median LOS in the CRBSI group were 56.0 days, which were significantly higher ( $P < 0.001$ ) than that in the control group (36.0 days). The median LOS attributable to CRBSI was 20.0 days.

**Table 3** The Distribution of Various Isolates Obtained from Cases of CRBSI

Pathogen	MDRB N (%)	N (%)
<b>Gram-positive bacteria</b>	12(42.86%)	28(31.11%)
<i>Enterococcus faecalis</i>	0(0.00%) <sup>a</sup>	2(2.22%)
<i>Enterococcus faecium</i>	2(22.22%) <sup>a</sup>	9(10.00%)
<i>Staphylococcus aureus</i>	2(100.00%) <sup>b</sup>	2(2.22%)
<i>Staphylococcus epidermidis</i>	6(85.71%) <sup>b</sup>	7(7.78%)
<i>Staphylococcus haemolyticus</i>	2(100.00%) <sup>b</sup>	2(2.22%)
<i>Streptococcus</i>	0(0.00%) <sup>a</sup>	6(6.67%)
<b>Gram-negative bacteria</b>	20(50.00%)	40(44.44%)
<i>Escherichia coli</i>	0(0.00%) <sup>c</sup>	7(7.78%)
<i>Klebsiella pneumoniae</i>	12(80%) <sup>c</sup>	15(16.67%)
<i>Acinetobacter baumannii</i>	4(66.67%) <sup>c</sup>	6(6.67%)
<i>Pseudomonas aeruginosa</i>	1(33.33%) <sup>c</sup>	3(3.33%)
<i>Pseudomonas maltophilia</i>	0(0.00%) <sup>d</sup>	3(3.33%)
Other Gram-negative bacteria	3(50.00%) <sup>c</sup>	6(6.67%)
<b>Fungus</b>	4(18.18%)	22(24.44%)
<i>Candida albicans</i>	0(0.00%) <sup>e</sup>	8(8.89%)
<i>Candida glabrata</i>	0(0.00%) <sup>e</sup>	2(2.22%)
<i>Candida parapsilosis</i>	0(0.00%) <sup>e</sup>	4(4.44%)
<i>Candida tropicalis</i>	4(50.00%) <sup>e</sup>	8(8.89%)
<b>Overall</b>	36(40.00%)	90(100.00%)

**Notes:** <sup>a</sup>Vancomycin resistant, <sup>b</sup>Oxacillin resistant, <sup>c</sup>Carbapenems resistant (including meropenem and imipenem), <sup>d</sup>Levofloxacin resistant, <sup>e</sup>Fluconazole resistant.

**Abbreviation:** MDRB, Multidrug-resistant bacteria.

## Evaluation of the Costs Attributable to CRBSI

The average costs in the CRBSI group were \$67,923 which was significantly higher ( $P < 0.001$ ) than that in the control group (\$34,227). The average total costs attributable to CRBSI was \$33, 696. Except for health care technical service, the difference between antimicrobial agent, non-antimicrobial agent, bed, nursing, laboratory testing, medical material, other cost of the two groups were all statistically significant (Table 6).

## Discussion

Central vascular access is vital for ICU patients and about 90% of bloodstream infection are related to it.<sup>22</sup> The overall incidence and incidence density of CRBSI of this study was 1.08% and 1.27 per 1000 CVC-days, respectively, which is similar to the CRBSI density of 1.1 per 1000 CVC-days in the United States as determined by the CDC NSHN and lower than the incidence density of 3.7 in Europe reported by the European Centre for Disease Prevention and Control, compared with developed countries.<sup>23</sup> Chopdekar et al reported the average CRBSI incidence density at 9.26 per 1000 CVC-days in ICUs in a tertiary care teaching hospital in Mumbai.<sup>24</sup>

This study revealed that the incidence and incidence density of CRBSI were highest in Hematology ICU (6.63% and 3.52 per 1000 CVC-days, respectively), which is higher than that in Rubenstein's study (2.6 per 1000 CVC-days).<sup>25</sup> The

**Table 4** Prognosis of CRBSI of *A. Baumannii*, *E. Coli* and *K. Pneumoniae*

	Discharge N (%)	Death N (%)	Overall
<i>Staphylococcus aureus</i>			
MRSA	1(50.00%)	1(50.00%)	
<i>Acinetobacter baumannii</i>	5(83.33%)	1(16.67%)	6
CR-AB	3(75%)	1(25%)	4
CS-AB	2(100%)	0(0%)	2
<i>Escherichia coli</i>	5(71.43%)	2(28.57%)	7
CRE	5(71.43%)	2(28.57%)	7
<i>Klebsiella pneumoniae</i>	5(33.33%)	10(66.67%)	15
CR-KP	4(33.33%)	8(66.67%)	12
CS-KP	1(33.33%)	2(66.67%)	3
<b>Overall</b>	15(53.57%)	13(46.43%)	28
MDRB	7(43.75%)	9(56.25%)	16
Non-MDRB	8(66.67%)	4(33.33%)	12

**Abbreviations:** MRSA, Methicillin-resistant *Staphylococcus aureus*; CR-AB, Carbapenem-resistant *Acinetobacter baumannii*; CS-AB, Carbapenem-sensitive *Acinetobacter baumannii*; CRE, Carbapenem-resistant Enterobacteriaceae; CR-KP, Carbapenem-resistant *Klebsiella pneumoniae*; CS-KP, Carbapenem-sensitive *Klebsiella pneumoniae*; MDRB, Multidrug-resistant bacteria.

**Table 5** Demographic Characteristics and Department Distribution of Patients in the Matched Group [ $\bar{x}(\pm s)$ , n (%)]<sup>a</sup>

	Case Group (n=51)	Control Group (n=51)
Age	50.0( $\pm$ 19.0)	50.3( $\pm$ 18.7)
Female	17(33.3%)	17(33.3%)
APACHE II score	12.6( $\pm$ 4.6)	12.4( $\pm$ 4.6)
<b>ICU Departments</b>		
Cardiac ICU	11(21.6%)	11(21.6%)
Hematology ICU	25(49.1%)	25(49.1%)
General ICU	7(13.7%)	7(13.7%)
Surgical ICU	7(13.7%)	7(13.8%)
Respiratory ICU	1(1.9%)	1(1.9%)

**Notes:** Continuous variables are represented by  $\bar{x}(\pm s)$  and categorical variables are represented by n (%); <sup>a</sup>p<0.05.

**Abbreviations:** CVC, central venous catheters; CRBSI, catheter related bloodstream infection; APACHE II score, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit.

incidence density of Hematology ICU was approximately 3-fold higher than the overall density. All patients in Hematology ICU had a bone marrow transplantation, who were in presence of inhibition of body immunity. They were in immunosuppressed state, and broad-spectrum antibiotics were routinely used to prevent infection. Since all

**Table 6** Medical Costs Attributable to CRBSI (\$)

	Average Cost in the CRBSI Group	Average Cost in the Control Group	Average Cost Attributable to CRBSI	P value
Antimicrobial agent	21,073	12,033	9030	<0.01
Non-antimicrobial agent	17,215	7473	9742	<0.01
Total drug cost <sup>a</sup>	38,288	19,507	18,781	<0.01
Bed	4608	3069	1539	<0.05
Health care technical service	135	115	21	>0.05
Nursing	783	417	365	<0.001
Laboratory testing	10,630	5529	5330	<0.001
Medical material	7450	3220	4230	<0.001
Other cost	6030	2601	3430	<0.001
Total medical cost <sup>b</sup>	29,636	14,720	14,915	<0.001
Total cost <sup>b</sup>	67,923	34,227	33,696	<0.001

Notes: <sup>a</sup>p<0.01; <sup>b</sup>p<0.001.

patients need chemotherapy treatment, and almost all of them had CVCs during hospitalization, which increased the risk of infection, likely leading to the incidence of CRBSI higher than these in other ICUs. It should be noted that due to disease and treatment related immunosuppression, the incidence of CRBSI in hematology ICU in this study was higher than other ICUs.<sup>25</sup>

The lowest incidence and incidence density were in Special Procurement ICU (0.37% and 0.14 per 1000 CVC-days, respectively). Mostly patients admitted in Special Procurement ICU were elderly people. Although their general conditions were not good, the high ratio of the ICU medical staff, adequate equipment security, and in-depth understanding of patients' situation can bring individualized diagnosis and prompt treatment to these patients. Those advantages could ensure every patient's condition stable with close monitoring, which may contribute to the lowest incidence and incidence density of CRBSI in SPICU.

In this study, the incidence of CRBSI in cardiac ICU was the second highest, while the incidence of CRBSI per 1000 CVC-days was the second lowest. The reason might be that most patients in cardiac ICU were observed for 48 hours and often transferred between cardiothoracic ICU and general wards. The high beds turnover rate led to very low average number of days of catheterization. Thus, there was a mismatch between the incidence and incidence density of CRBSI. The incidence of CRBSI varied in different areas, which may result from a variety of factors, such as the patient's condition, catheter selection, and catheter maintenance.

As most patients admitted to ICU are in complex and critical ill condition, a variety of invasive operations such as central venous catheters are usually required, due to the needs of monitoring and treatment. All these factors could increase the possibility of bloodstream infection in these patients. Once bloodstream infection occurs, especially CRBSI, the patient's condition may rapidly worsen, causing sepsis easily and even leading to death, bringing great challenges to medical staffs. Studies have shown that the mortality rate of ICU patients with CRBSI is generally higher than those without CRBSI.<sup>26</sup> The mortality rate of patients with CRBSI was 46.34% in this study, with no difference in different intubation sites (P=0.24).

In the past, Gram-positive cocci were the most frequent microorganism causing BSI associated with catheter,<sup>27</sup> yet nowadays GNB has overtaken it as shown in this study.<sup>28</sup> Notably, methicillin-resistant *S. aureus* (MRSA) and carbapenem-resistant *K. pneumoniae* (CRKP) accounted for the majority of the pathogens, respectively. This study



found that the mortality of patients with *K. pneumoniae* CRBSI was the highest. To fight against the infection caused by drug-resistant bacteria, especially CRKP, more advanced antibacterial drugs should be used, such as tigecycline and polymyxin, which will greatly increase the medical costs. Moreover, CRBSI caused by these drug-resistant microorganisms may lead to worse prognosis.

Studies have shown that CRBSI could prolong the LOS in ICU and the total LOS in hospital.<sup>15,29</sup> However, the results of different studies varied significantly due to the differences in medical charge patterns and statistical methods such as patient grouping in different regions. If patients are simply divided into infected and uninfected groups, and then the difference in average LOS between the two groups is compared, it will generate biased estimates due to the influence of basic diseases and physical states of patients. By means of matching, confounding factors are controlled between the case group and the control group. It can relatively reduce the differences between the underlying influence factors of the patients.

With proper matching method, we found the median LOS attributable to CRBSI was 20.0 days, which was much higher than the extra LOS (7 days) of previous studies.<sup>15,30</sup> A study by Rosenthal et al in six ICUs among three hospitals in Argentina found that the LOS attributable to CRBSI was 11.9 days.<sup>31</sup> Dimick et al found the attributable LOS to CRBSI was 20 days in severe surgical ICU patients, which was quite similar as our result.<sup>13</sup>

More LOS naturally leads to higher hospitalization costs. Multiple studies have demonstrated that the extension of hospital stay is one of the important factors affecting the increased nosocomial infection.<sup>26,32</sup> In this study, patients with CRBSI extended the LOS by a median of 20 days compared with patients without CRBSI. Therefore, the LOS of patients is positively correlated with the occurrence of nosocomial infection, and these two may be mutually causal. Compared to health care-associated bloodstream infections, CRBSI contributes more hospital stay days.<sup>33</sup> Patients with CRBSI need targeted treatment, increased use of antimicrobial agents and corresponding supportive treatment, so as to prolong the course of disease, thus leading to reduced ICU bed turnover rate and bed utilization rate. The excessively LOS and low utilization rate of hospital beds not only lead to more risk of other infection, but also the delay of treatment of patients in need of treatment because there is no spare bed, and increase the potential of doctor-patient disputes.<sup>29</sup>

The average costs of each case of CRBSI in the ICU was \$ 67,923. The average drug costs attributable to CRBSI is \$18,781, for which antibiotic agents mostly account, almost twice as much as the costs in the control group. Dimick's study found the additional costs of CRBSI was \$11,523 to \$165,735 in surgical ICU in US.<sup>13</sup> David et al found the hospital costs attributable to CRBSI was \$11,971 in ICU in Canada.<sup>34</sup> Another study on the costs of CRBSI found the costs of CRBSI acquired ICU is \$12,321 in Canada.<sup>35</sup>

Since October 1st 2008, the United States has stipulated that the medical costs caused by CRBSI should be paid by the hospital, and patients do not have to pay for it. Currently, China has not established similar regulations. In China, most of the special antibiotics for the antimicrobial resistant bacteria infection treatment, such as carbapenem-resistant Enterobacteriaceae bacteria, are quite expensive and not covered by the basic medical reimbursement.

First of all, the occurrence of CRBSI increases the costs of microorganism culture and drug sensitivity test. In addition, the costs of antibiotics such as linezolid, tigecycline, and polymyxin used in the early empirical treatment and targeted treatment of pathogenic bacteria is quite expensive, which greatly increases the costs of treatment for patients. The overuse of antibiotics not only consumes excessive health resources, but also increases the risk of nosocomial infection and the emergence and spread of drug-resistant bacteria. Therefore, reducing the incidence of CRBSI can not only reduce the disease burden of patients, but also reduce the occurrence of nosocomial infection and the spread of drug-resistant bacteria, which is of great significance for improving the quality of medical care and ensuring the safety of patients.

Once CRBSI occurs, lots of high-level antibiotic agents would be used, which are substantially expensive and less covered by medical insurance service. Our study innovatively considered the costs of antibiotics which was closely related to the incidence of CRBSI. As a proactive anticipative strategy, microscopic examination of CVC blood samples might be used to anticipate CRBSI in an earlier stage.<sup>36</sup>

Certainly, this study has some limitations. 1) Except CVC, whether these patients had other medical device use was not considered. 2) According to the antibacterial spectrum of antibiotics, multiple antibiotics could be used for a specific microbial infection. In addition, the record of prescription time was not contained in the database, which could otherwise



be used to match the microbial infection and treatment plan. 3) Patients with other concurrent infections were not excluded, which may further increase the costs and prolong LOS. 4) This was a single-center retrospective study with a relatively small sample group. More studies with multi-center and large sample groups are needed to further clarify the effect of CRBSI rates on the medical costs of ICU patients.

## Conclusion

In conclusion, if CRBSI happened, the hospitalization costs and LOS of the patient will increase. It is worth noting that CRBSI could be prevented and imperative measures should be taken to prevent the occurrence of CRBSI in ICU patients, not only to reduce the burden of patients and antibiotics use, but also to improve the prognosis.

## Data Sharing Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on a reasonable request.

## Ethics Approval

This study is approved by the Ethics Committee of Ruijin Hospital, Jiaotong University School of Medicine with a waiver of informed consent for the following reasons: (1) the retrospective nature of the study, (2) all identifiable personal information was removed for privacy protection, (3) only medical records and charges were reviewed. This study complies with the Declaration of Helsinki.

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## Disclosure

The authors report no conflicts of interest in this work.

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