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Original Article

Outcomes and mortality risk scoring for infections caused by carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae*

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Abstract

Introduction: Carbapenem-resistant Enterobacterales (CRE) are becoming increasingly prevalent and have been associated with increased mortality. Due to the paucity of data from the region, we evaluated the risk factors and outcomes of infections caused by CRE at a tertiary care center in Lebanon.

Methodology: The study had three arms in a case-case-control design: patients with CRE infections, patients with infections due to ceftriaxone-resistant carbapenem-susceptible Enterobacterales (CSE), and uninfected controls (UC). Logistic regression was performed to identify risk factors uniquely associated with CRE. A CRE infection score was also created to assess the likelihood of having a CRE infection.

Results: We included 337 patients (112 CRE, 75 CSE, 150 UC). Predictors unique to CRE infection included recent surgery (Odds Ratio (OR) 25.7; 95% confidence interval (CI_{95} 5.7-115.2), carbapenem use within 30 days (OR 19.1; CI_{95} 3.3-109.6), and malignancy (OR 4.2; CI_{95} 1.6-10.5). The mean CRE score was 4.2 ± 2.2 in the CRE group and 2.4 ± 2.4 in the CSE group ($p < 0.001$). Infection-related mortality was higher among CRE patients (63.6% vs. 20.0%; $p = 0.015$), and CRE was independently associated with all-cause in-hospital mortality.

Conclusions: We developed a scoring system that would allow risk stratification and would guide empiric antibiotic therapy. CRE infections were associated with a worse outcome compared to CSE infections.

Key words: Carbapenem resistance; risk stratification; Enterobacterales.

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Introduction

Carbapenems, a subclass of the beta-lactam antibiotics family, are used for broad-spectrum antibiotic coverage [1]. With the emergence of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae during the last 30 years [2], carbapenem use to treat infections with these organisms has increased significantly [3]. This rise in the use of carbapenems has led to the development of resistance to carbapenems among Enterobacterales via several mechanisms, including, but not limited to, carbapenemases [4,5], porin loss, and up-regulation of efflux pumps [6,7]. Infections with carbapenem-resistant Enterobacterales (CRE) are often associated with a higher mortality rate and decreased clinical cure rates [8]. Mortality attributable to CRE is, however, more difficult to determine, and the true role of CRE as a cause of death still needs to be determined.

Several studies have evaluated the risk factors associated with the acquisition of infections caused by CRE. A study by Cendejas *et al*., showed that infection with CRE was associated with long-term hospitalization, major surgery, and broad-spectrum antibiotic therapy [9]. Another study by *Marchaim et al*., showed that recent exposure to antibiotics was an independent risk factor for the acquisition of infections by CRE [10]. More specifically, prior treatment with vancomycin, metronidazole, and carbapenems was associated with infection with carbapenem-resistant *E. coli* [11]. Other antibiotics that have been possibly incriminated in selecting for carbapenem-resistant *Klebsiella pneumoniae* were anti-pseudomonal penicillins and quinolones, in addition to glycopeptides and carbapenems [11]. Patient-specific risk factors for CRE infections include older age, longer time-at-risk, recent ICU admission, and presence of a central venous catheter [10,11].

The aim of the study is to identify clinical risk factors that are unique to CRE infections compared to infections with CSE isolates. By identifying risk factors predisposing to CRE but not CSE, the clinician will be able to risk stratify patients upon presentation, thereby providing prompt and appropriate empiric therapy in high-risk patients, while preserving broad-spectrum antibiotics in low-risk patients. This study provides region-specific data on risk factors and outcomes associated with CRE and CSE, contributing to the existing literature by addressing gaps in data from our geographical area. We also compare the complications and final outcomes of patients with CRE and CSE infections.

Methodology

Study design and study population

We used a retrospective case-control study design, which is known to be an effective method for identifying risk factors for antimicrobial-resistant pathogens**.** The first group of cases consisted of hospitalized patients with infections due to CRE between 2008 and 2020, and the second group of cases consisted of patients with infections due to ceftriaxone-resistant CSE who were admitted during the same time period. Controls included patients who were hospitalized for at least 72 hours but did not develop CRE or CSE infections during their hospital stay. The controls were chosen randomly from the hospital database and were matched to the cases by year of infection. Only adult patients (> 18 years of age) were eligible for the study. All patients were followed throughout the index admission until death or hospital discharge. The uninfected controls in this study were chosen randomly, selected based on their admission to the hospital during the same timeframe as the cases and a minimum hospital stay of 72 hours. This selection process ensures temporal alignment with the cases and controls for differences in baseline admission timing.

Data collection and definitions

A case report form was designed for data collection with sections on patient demographics, comorbidities, clinical signs and symptoms upon presentation, laboratory findings, and risk factors for infection, in addition to the treatment regimen chosen and the final outcome. Data collected from the control group was limited to demographics and comorbidities. Infection-related in-hospital mortality was judged upon chart review independently by two trained study coordinators and was confirmed by the principal investigator. Inclusion criteria for patients in the CRE included Enterobacterales that are resistant to third-generation cephalosporins and to at least one of the carbapenem antibiotics (ertapenem, meropenem, or imipenem). Inclusion criteria for the CSE group included Enterobacterales resistant to third-generation cephalosporins but sensitive to all carbapenems. Patients were excluded from the study if they met any of the following criteria: age under 18 years; insufficient clinical data available in the medical records; presence of polymicrobial infections where CRE or CSE was not the primary pathogen. Hospital-acquired infection was defined as an infection that manifested 48 hours of more after hospital admission. Healthcare-associated infection was defined as an infection occurring in patients receiving home and/or ambulatory intravenous therapy, chemotherapy, hemodialysis, wound care, specialized nursing care, or who had attended a hospital clinic within the last 30 days; patients hospitalized in an acute care hospital for ≥ 2 days within the last 90 days; and those residing in a nursing home or long-term care facility [12].

Microbiological Testing and Data Collection

Bacterial isolates

Clinical isolates of ESBL-producing *E. coli* and *K. pneumoniae* that were recovered from different specimens submitted to the clinical microbiology laboratory of AUBMC were analyzed. Identification of isolates was based on growth characteristics, colonial and microscopic morphology, and by using the relevant Analytical Profile Index (API) identification strips. Only one isolate of the same bacterial species was included per patient. All isolates were tested by disk diffusion against relevant antimicrobial agents according to the Clinical Laboratory Standards Institute (CLSI) guidelines that were current at the time of specimen processing.

Suspicion and confirmation of carbapenem resistance

The disk diffusion susceptibility testing was done using Mueller-Hinton agar according to the CLSI guidelines. 10 microgram disks of ertapenem and imipenem are used. In case of intermediate susceptibility or resistance (according to the CLSI guidelines), the E-test was done using strips for imipenem, ertapenem, and meropenem on the Mueller-Hinton agar. The MIC was identified using the E-test and interpreted according to CLSI guidelines.

All microbiological testing and susceptibility experiments were performed on isolates collected shortly after the diagnosis of infection, throughout the study period from 2008 to 2020.

Quality control

The proper performance of the disk diffusion test method was ensured by using the American Type Culture Collection (ATCC) quality control strains *E. coli* ATCC 25922 and *P. aeruginosa* (ATCC 27853).

Statistical analysis

Continuous variables are presented as a mean ± standard deviation. Categorical variables are presented as percentages. Data was entered and analyzed using SPSS (Statistical Package for the Social Sciences). Bivariable analysis was used to detect statistical associations. Multivariable analysis was performed by logistic regression to detect independent associations. Using logistic regression, three multivariable models were constructed (CRE vs. uninfected controls, CSE vs. uninfected controls, and CRE vs. CSE). The primary objective of these multivariable analyses was to assess the independent impact of various factors on the risk of isolation of CRE and CSE while controlling for potential confounders. The candidate variables for inclusion in the logistic models included all variables with $p \leq 0.05$ on bivariable analyses. A backward stepwise selection procedure was used to select variables for inclusion in the final model. The variables that were significant in the CRE vs. CSE model were used to create a clinical scoring system to estimate the likelihood of a CRE infection. Variables were assigned points based on their respective adjusted odds ratio obtained on multivariable analysis. Receiver operating characteristic (ROC) analysis was used to determine the best cutoff score. As for the mortality analysis, all patients who had a fatal outcome in both the CRE and CSE groups were included in a multivariable model with mortality as the dependent variable in order to evaluate whether CRE is an independent risk factor for mortality.

Ethical approval

This study was approved by the Institutional Review Board of the American University of Beirut, and a waiver of informed consent was granted due to the retrospective nature of the research. All patient-identifying data were anonymized to ensure confidentiality and privacy.

Results

A total of 337 cases were included in the study, of which 112 were CRE cases, 75 were CSE cases and 150 were randomly selected uninfected controls. A bivariable analysis was performed comparing the CRE cases and CSE cases to the uninfected controls; results are shown in Tables 1 and 2, respectively. When comparing the CRE subjects to the uninfected controls (Table 1), patients infected with CRE generally had a higher prevalence of comorbidities compared to the controls. They were also more likely to have received steroids or immunosuppressive therapy, had a surgical intervention, stayed in the hospital, used antibiotic, and used carbapenem. As shown in Table 2, CSE-infected patients were also more likely to have comorbid conditions compared to uninfected controls, with the exception of chronic pulmonary disease. Moreover, similar to the CRE infected group, the CSE infected group was more likely to have been hospitalized, undergone surgery, received steroids or immunosuppressive therapy, and used antibiotics, particularly carbapenems, within the past 30 days compared to the uninfected controls. In analyzing the relationship between surgery and hospital stay, we categorized the duration of stay into three groups: 0-2

Table 1. Bivariable analysis of patients with CRE infections vs. uninfected controls.

Variable	CRE (n = 112)	Uninfected controls (n = 150)	*p*
Age	58.6 ± 17.8	54.1 ± 19.4	0.06
Male sex	69 (61.6)	88 (58.7)	0.63
Renal insufficiency	35 (31.3)	10 (6.7)	< 0.001
Diabetes mellitus	46 (41.1)	32 (21.3)	0.001
Chronic pulmonary disease	19 (17.0)	26 (17.3)	0.94
Malignancy	52 (46.4)	36 (24.0)	< 0.001
Steroids or IS therapy*	25 (22.3)	10 (6.7)	0.001
Hospital stay*			< 0.001
0-2 days	28 (25.0)	136 (90.7)	
3-5 days	16 (14.3)	10 (6.7)	
> 6 days	68 (60.7)	4 (2.6)	
Surgery*	53 (47.3)	3 (2.0)	< 0.001
Antibiotic use*	65 (58.0)	15 (10.0)	< 0.001
Carbapenem use*	34 (30.4)	2 (1.3)	< 0.001

*Within the past 30 days. CRE: carbapenem-resistant Enterobacterales; IS: immunosuppressive. All numbers represent n (%) except for continuous variables, which are mean ± standard deviation.

Table 2. Bivariable analysis of patients with CSE infections vs. uninfected controls.

Variable	CSE (n = 75)	Uninfected controls (n = 150)	*p*
Age	64.6 ± 18.7	54.1 ± 19.4	0.004
Male sex	31 (41.3)	88 (58.7)	0.014
Renal insufficiency	21 (28.0)	10 (6.7)	< 0.001
Diabetes mellitus	29 (38.7)	32 (21.3)	0.006
Chronic pulmonary disease	19 (25.3)	26 (17.3)	0.16
Malignancy	24 (32.0)	36 (24.0)	< 0.001
Steroids or IS therapy*	17 (22.7)	10 (6.7)	< 0.001
Surgery*	17 (22.7)	3 (2.0)	< 0.001
Hospital stay*			0.005
0-2 days	33 (44.0)	136 (90.7)	
3-5 days	10 (13.3)	10 (6.7)	
> 6 days	32 (42.7)	4 (2.7)	
Antibiotic use*	32 (42.7)	15 (10.0)	< 0.001
Carbapenem use*	10 (13.3)	2 (1.3)	< 0.001

*Within the past 30 days. CSE: carbapenem-susceptible Enterobacterales; IS: immunosuppressive. All numbers represent n (%) except for continuous variables, which are mean ± standard deviation.

days, 3-5 days, and > 6 days. We found a significant association, with patients who underwent surgery being more likely to have a hospital stay exceeding 6 days. This association was further assessed in our regression model, where both surgery and recent hospital stay were included as covariates. Notably, only surgery retained a significant association, underscoring its independent impact on extended hospitalization.

A multivariable analysis comparing the CRE dataset to the uninfected controls (Table 3) showed that recent surgery and carbapenem use were associated with the highest risk for CRE infection, with adjusted odds ratios of 25.7 (95% CI 5.7-115.2) and 19.1 (95% CI 3.3-109.6), respectively. In this study it was found that 81.4% of the surgeries were major surgeries, with upper gastrointestinal (GI) surgery being the most common type, followed by orthopedic surgery and laparotomy. Importantly, all surgeries, whether classified as major or minor, were performed in the same operating room theater. This distribution and operational detail have been included to clarify surgical procedures within the studied cohort. Other independent risk factors were renal insufficiency, malignancy, recent hospital stay, and diabetes. Another multivariable analysis compared the CSE dataset to the uninfected controls (Table 3) and found that recent hospital stay was the strongest predictor of CSE infections, with an adjusted odds ratio of 3.9 (95% CI 2.3-6.8), followed by steroids or immunosuppressive therapy and renal insufficiency. Finally, in the third regression model comparing the CRE group to the CSE group, carbapenem use within 30 days showed the strongest association (aOR 3.8; 95% CI 1.6-9.1), followed by surgery, renal insufficiency, and malignancy. We conducted an additional regression analysis that included only major surgeries and found that the results were consistent with the original analysis: adjusted odds ratios (aOR) for carbapenem use were 3.3; surgery, 3.1; renal insufficiency, 1.8; and malignancy, 2.0. Despite these similar findings, we chose to use the model inclusive of both major and minor surgeries in the final analysis. This decision reflects the consideration that exposure to the operating room environment, regardless of surgery classification, may influence infection risk.

Using the standard method [13], a CRE infection score was created to assess the likelihood of having a CRE infection (Figure 1). The score was calculated by assigning a value to clinical characteristics based on their aOR. Renal insufficiency was assigned 2 points, malignancy was assigned 2 points, surgery in the past 30 days was assigned 3 points, and carbapenem use in the past 30 days was assigned 4 points, for a maximum total of 11 points. The predicted probability of having a CRE infection was 31.4% if no risk factors were present and increased with additional risk factors, reaching a

Table 3. Multivariable analysis of CRE vs. uninfected controls, CSE vs. uninfected controls, and CRE vs. CSE.

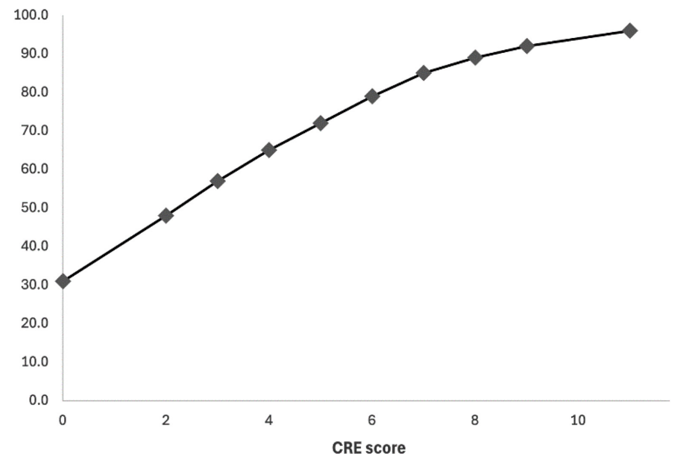
Variable	CRE vs. uninfected controls		CSE vs. uninfected controls		CRE vs. CSE	
	aOR	*p*	aOR	*p*	aOR	*p*
Carbapenem use*	19.1 (3.3-109.6)	0.001	—	—	3.8 (1.6-9.1)	0.002
Surgery*	25.7 (5.7-115.2)	< 0.001	—	—	3.0 (1.5-6.2)	0.003
Renal insufficiency	6.9 (2.0-23.6)	0.002	2.9 (1.1-7.9)	0.03	2.3 (1.1-5.0)	0.03
Malignancy	4.2 (1.6-10.5)	0.003	—	—	2.2 (1.1-4.4)	0.02
Hospital stay*	4.1 (2.2-7.9)	< 0.001	3.9 (2.3-6.8)	< 0.001	—	—
Diabetes mellitus	3.1 (1.1-8.8)	0.03	—	—	—	—
Steroids of IS therapy*	—	—	3.5 (1.1-10.6)	0.03	—	—

*Within the past 30 days. CRE: carbapenem-resistant Enterobacterales; CSE: carbapenem-susceptible Enterobacterales; aOR: adjusted odds ratio; CI: confidence interval; IS: immunosuppressive.

maximum of 96.0% at a risk score of 11. The mean CRE score was 4.2 ± 2.2 in the CRE group and 2.4 ± 2.4 in the CSE group ($p < 0.001$). The area under the receiver operating characteristic (ROC) curve was 0.72 ($p < 0.001$). ROC analysis of the CRE score showed that a cutoff of 1 point is appropriate to maximize sensitivity (96%) but not specificity (33%) in predicting CRE infections. On the other hand, a cutoff of 2.5 points maximizes both sensitivity (75%) and specificity (68%).

Table 4 shows the characteristics of CRE and CSE infection episodes. Regarding the source of the infection, CRE isolates were almost equally distributed between urine and respiratory specimens (29.4% and 22.3%, respectively), followed by surgical wounds and blood, and non-surgical wounds. On the other hand, CSE infections originated mostly from the urine (62.7%), and this difference in distribution was statistically significant ($p < 0.001$). There was a higher prevalence of *Klebsiella* isolates in the CRE group compared to the CSE group where the vast majority were *E. coli* isolates ($p < 0.001$). CRE infections were predominantly hospital-acquired (n = 80; 71.4%) and rarely community-acquired (n = 3; 25.9%), whereas CSE was almost equally distributed between hospital-acquired, healthcare-associated, and community-acquired ($p < 0.001$ between CRE and CSE). As far as outcomes are concerned, the hospital stay of patients with CRE infection was more likely to be complicated by an adverse event compared to CSE infected patients. Patients infected with CRE were more likely to develop septic shock (33; 29.5%) compared to patients infected with CSE (8; 10.7%) ($p = 0.002$), persistence or progression of the infection, persistent bacteremia, and metastatic infection. In addition, patients infected with CRE were more likely to develop acute renal failure (27; 24.1%) compared to CSE infected patients (6; 8.0%) ($p = 0.005$). Finally, all-cause in-hospital mortality and infection-related in-hospital mortality were both significantly higher in the CRE group compared to the CSE group (29.5% and 63.6% vs. 13.3% and 20.0%, respectively; $p = 0.01$). A regression

Figure 1. Association between the CRE score and the probability of developing a CRE infection.



CRE: carbapenem-resistant Enterobacterales. CRE score = sum of individual risk factors (2 points for renal insufficiency, 2 points for malignancy, 3 points for surgery in the past 30 days, 4 points for carbapenem use in the past 30 days).

Table 4. Characteristics of infection episodes CRE vs. CSE.

Variable	CRE (n = 112)	CSE (n = 75)	*p*
Source of infection			**< 0.001**
Urine	33 (29.4)	47 (62.7)	
Respiratory	25 (22.3)	9 (12.0)	
Surgical wound	19 (17.0)	4 (5.3)	
Non-surgical wound/cutaneous abscess	16 (14.3)	7 (9.3)	
Blood	19 (17.0)	8 (10.7)	
Organism			**< 0.001**
E. coli	62 (55.4)	68 (90.7)	
Klebsiella spp.	43 (38.4)	4 (5.3)	
Other	7 (6.2)	3 (4.0)	
Route of acquisition			**< 0.001**
Hospital-acquired	80 (71.4)	30 (40.0)	
Healthcare-associated	29 (25.9)	23 (30.7)	
Community-acquired	3 (2.7)	22 (29.3)	
Complications			
Septic shock	33 (29.5)	8 (10.7)	0.002
Acute renal failure	27 (24.1)	6 (8.0)	0.005
Persistence/progression	44 (39.3)	13 (17.3)	0.001
Persistent bacteremia	9 (8.0)	1 (1.3)	0.04
Metastatic infection	7 (6.3)	0	0.03
ICU admission	46 (41.1)	6 (8.0)	< 0.001
Hospital-acquired infection	46 (41.1)	13 (17.3)	0.001
All-cause in-hospital mortality	33 (29.5)	10 (13.3)	0.01
Infection-related in-hospital mortality	21/33 (63.6)	2/10 (20.0)	0.01

CRE: carbapenem-resistant Enterobacterales; CSE: carbapenem-susceptible Enterobacterales.

analysis revealed that CRE infection is an independent predictor of all-cause in-hospital mortality (aOR = 3.6; 95% CI 1.5-8.7; $p = 0.004$) along with recent hospital stay (aOR 2.1; 95% CI 1.3-3.5; $p = 0.002$)

Discussion

In this study, we found that patients infected with CRE and CSE have different characteristics that would be useful in risk stratification. When compared to uninfected controls, the CRE and CSE groups were both more likely to have a history of chronic comorbid diseases, to have undergone invasive procedures, and to have received prior antibiotics, as shown in the two bivariable analyses.

Several risk factors were generated from the case-control multivariable analysis, and comparing the first two models (CRE vs. uninfected controls and CSE vs. uninfected controls) allows for the identification of variables uniquely associated with CRE infection. Prior antibiotic exposure has been reported in multiple publications as a risk factor for CRE infections, particularly prior exposure to carbapenems [14-19] and fluoroquinolones [20-22], and our study is no exception. Our findings reiterate the need for wise antibiotic selection prior to treating infection to prevent the selection of carbapenem resistance, particularly in view of the limited antibiotic options. In another case-control study by Kofteridis *et al*., similar results were seen for carbapenem-resistant *Klebsiella pneumoniae*, where previous surgery and the presence of renal disease were risk factors [23]. Recent hospital stay was a shared risk factor between CRE and CSE infections with similar odds ratios. Therefore, although it is important in predisposing to infection in general, it cannot be used to predict a CRE infection. While the distinction between major and minor surgeries is clinically relevant, we believe that exposure to the operating room environment itself represents a significant factor in infection risk. This supports our decision to use a model that includes all surgeries, capturing the comprehensive impact of operative exposure on patient outcomes.

In this study, one goal was to develop a risk score to predict the likelihood of patients developing CRE infections by utilizing baseline variables that can identify patients at high risk at an early stage. The aim of this risk-stratification process is to aid in the management of patients with CRE infections. To achieve this, we combined several independent risk factors and presented them in a quantifiable format that is easy to use in a clinical setting. This score provides a comprehensive assessment of patients, allowing clinicians to identify those at the highest risk of developing CRE infections and implement appropriate preventive measures. By having this information, healthcare providers can take proactive steps to minimize the occurrence and spread of CRE infections, ultimately leading to improved patient outcomes. Recently, a group of investigators from Argentina developed a risk score for CRE bacteremia in patients with cancer and hematopoietic stem cell transplantation in which they included three variables, ≥ 10 days of hospitalization until bacteremia (2 points; OR 4.03, previous antibiotics > 7 days (2 points; OR 4.65), and current colonization with KPC-carbapenemase-producing Enterobacterales (5 points; OR 33.08) [24]. Our model was able to identify the unique importance of previous carbapenem use. In addition, we assigned points to each variable proportionate to the respective adjusted odds ratio. Hence, we believe our model is valuable and adds to the existing literature on risk stratification for patients with Enterobacterales infections.

We acknowledge that the scoring system developed in this study has not yet been externally validated. Future studies should aim to validate the scoring system using data from different hospitals or patient populations to confirm its generalizability and enhance its validity. One limitation of this study is the low number of uninfected controls who had undergone surgery. While increasing this number might allow for a more extensive comparison, doing so would prevent us from effectively analyzing surgery as an independent variable. Importantly, the lower frequency of surgeries among uninfected controls does not impact the CRE vs. CSE model or the predictive model outcomes.

Complications were found to be more prevalent in the CRE group compared to the CSE group. This may suggest that the carbapenem resistant pathogens are more virulent strains compared to their susceptible counterparts, leading to the various complications. However, patients infected with CRE infections often carry serious comorbidities that may predispose them to frequent hospitalizations, antibiotic exposure, and infections [25]. In considering infection risk factors related to surgical procedures, we also examined compliance with surgical antimicrobial prophylaxis. At our institution, compliance rates with prophylaxis exceed 90% across all types of surgeries. This high compliance rate underscores our institution's commitment to minimizing infection risk and may influence the observed outcomes related to surgery-associated infections.

There is conflicting evidence in the literature on whether carbapenem resistance is in itself a risk factor for mortality. We found that the percentage of all-cause in-hospital mortality and infection-related in-hospital mortality were both significantly higher in the CRE group compared to the CSE group. In support of these findings is a meta-analysis conducted by Falagas *et al.*, where the number of deaths was significantly higher in patients who were infected with CRE, and in 7 studies, deaths attributable to CRE infections ranged from 26-44% [26]. However, these findings are contradicted by a number of studies where carbapenem resistance was not associated with mortality [26,27]. In our study, CRE infection was not an independent predictor of mortality in the multivariable model. Multiple factors can come into play when addressing the increased mortality in patients infected with CRE. First, the fact that the organisms themselves are resistant to antibiotics would inherently make them more difficult to target with empirical antibiotic regimens where the spectrum may not be broad enough to cover CRE, thereby leading to a delay in appropriate therapy while awaiting culture results. Although not explored in our study, time to appropriate therapy initiation has already been evaluated as a predictor of mortality in patients infected with CRE in the literature and has been found to be predictive of mortality [27]. As mentioned previously, patients who are infected with CRE are generally sicker with a greater number of comorbid conditions, which can be cofounders in patients infected with CRE, leading to higher mortality rates.

Conclusions

We were able to identify risk factors that were uniquely associated with CRE infections. We also developed a simple scoring system that can be used at the bedside to quantify the risk of acquiring a CRE infection. These can be used to risk stratify patients upon diagnosis of infection and before susceptibility testing is available in order to initiate appropriate empiric therapy that would target CRE. CRE infections are associated with increased mortality. Our study further exemplifies the recurring association of CRE infections with prior use of antibiotics, particularly carbapenems, and calls for the judicious use of these broad-spectrum agents.

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Authors' Contributions

Project inception: ZK; Data collection: JES, JA, RWM, TN, AS; Data analysis: GD, ZK; Manuscript writing: JES, RWM, GD, ZK; Manuscript proofing: SK, ZK; Manuscript final editing: ZK

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Conflict of interests

No conflict of interests is declared.

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