Chron Precis Med Res 2024; 5(2): 84-88
DOI: 10.5281/zenodo.12805654

ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

The Effect of Risk Factors on Mortality in Central Line Associated Bloodstream Infections Developing in the Intensive Care Unit

Yoğun Bakım Ünitesinde Gelişen Santral Venöz Kateter İlişkili Kan Dolaşım Yolu Enfeksiyonlarında Risk Faktörlerinin Mortalite Üzerine Etkisi

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ABSTRACT

Aim: Central venous catheters (CVCs) are commonly used for treatment and monitoring in intensive care units. Despite its benefits, CVCs can also result in infectious complications. Central venous catheter associated-bloodstream infection (CVC-BSI) is one of the most common complications of CVC. The aim of the study is to examine the clinical features of CVC-BSIs developing in the intensive care unit and the risk factors affecting mortality.

Material and Method: From 2017 to 2021, a total of 245 patients aged 18 years and older who had developed CVC-BSI and had been admitted to all intensive care units of the hospital were retrospectively evaluated. Patient age, gender, comorbidities, length of stay in the ICU, ICU unit monitored, use of total parenteral nutrition (TPN), isolated microorganism, infection rate, and APACHE 2 score were evaluated.

Results: From 2017 to 2021, a total of 245 patients aged 18 years and older who had developed CVC-BSI and had been admitted to all intensive care units of the hospital were retrospectively evaluated. 171 of 245 patients were 65 years or older. There was a significant difference between being 65 years of age and older and mortality (p:0.002). There was a significant relationship between female gender and mortality (p:0.045). Fifty-seven patients (%32) had femoral catheters, 117 (%65.7) had subclavian/jugular catheters, and 4 (%2.2) had hemodialysis catheters. The study found no significant relationship between the site of CVC insertion and mortality (p:0.539). Likewise, no significant relationship was found between TPN use, secondary infection development, and mortality. While gram-negative bacteria were the most commonly isolated causative agents CNS (coagulase-negative staphylococcus) was the most commonly isolated microorganism in CVC-BSI.

Conclusion: Central venous catheter-related blood stream infections are common and life-threatening infections in intensive care units. It was found that this type of infections particularly increases mortality in female and geriatric patient groups. However, it was revealed that the APACHE 2 score, catheter site, and TPN use are not effective on mortality.

Keywords: Central venous catheter-related bloodstream infectin, Healthcare-associated infection, mortality, APACHE 2

ÖZ

Amaç: Santral venöz kateterler (SVK 'ler) yoğun bakım ünitelerinde tedavi ve izlem amacıyla yaygın olarak kullanılmaktadır. Yararlı etkilerine rağmen CVC enfeksiyöz komplikasyonlara yol açabilir. Santral venöz kateter ilişkili kan dolaşımı enfeksiyonu (SKİ-KDE), SVK' nin en sık görülen komplikasyonlarından biridir. Çalışmanın amacı yoğun bakım ünitesinde gelişen SVK-KDE'lerin klinik özelliklerini ve mortaliteyi etkileyen risk faktörlerini incelemektir.

Gereç ve Yöntem: Hastanemiz tüm yoğun bakım ünitelerinde 2017-2021 yılları arasında yatmış 18 yaş ve üzeri olan, SKİ-KDE gelişmiş 245 hastayı retrospektif olarak değerlendirdik. Hastaların yaş, cinsiyet, ek hastalık, yoğun bakım yatış süresi, takip edildiği yoğun bakım birimi, total parenteral nutrisyon (TPN) kullanımı, izole edilen mikroorganizma, enfeksiyon hızı, APACHE 2 skoru değerlendirildi.

Bulgular: 2017-2021 yılları arasında hastanenin tüm yoğun bakım ünitelerine başvuran, CVC-BSI gelişen 18 yaş ve üzeri toplam 245 hasta retrospektif olarak değerlendirildi. Hastalar 18-99 yaş aralığındaydı. 245 hastanın 171 tanesi 65 yaş ve üzerindeydi. 65 yaş ve üzeri olmanın mortaliteyle arasında anlamlı fark olduğu görüldü (p:0,002). Hastaların 129 (%52,6)'u kadın, 116 (%47,3) erkekti. Kadın cinsiyetle mortalite arasında anlamlı ilişki bulunmuştur (p:0,045). Hastaların 57'sinde (%32) femoral kateter, 117'sinde (%65,7) subklavian/juguler kateter, 4'ünde (%2,2) hemodiyaliz kateteri vardı. Çalışmada SVK'nin yerleştirildiği yer ile mortalite arasında anlamlı bir ilişki bulunamadı (p:0,539). Benzer şekilde TPN kullanımı, sekonder enfeksiyon gelişimi ve mortalite arasında da anlamlı bir fark bulunamadı. SKİ-KDE' de en sık izole edilen patojen gram negatif bakteriler iken, KNS (koagülaz negatif stafilokok) en sık izole edilen mikroorganizmaydı.

Sonuç: Santral venöz kateterle ilişkili kan dolaşım enfeksiyonları yoğun bakım ünitelerinde sık görülen ve yaşamı tehdit eden enfeksiyonlardır. Bu enfeksiyonların özellikle kadın cinsiyet ve yaşlı hasta gruplarında mortaliteyi artırdığı belirlendi. Ancak APACHE 2 skoru, kateter yeri ve TPN kullanımının mortalite üzerine etkili olmadığı saptandı.

Anahtar Kelimeler: Santral venöz kateter ilişkili kan dolaşımı enfeksiyonu, sağlık hizmeti ilişkili enfeksiyon, mortalite, APACHE 2

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Başvuru Tarihi/Received: 02.07.2024
Kabul Tarihi/Accepted: 25.07.2024

INTRODUCTION

Central venous catheters (CVC) are widely used in intensive care units (ICU) and especially in critically ill patients. Considering the critical condition of patients, the use of CVC plays a vital role in hemodynamic monitoring. It allows the administration of intravenous fluids, antibiotics and other drugs, blood products if necessary, and total parenteral nutrition (TPN). Correlated with the increase in catheter use, the incidence of catheter-related bloodstream infections (CVC-BSI) is increasing yearly1. The development of catheter-related bloodstream infection significantly affects the patient's hospitalization duration, mortality rates, hospital costs, prognosis of the disease and patient's life quality (1-3). Due to factors such as patients having chronic illnesses, broad-spectrum antibiotic use, prolonged hospital stays, and multiple invasive procedures, infections are more common in intensive care units. While the infection rate among patients in regular hospital wards is 5-10%, it is 20-25% in intensive care patients. On the other hand, the mortality rate is 53.6% (4,5).

Catheter use is the most common cause of infection (6). Despite many studies on catheter-related infections, the lack of data from developing countries such as Türkiye regarding intensive care units, primarily the surveillance of healthcare-associated infections (HAIs), including CVC-BSI, makes it mandatory to establish such surveillance.

The aim of the study is to examine the clinical features of CVC-BSIs developing in the intensive care unit and the risk factors affecting mortality.

MATERIAL AND METHOD

The study was approved by local ethics committee, dated on 21.11.2022 and with the registration number of 2022/024. From 2017 to 2021, a total of 245 patients aged 18 years and older who had developed CVC-BSI and had been admitted to all intensive care units of our Hospital were retrospectively evaluated. The diagnosis of Healthcare-Associated Infections was made based on the criteria of the Centers for Disease Control and Prevention and the National Health hospital care-Associated Infections Surveillance System. Infectious agents isolated from patients admitted to the ICU were identified using conventional methods and the VITEK2 Compact® (bioMérieux, France) automated system, while antibiotic susceptibility was determined by the disk diffusion method and automated system according to the Clinical and Laboratory Standards Institute (CLSI) criteria.

In patients with clinical signs and symptoms and no other infection focus except the central venous catheter, a diagnosis was made based on the growth of the same microorganism in blood culture samples obtained from the catheter tip or a peripheral vein (7). The second infection episode that occurred in the patient and the microorganisms accepted as skin flora in the culture were not included in the study. Patient age, gender, comorbidities, length of stay in the ICU, ICU unit monitored, use of total parenteral nutrition, isolated microorganism, infection rate, and APACHE 2 score were evaluated.

Statistical Analysis

IBM SPSS v24.0 software was used for data analysis. Minimum, maximum, mean, and standard deviation were used to evaluate demographic data. Chi-square and Fisher's Exact tests were used to evaluate categorical data. Student t-test was used for the analysis of numerical variables. A one-way ANOVA test was used when comparing more than two groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

245 patients who developed CVC-BSI during a 4-year period between 2017 and 2021 were included in our study. The age range of the patients was 18-19. The age range is 70.4±17.4. 129 (52.6%) of the patients were female and 116 (47.3%) were male. 171 of 245 patients were 65 years or older.

There was a significant relationship between older age and mortality (p:0.002). Demographic data and risk factors of patients diagnosed with CVC-BSI are shown in **Table 1**. There was a significant relationship between female gender and mortality (p:0.045). The CRBSI rates are reported as: the percentage of catheters that developed CRBSI; the number of CRBSIs per 1,000 catheter-days. Comparison of the densities of incidence per 1,000 catheter-days of CRBSI, and between the different accesses were done using regression analysis. The central catheter-associated infection rates for the years included in the study are shown in **Figure 1**. There was no statistically significant difference in infection rates between years (p: 0.406). Fifty-seven patients (%32) had femoral catheters, 117 (%65.7) had subclavian/jugular catheters, and 4 (%2.2) had hemodialysis catheters. The study found no significant relationship between CVC insertion site and mortality (p:0.539). Likewise, no significant difference was found between TPN use, secondary infection development, and mortality (**Table 1**). There was a significant difference between APACHE 2 score, TPN use, day of admission, development of the secondary Protocol and death (**Table 1**)

While gram-negative bacteria were the most commonly isolated causative agents, CNS (coagulase-negative staphylococcus) was the most commonly isolated microorganism in CVC-BSI. The isolated microorganisms and their survival status are shown in **Table 2**.

Table 1. The clinical features of the patients and their relationship with mortality

Variable	All (n: 245)	Surviving patients (n: 102)	Deceased patients (n: 143)	p
Age	70.4±17.4	65±18.9	74.3±15	<0.001*
Gender				0.045*
Female	129	46 (35.6%)	83 (64.3%)	
Male	116	56 (48.2%)	60 (51.7%)	
Geriatric status				0,002*
≥65 years	171	60 (35.1%)	111 (64.9%)	
<65 years	74	42 (56.8%)	32 (43.2%)	
Total Parenteral Nutrition Usage				0.581
Yes	118	47 (39.8%)	71 (60.2%)	
No	127	55 (43.3%)	72 (56.7%)	
Site of CVC insertion				0.539
Jugular/subclavian	117	56 (47.9%)	61 (52.1%)	
Femoral	57	26 (45.6%)	31 (54.4%)	
Hemodialysis	4	1 (25%)	3 (75%)	
Secondary infection development				0.496
Yes	4	1 (25%)	3 (75%)	
No	241	101 (41.9%)	140 (58.1%)	
The reason for hospitalization				<0.001*
CVD	53	31 (58.4%)	22 (41.5%)	
COVID-19	37	3 (8.1%)	34 (91.8%)	
Renal failure	25	10 (40%)	15 (60%)	
Trauma	23	15 (65.2%)	8 (34.7%)	
Pneumonia	20	9 (45%)	11 (55%)	
CHF	14	3 (21.4%)	11 (78.5%)	
General condition disorder	12	4 (33.3%)	8 (66.6%)	
Malignancy	8	6 (75%)	2 (25%)	
Sepsis	7	2 (28.5%)	5 (71.4%)	
Postoperative follow-up	6	1 (16.6%)	5 (83.3%)	
CAD	6	4 (66.6%)	2 (%33.3%)	
Other neurological disorders	3	3 (100%)	0 (0.0%)	
Other	26	10 (38.4%)	16 (61.5%)	
Microorganism				0.126
Gram negative	112	40 (35.7%)	72 (64.2%)	
Gram positive	76	39 (51.3%)	37 (48.6%)	
Candida	57	23 (40.3%)	34 (59.6%)	

CVC: central venous catheter, CVD: cerebrovascular disease, CHF: congestive heart failure, COPD: chronic obstructive pulmonary disease, CAD: coronary artery disease. *: p<0.05

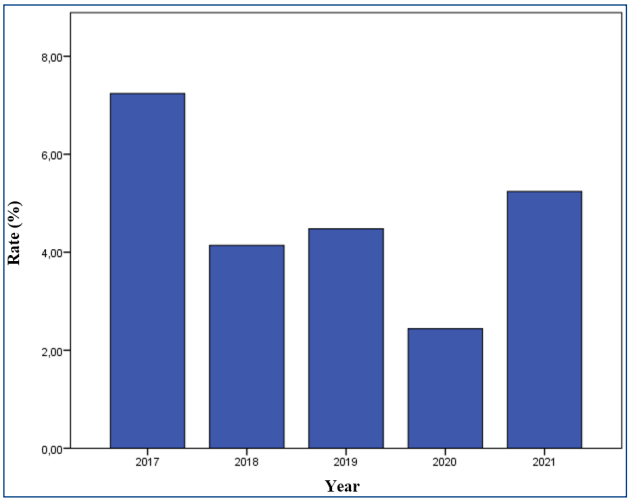

Figure 1. Catheter-related infection rates

Table 2. CVC-BSI causative microorganisms

Microorganism	All	Alive	Not alive
CNS	60	29 (48.3%)	31 (51.6%)
Candida nonalbicans	45	17 (37.7%)	28 (62.2%)
Acinetobacter baumanii	38	8 (21.0%)	30 (78.9%)
Klebsiella pneumonie	32	12 (37.5%)	20 (62.5%)
Enterococcus faecium	10	4 (40%)	6 (60%)
Enterococcus faecalis	9	4 (44.4%)	5 (55.6%)
Pseudomonas aeruginosa	8	3 (37.5%)	5 (62.5%)
Staphylococcus aureus	7	6 (85.7%)	1 (14.2%)
Enterobacter cloaca	3	1 (33.3%)	2 (66.6%)
Klebsiella spp.	3	0 (0.0%)	3 (100%)
Acinetobacter lwafii	3	1 (33.3%)	2 (66.6%)
Serratia marcescens	2	2 (100%)	0 (0.0%)
Other	7	6 (85.7%)	1 (14.2%)

CNS: Coagulase-negative staphylococcus CVC-BSI: Central venous catheter associated-bloodstream infection

DISCUSSION

Central venous catheter-related infections, particularly CVC-BSI, are common and life-threatening infections in intensive care units. In our study, It was found that this type of infection particularly increases mortality in female and geriatric patient groups. In our study, when examining the factors influencing the development of CVC-BSI in patients in the ICU, it was found that being over 65 years old and being female had an effect on mortality. It has been observed that there is a significant increase in mortality in the geriatric patient group (65 years and older) admitted to intensive care, especially compared to younger patients.

The rate of CVC-BSI in our intensive care unit is higher compared to the rate reported by the National Nosocomial Infection Surveillance Network (NNISN). In the study conducted by Meriç et al., the presence of comorbidity. was not a risk factor for CVC-BSI development, but having more than two comorbid diseases was significant in terms of mortality (8). In the same study, the relationship between healthcare-associated infections and mortality in intensive care units of public hospitals was examined; being over 60 years old, having a high APACHE 2 score, and undergoing intubation and central venous catheterization were defined as risk factors. On the other hand, influential risk factors for the development of infection included staying in the ICU for more than seven days, receiving sedation, having a history of surgical intervention, and having respiratory failure. When the risk factors of device-related infections were examined, advanced age was found to be an important risk factor for CI-BSI (9). The most common comorbid disease in our study was cerebrovascular disease and there was no relationship with infection or mortality. In a study by Ahsen et al., cerebrovascular disease was the most common comorbid disease (10).

Immunosuppression, burns, TPN use, extreme ages, hospitalization for more than 3 days, femoral and jugular catheterization are reported as risk factors for CRBSI (11). In our study, a significant relationship between APACHE 2 score and mortality was not found. It is thought that the fact that only patients who developed CVC-BSI were evaluated in our study may have had an effect on this result. Knaus et al. showed a relationship between APACHE 2 score and mortality (12). In another study, CVC-BSI in intensive care patients was associated with total parenteral nutrition (TPN) use, increasing disease severity, and the number of days on mechanical ventilation (13). In catheter-related infections, there is an increase in infections when the catheterization period exceeds 5-7 days. Some studies have indicated that planned catheter replacement does not provide any advantage over clinical indication-based replacement. However, as catheter tip colonization and bloodstream infections increase with the duration of catheterization, debates continue regarding planned replacement (14).

The rate of CVC-BSI ranges from 3-20%, depending on the catheter types used. On the other hand, it is still controversial which catheterization site carries a higher infection risk. Some studies indicate that the femoral entry site is more risky, while others indicate the jugular entry site (15,16). In the studies by Menteş et al., it was determined that subclavian catheterization is associated with a lower incidence of infection compared to other sites and carries a 2.5 times lower risk of catheter-related bacteremia than jugular catheterization (14). It was emphasized that the subclavian vein should be preferred over other catheter insertion sites to minimize catheter-related infections. The infection rate also increases in urgently applied catheters that remain in place for more than 72 hours (15,16). Lorente et al. found that the risk of developing CVC-BSI is higher in catheters inserted through the femoral vein (17). Other studies have also recommended minimizing the use of the femoral vein to prevent catheter-related bloodstream infections (18,19). However, in our study, despite the most commonly used catheter being inserted through the femoral vein, no significant difference was found between the catheter site and the development of infection. The virulence factors of microorganisms that cause CVC-BSI are essential in the development of catheter infections. Particularly, *S. epidermidis* and *P. aeruginosa* attach to the catheter through the adhesive glycocalyx "slime" factor and are protected in the host's defense cells (15). In our study, the most commonly encountered causative agents were *K. pneumoniae* and *S. aureus*, which had high virulence.

According to the Türkiye National Healthcare-Associated Infections Surveillance Network 2021 report, the rate of CVC-BSI in adult intensive care units has a weighted overall average of 2.9-6.7 per thousand (20). In our study, conducted between 2017-2021, the overall infection rate for all intensive care units was found to be 4.7, which falls within the average range for Türkiye. There was no significant difference in infection rates between the years.

CONCLUSION

Central venous catheter-related infections, particularly CVC-BSI, are common and life-threatening infections in intensive care units. It was found that this type of infection particularly increases mortality in female and geriatric patient groups. However, it was revealed that the APACHE 2 score, catheter site, and TPN use are not effective on mortality. It should be highlighted that it

is crucial to prevent these infections that can lead to mortality and morbidity. Therefore, placing the correct indication for central venous catheterization, following sterilization rules, knowing the common causative agent and initiating appropriate antibiotic therapy are essential factors that can be changed to prevent CVC-related infections.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Karatay University Faculty of Medicine Ethics Committee (Date: 21.11.2022, Decision No: 2022/024).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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