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# Investigation of the Factors Associated with Mortality in Catheter-Related Bloodstream Infections: Five-Year Observation

## Kateter İlişkili Kan Dolaşımı Enfeksiyonlarında Mortalite ile İlişkili Faktörlerin Araştırılması: Beş Yıllık Gözlem

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**ABSTRACT**

**Aim:** Intravenous catheter use can cause various infections ranging from infection at the site of catheter entry to bacteremia and colonization. The purpose of this study was to identify the causative micro-organisms, and effects on morbidity-mortality of catheter-related bloodstream infections developing over the last five years.
**Material and Methods:** Data for 194 patients who underwent central intravenous catheter insertion in our hospital's intensive care unit and other departments between November 2014 and August 2019 were analyzed retrospectively. Blood samples taken from the catheter or the catheter tip, and blood samples collected simultaneously from the peripheral vein were included in the study, and culture results were recorded. Patients' demographic data and the effects of the factors identified on morbidity and mortality were subjected to statistical analysis.
**Results:** Ninety-two (47.4%) of the 194 patients included in the study were female and 102 (52.6%) were male, and mortality rate was 62.4% (n=121). The frequency of underlying medical conditions such as asthma, congestive heart failure, and cerebrovascular event, and receiving treatments such as immunosuppression, transfusion, tracheostomy, nasogastric tube, and mechanical ventilation were higher in mortal cases than non-mortal cases. A total of two hundred and forty microorganisms were detected in 194 patients, 121 (50.4%) of which were Gram negative bacteria, while 68 (28.3%) were Gram positive bacteria, and 51 (21.3%) were Candida species.
**Conclusion:** As a result, it was observed that the advanced age, underlying diseases and presence of resistant microorganisms were higher in mortal cases.
**Keywords:** Catheter-related bloodstream infections; mortality; advanced age.

**ÖZ**

**Amaç:** İntravenöz kateter kullanımı hastalarda kateter girişindeki enfeksiyondan bakteriyemi ve kolonizasyona kadar çeşitli enfeksiyonlara neden olabilir. Bu çalışmanın amacı, son beş yılda gelişen kateter ilişkili kan dolaşımı enfeksiyonlarının etken mikroorganizmalarını tanımlamak ve morbidite-mortalite üzerine etkisini ortaya koymaktır.
**Gereç ve Yöntemler:** Kasım 2014 ve Ağustos 2019 tarihleri arasında hastanemizin yoğun bakım ünitesinde ve hastanemizin diğer bölümlerinde santral intravenöz kateter yerleştirilen 194 hastanın verileri geriye dönük olarak incelendi. Kateterden veya kateter ucundan alınan kan örnekleri ve periferik venden aynı anda toplanan kan örnekleri çalışmaya dahil edildi ve alınan kan örneklerinin kültür sonuçları kaydedildi. Hastaların demografik verileri ile saptanan faktörlerin morbidite ve mortalite üzerine olan etkileri istatistiksel olarak değerlendirildi.
**Bulgular:** Çalışmaya dahil edilen 194 hastanın 92'si (%47,4) kadın, 102'si (%52,6) erkek cinsiyette idi ve mortalite oranı %62,4 (n=121) idi. Astım, konjestif kalp yetmezliği ve serebrovasküler olay gibi altta yatan tıbbi durumların sıklığı ve immünosupresyon, transfüzyon, trakeostomi, nazogastrik tüp ve mekanik ventilatör uygulanması gibi tedavilerin sıklığı mortal olgularda mortal olmayan olgulardan daha fazla idi. Yüz doksan dört hastada toplam 240 adet mikroorganizma üremesi saptanmış olup bunların 121 (%50,4)'i Gram negatif bakteri, 68 (%28,3)'i Gram pozitif bakteri ve 51 (%21,3)'i *Candida* spp idi.
**Sonuç:** Sonuç olarak ileri yaş, altta yatan hastalıklar ve dirençli mikroorganizma varlığının mortal olgularda daha fazla olduğu görülmüştür.
**Anahtar kelimeler:** Kateter ilişkili kan dolaşımı enfeksiyonu; mortalite; ileri yaş.

## INTRODUCTION

In addition to raising costs, healthcare-related infections extend hospital stays and exacerbate poor prognosis and mortality (1). Catheter-related bloodstream infection (CRBSI) is the third most common nosocomial infection after ventilator-associated pneumonia and catheter-related urinary tract infection. The incidence of CRBSI decreases when protective bundles and infection control measures are applied, although the rate of infection may vary depending on the site of the catheter, the size of the hospital, and intensive care conditions (2). More than two billion intravenous devices are applied annually worldwide (3). In the USA, 250,000 patients are diagnosed with CRBSI every year, an average of 80,000 of whom are being treated in intensive care units (4). In addition to prolonging hospital stays and causing higher costs, CRBSI is one of the deadliest infections, with a mortality rate of 12-25% (5-7). Central venous catheters (CVCs) allow micro-organisms to enter and colonize the body. These pathogenic micro-organisms adhere to the surface of the catheter within the first 24 hours and form a biofilm layer that prepares the ground for infection by competing with the host cells (8,9). This allows micro-organisms to protect themselves against both antimicrobials and the immune system, and catheters need to be removed in most cases (10). Micro-organisms frequently implicated in CVC infections include *Acinetobacter baumannii*, *Staphylococcus epidermidis*, *Enterococcus faecium*, and *Candida albicans* (9,11).

The purpose of this study was identify the causative micro-organisms, and the effects on morbidity-mortality of CRBSI developing in our hospital over the last five years.

## MATERIAL AND METHODS

Data for 194 patients in whom CVCs were inserted in our hospital's intensive care unit and other departments between November 2014 and August 2019 were analyzed retrospectively. Development of CRBSI was identified from data from the laboratory and clinic-based active surveillance system based on US Centers for Disease Control and Prevention criteria (2). The culture results of blood samples taken from the catheter or the catheter tip and blood samples taken from the peripheral vein were examined. Catheter samples were seeded using the semi-quantitative culture method. Culture plates were incubated at 37° C for 48 hours. Cultures from peripheral venous and catheter blood were incubated in a BACTEC 9120 (Becton Dickinson, USA) automated blood culture device. Conventional methods and/or the VITEK 2 automated system (bioMérieux, France) were used to identify the growing bacteria. Antibiotic susceptibility tests were performed according to "Clinical and Laboratory Standards Institute (CLSI)" standards (12) before 2016, and in line with "European Committee on Antimicrobial Susceptibility Testing (EUCAST)" standards (13) after 2016. Additional diseases such as asthma, hypertension, diabetes, and risk factors including mechanical ventilation, transfusion and immunosuppression were investigated. Infection Control Committee surveillance records were used to collect all data.

This study was approved by the Clinical Research Ethics Committee of Düzce University Medical Faculty on 15.06.2020 with decision number 130 and was conducted according to the Helsinki Declaration principles.

### Statistical Analysis

SPSS v.22 software was used for data analysis. The data were expressed as numbers and percentages. Relationships between categorical variables were examined by Pearson chi-square, Fisher's exact and Fisher-Freeman-Halton tests. A p value of $<0.05$ was considered significant.

## RESULTS

One hundred ninety-four patients, 92 (47.4%) female and 102 (52.6%) male, were included in the study. One hundred twenty-one (62.4%) patients with CRBSI died. One hundred eleven (57.2%) patients were aged 65 and over, and 83 (42.8%) were under 65. The mortality rate was significantly higher in patients aged 65 and over ($p<0.001$). Twenty-eight (14.4%) patients were treated on the wards and 166 (85.6%) in intensive care units. While the frequency of patients hospitalized in the internal intensive care unit (IICU) was higher in mortal cases than the non-mortal cases, the frequency of patients hospitalized in internal ward and pediatric intensive care unit (PICU) were lower in mortal cases than the non-mortal cases ($p<0.001$). Analysis of catheter sites revealed similar relationships between jugular, femoral, umbilical, or subclavian catheter applications and mortality rates ($p=0.903$). Analysis of comorbidities and risk factors revealed that the presence of asthma, congestive heart failure (CHF) and cerebrovascular event (CVE) were associated with mortality rates ($p=0.015$, $p=0.033$ and $p=0.039$, respectively). While the frequency of immunosuppression ($p=0.048$), transfusion ($p=0.046$), nasogastric tube ($p<0.001$), and mechanical ventilation ($p=0.005$) in mortal cases was higher than the non-mortal cases, the frequency of enteral nutrition ($p=0.011$) was lower in mortal cases than the non-mortal cases. While infection with single or multiple factors caused no statistically significant difference in mortality rates ($p=0.167$), the mortality rate in resistant microorganism growth was higher than that in susceptible agent growth ($p=0.004$). All these data are summarized in Table 1.

A total of 240 microorganisms were detected in 194 patients in the study. Infection occurred in 149 (76.8%) patients with a single agent and in 45 (23.2%) of patients with multiple agents. One hundred twenty-one (50.4%) of the 240 micro-organisms were identified as Gram negative bacteria, 68 (28.3%) as Gram positive bacteria, and 51 (21.3%) as Candida species. The distribution of agents is shown in Table 2. Extended spectrum beta-lactamase (ESBL) positivity rates were 62% in *Klebsiella pneumoniae* strains and 60% in *Escherichiae coli* strains, while the carbapenem resistance rate was 34% in *K. pneumoniae* strains. In addition, two carbapenem-resistant *Enterobacter aerogenes* and one colistin-resistant *Acetinobacter baumannii* strain were detected. Vancomycin resistance was detected in three out of 17 *E. faecium* strains among the enterococci.

## DISCUSSION

The 2019 National Vascular Access Management Guide lists risk factors as prolonged hospitalization before catheter insertion, colonization of the inserted area and lumen, long-term catheter insertion, presence of internal jugular and femoral catheter in adults, prematurity, neutropenia, lack of intensive care nurses, catheter care

errors, total parenteral nutrition (TPN) support, and blood transfusion in children (10,11). The site of CVC is important for the risk of developing complications such as thrombophlebitis due to the local skin flora causing the infection (14-16). One randomized controlled study comparing the femoral and subclavian catheter insertion sites reported a higher colonization rate in the femoral region (17). Another study compared the subclavian and internal jugular veins and reported that catheters inserted into the internal jugular vein were exposed to higher colonization (18). A study conducted in 2017 reported infection rates of 36% for the internal jugular vein, 35.5% for the femoral vein, and 30% for the subclavian vein (19).

**Table 1.** Distribution of the features of patients and agents in mortal and non-mortal cases, n (%)

| | Mortal (n=121) | Non-mortal (n=73) | p |
|---|---|---|---|
| **Gender** | | | |
| Female | 62 (51.2) | 30 (41.1) | 0.170 |
| Male | 59 (48.8) | 43 (58.9) | |
| **Age** | | | |
| ≥65 | 82 (67.8) | 29 (39.7) | **<0.001** |
| <65 | 39 (32.2) | 44 (60.3) | |
| **Clinics** | | | |
| SICU | 62 (51.2)[a] | 35 (47.9)[a] | **<0.001** |
| IICU | 48 (39.7)[a] | 11 (15.1)[b] | |
| Internal ward | 9 (7.4)[a] | 17 (23.3)[b] | |
| PICU | 1 (0.8)[a] | 9 (12.3)[b] | |
| Surgical ward | 1 (0.8)[a] | 1 (1.4)[a] | |
| **Catheter type** | | | |
| Femoral | 72 (59.5) | 42 (57.5) | 0.903 |
| Juguler | 35 (28.9) | 21 (28.8) | |
| Subclavian | 13 (10.7) | 10 (13.7) | |
| Umbilical | 1 (0.8) | 0 (0.0) | |
| **Risk factors*** | | | |
| Asthma | 9 (7.4) | 0 (0.0) | **0.015** |
| CHF | 26 (21.5) | 7 (9.6) | **0.033** |
| CVE | 16 (13.2) | 3 (4.1) | **0.039** |
| Hypertension | 60 (49.6) | 36 (49.3) | 0.971 |
| Diabetes | 39 (32.2) | 17 (23.3) | 0.183 |
| CAD | 22 (18.2) | 8 (11.0) | 0.178 |
| CRF | 19 (15.7) | 14 (19.2) | 0.533 |
| COPD | 13 (10.7) | 3 (4.1) | 0.104 |
| Enteral feeding | 109 (90.1) | 56 (76.7) | **0.011** |
| TPN | 53 (43.8) | 29 (39.7) | 0.578 |
| Immunosuppression | 52 (43.0) | 21 (28.8) | **0.048** |
| Transfusion | 91 (75.2) | 45 (61.6) | **0.046** |
| Nasogastric tube | 108 (89.3) | 46 (63.0) | **<0.001** |
| Mechanical ventilation | 93 (76.9) | 42 (57.5) | **0.005** |
| Hemodialysis | 43 (35.5) | 21 (28.8) | 0.331 |
| **Agent features** | | | |
| Single agent | 89 (73.6) | 60 (82.2) | 0.167 |
| Multiple agent | 32 (26.4) | 13 (17.8) | |
| **Resistancy state** | | | |
| Group of resistant agent | 95 (78.5) | 43 (58.9) | **0.004** |
| Group of sensitive agent | 26 (21.5) | 30 (41.1) | |

SICU: Surgical intensive care unit, IICU: Internal intensive care unit, PICU: Pediatric intensive care unit, *: more than one factors in a patient, CHF: Congestive heart failure, CVE: Cerebrovascular event, CAD: Coronary artery disease, CRF: Chronic renal failure, COPD: Chronic obstructive pulmonary disease, TPN: Total parenteral nutrition, Group of resistant agent: Carbapenem resistant Gram negative bacteria, methicillin resistant staphylococcus, vancomycin resistant enterococcus and Candida spp., Group of sensitive agent: Vancomycin sensitive enterococcus, methicillin sensitive staphylococcus, carbapenem sensitive Gram negative bacteria and others

In the present study, rates of use were 58.5% in the femoral vein, 29% in the jugular vein, 12% in the subclavian vein, and 0.5% in the umbilical vein. Although the highest rate of use was observed in the femoral vein, analysis of mortality rates revealed identical values for the femoral catheter and jugular catheter, at 63%, and a rate of 57% for the subclavian catheter. Although mortality rates for the subclavian catheter were relatively low, no significant difference in mortality rates was detected among the groups.

Age and the presence of risk factors such as immunosuppression and malignancy are important factors in the diagnosis of CRBSI (20). In a study by Hajjej et al. (21), the presence of diabetes mellitus or presence of sepsis at the time of catheter insertion, prolonged catheterization, and the use of antibiotics before insertion, even in a single dose, were identified as independent risk factors for the development of infection, with a reported mortality rate of 21.8%. In Wittekamp et al. (22), the incidence of infection was high in central venous and arterial catheters, but even higher in arterial catheters. In a study from Turkey, advanced age, being treated in intensive care, use of antibiotics during catheterization, and prolonged catheterization were associated with the development of infection (14). In the present study, 57.2% of patients were over 65, 85.6% were being treated in the intensive care unit, and 37.6% were immunosuppressive. When the departments in which patients were hospitalized were compared, mortality rates were higher in the IICU. We attributed this to patients receiving treatment in IICU being hospitalized for longer periods due to advanced age and

**Table 2.** Distribution of causative microorganism species

| Microorganism (n=240) | n (%) |
|---|---|
| **Gram negative bacteria species** | **121 (50.4)** |
| *Acinetobacter baumanni* | 44 (18.3) |
| *Klebsiella pneumonia* | 29 (12.1) |
| *Pseudomonas aeruginosa* | 18 (7.5) |
| *Escherichiae coli* | 5 (2.1) |
| *Serratia marcescens* | 5 (2.1) |
| *Enterobacter cloacae* | 5 (2.1) |
| *Enterobacter aerogenes* | 4 (1.7) |
| *Klebsiella oxytoca* | 3 (1.3) |
| *Pseudomonas putida* | 2 (0.8) |
| *Stenotrophomonas maltophilia* | 2 (0.8) |
| *Burkholderia cepaciae* | 2 (0.8) |
| *Morganella morganii* | 1 (0.4) |
| *Pantoae* spp | 1 (0.4) |
| **Gram positive bacteria species** | **68 (28.3)** |
| MRCNS | 31 (12.9) |
| *Enterococcus faecium* | 17 (7.1) |
| *Enterococcus faecalis* | 8 (3.3) |
| MRSA | 7 (2.9) |
| MSSA | 4 (1.7) |
| *Corynebacterium* spp. | 1 (0.4) |
| **Fungal types** | **51 (21.3)** |
| *Candida albicans* | 26 (10.8) |
| *Candida tropicalis* | 10 (4.2) |
| *Candida parapsilosis* | 9 (3.8) |
| *Candida glabrata* | 3 (1.3) |
| *Candida famata* | 1 (0.4) |
| *Candida lipolytica* | 1 (0.4) |
| *Candida guilliermondi* | 1 (0.4) |

MRCNS: Methicillin-resistant coagulase negative staphylococcus, MRSA: Methicillin-resistant *Staphylococcus aureus*, MSSA: Methicillin-sensitive *Staphylococcus aureus*

comorbid disease, and to infections that developed with more resistant agents.

The present study also examined the effects of comorbid conditions, enteral nutrition, TPN, and mechanical ventilation on mortality rates. Asthma, CHF, CVE, and other risk factors such as transfusion, immunosuppression, tracheostomy, nasogastric tube, mechanical ventilation, and pulmonary artery catheter (PAC) were associated with mortality. While enteral nutrition is associated with mortality, it has been reported that TPN is not (10). This may be due to enteral nutrition, tracheostomy, nasogastric tube, PAC and mechanical ventilation being the most frequently applied interventions or treatments, especially in long-term hospitalizations and intensive care patients, and to the majority of our patients being treated in the ICU. Pichitchaipitak et al. (23) reported that long-term TPN use increased the rate of CRBSI.

While Gram-negative bacilli or *S. aureus* may be an agent in catheters inserted for a short period, Coagulase-negative staphylococci are generally factors in extended catheter insertion (10,24). In their study of hematology, oncology, and intensive care patients, 78% of whom were immunosuppressive, Demirel et al. (25) observed that half of the factors consisted of Gram negative bacteria (50%) and that Gram positive bacteria consisted of only 24.5%. The rate of Candida species was 23.9%. In a study involving hemodialysis patients, catheter infection factors were reported to be 60% Gram positive bacteria, 38% Gram negative bacteria, and 2% *Candida* spp. The authors of that study reported that only 20% of these patients had temporary catheters, the remaining 80% having permanent catheters, and that the incidence of infection in the temporary catheter group was higher than that in the permanent catheter group (26). All patients in the present study had temporary catheters, and the fact that information of the numbers of days with catheters could not be provided is a limitation of our study.

The relationship between susceptibility and mortality has also been investigated in recent research. In one study conducted in the hemodialysis unit, the reported carbapenem susceptibility of Gram-negative bacteria was 87.5%, with an overall mortality rate of 10% (26). Analysis of the effects of micro-organisms on mortality in the present study revealed no significant difference between infections with single or multiple factors in terms of mortality rates. At least one resistant agent or *Candida* spp. was detected in the cultures of 95 patients who died (78.5%). When our patients were divided into two groups based on the resistance status of microorganisms, the mortality rate was significantly higher in the group with resistant agents compared to the other group.

## CONCLUSION

In conclusion, central catheter insertion is an invasive procedure and may result in morbidity and mortality by preparing the ground for infection. The purpose of this study was to contribute to the literature for Turkey by evaluating our own hospital's catheter infection data in the preceding five years. Advanced age and hospitalization in the IICU were more common in the mortal cases than the non-mortal cases. In addition, the frequency of resistant microorganisms in CRBSI was higher in mortal cases than non-mortal cases.

**Ethics Committee Approval:** The study was approved by the Ethics Committee of Düzce University Faculty of Medicine (15.06.2020, 130).

**Conflict of Interest:** None declared by the authors.

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