

Kardiyovasküler Girişimler için Kullanılan Santral Venöz Kateterlerden İzole Edilen Patojenlerin Değerlendirilmesi

Evaluation of Pathogens Isolated from Central Venous Catheters Used for Cardiovascular Interventions

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ÖZ

Amaç: Bu çalışmanın amacı kardiyovasküler girişimler nedeniyle santral venöz kateterizasyon uygulanan hastalarda izole edilen patojenleri değerlendirmektir.

Materyal ve Metot: Hastalar, kateter ilişkili infeksiyonların gelişimi için günlük olarak izlendi. Nisan 2017 ile Temmuz 2019 tarihleri arasında, kateterizasyondan sonra akıntı, ateş, ağrı, lenfadenopati ve kaşıntı gibi infeksiyon semptomları gösteren hastalar geriye dönük çalışmaya dahil edildi. Hastaların kateter tipleri, kateter yerleştirme bölgeleri, toplam kateterizasyon süreleri, kültür sonuçları, patojenlerin antimikrobiyal ilaçlara karşı duyarlılıkları ve dirençleri kaydedildi ve analiz edildi.

Bulgular: Çeşitli endikasyonlar nedeniyle santral venöz kateterizasyon uygulanan 86 hasta çalışmaya alındı. Hastaların ortalama yaşı 52,70±17,82 yıl idi. Hastaların % 62,79'unda bakteri üremesi mevcuttu. En sık kateter yerleştirme yerleri sağ subklavyen ven, sağ juguler ven ve sağ femoral venlerdi. En sık izole edilen mikroorganizma % 25,58 ile *S.aureus* idi ve onu *E. coli* (%6,98), *S. haemolyticus* (%5,81) ve *K. pneumonia* (%5,81) izlemekte idi. *S. aureus*'un vankomisin ve linezolid duyarlı olduğu tespit edildi.

Sonuç: Bu infeksiyonların insidansını etkileyen faktörler arasında kateter yerleştirme bölgesi, kateterizasyon süresi, kateter seçimi ve uygulayıcıların becerileri bulunur. Literatürdeki kateterle ilişkili infeksiyonlarda izole edilen patojenler ve bunların antimikrobiyal ajanlara duyarlılığı ve direnci hakkındaki veriler çoğunlukla eskidir. Bu konuda daha kapsamlı, çok merkezli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Kateterizasyon, kateterle ilişkili kan dolaşımı infeksiyonları, patojenler, *S. aureus*.

ABSTRACT

Objective: To evaluate the isolated pathogens in patients who underwent central venous catheterization due to cardiovascular procedures.

Materials and Methods: Patients were monitored daily for the development of catheter related infections. Between April 2017 and July 2019, patients who exhibited infection symptoms like discharge, fever, pain, lymphadenopathy and itching after the catheterization were included in this retrospective study. Patients' catheter types, catheter insertion sites, total catheterization durations, culture results, sensitivities and resistances of pathogens against antimicrobial drugs were recorded and analyzed.

Results: Eighty-six patients who underwent central venous catheterization due to various indications were included. Mean age of patients was 52.70±17.82 years. Bacterial growth was found in 62.79% of patients. The most common catheter insertion sites were right subclavian vein, right jugular vein and right femoral vein. The most commonly isolated microorganism was *S. aureus* by 25.58% followed by *E.coli* (6.98%), *S. haemolyticus* (5.81%) and *K.pneumonia* (5.81%). *S. aureus* was detected to be sensitive to vancomycin and linezolid.

Conclusion: Factors affecting incidence of these infections include catheter insertion site, catheterization duration, catheter selection and skills of the practitioners. Data in literature about the pathogens isolated in catheter-related infections and their sensitivity and resistance to antimicrobial agents are mostly old. Further comprehensive, multicenter studies are needed on this issue.

Keywords: Catheterization, catheter related bloodstream infections, pathogens, *S.aureus*.

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INTRODUCTION

Cardiac catheterization is an invasive intervention used for achieving an acceptable vascular access for diagnosis and treatment of various cardiovascular diseases. Cardiac catheterization is used to diagnose a condition or to fix a problem by reaching the right or left side of the heart with a fine-bore tube passing through a cannula inserted into peripheral arteries or.¹ The catheter is inserted from the groin or arm under the guidance of fluoroscopy, and has a camera at the top, which is used to display the desired position.² Advancements in the catheterization techniques, increased experience and pharmacologic developments have increased indications for catheterization procedures. Although these procedures are safe, they have numerous systemic and local potential complications. Among these complications, catheterization-related bloodstream infections (CRBSIs) are infrequent, but they can be dangerous and fatal if the recommended measures are not considered by healthcare providers. In addition, even a low incidence of these infections can have serious consequences, as these procedures are performed in great numbers each year. CRBSIs may lead to prolongation of hospital stay, increased costs and even death. Several risk factors have been described for CRBSIs, which can be widely categorized as patient-related, catheter-related and medical staff-related factors.³ In patients with intravenous catheters, CRBSI should be clinically suspected when fever, chills, and other signs of sepsis begin, even if there are no local signs of infection, especially if an alternative source cannot be detected.⁴

The pathogenesis of CRBSI is a complex process. CRBSI begins either by the colonization of the catheter by skin flora or as a local infection of the intradermal part of the catheter site. Microorganisms adhere to the catheter surface and extend to the catheter portion within the vasculature. From here, colonized organisms enter the bloodstream and seed into the distant tissues of the body. Once the colonization occurs, there is an opportunity for the development of infection. Although the relationship between the level of colonization and infection is not easily understandable, there is evidence that local and bloodstream infections are associated with the number of microorganisms on the catheter. The most commonly encountered pathogens in CRBSI include *S. aureus*, coagulase negative *staphylococci*, yeasts,

enterococci and various gram negative bacilli.

The annual incidence of CRBSI is 80,000 in the USA with 28,000 deaths and 2.3 billion dollars cost.⁵ However, this incidence may be actually underestimated because of the 5 to 10 day delay between the procedure performed and the development of common signs and symptoms of the infection. CRBSI have been shown to prolong the stay in the intensive care unit (ICU) for 2.4 days and the duration of hospitalization for 7.5 days on average.⁶

It is crucial to continuously perform epidemiologic studies and to keep data updated on CRBSIs that are rare, but important complications leading to significant increase in costs, morbidity and mortality. Therefore, the objective of this study was to evaluate CRBSI and the pathogens isolated in the patients who underwent catheterization due to various reasons in the cardiovascular clinics of our hospital.

MATERIALS AND METHODS

Before the beginning of the study, the necessary approval was received from the local ethics committee of Mogadishu Somali Turkey Recep Tayyip Erdogan Training and Research Hospital (Date: 07.08.2019, decision no: 132). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Data of 86 patients hospitalized in the cardiovascular clinic and catheterized for several cardiovascular procedures such as hemodialysis access, peripheral bypass operations and repair of vascular injury following blunt or penetrating trauma between April 2017 and July 2019 were obtained from the hospital recording system and retrospectively evaluated. Catheters were inserted during the cardiovascular procedures into the right or left subclavian veins, jugular veins or femoral veins with Seldinger technique under aseptic precautions. Temporary or permanent hemodialysis catheters, or large lumen central venous catheters for blood and fluid replacement were inserted to the patients. Patients were monitored daily for the development of CRBSI during the study period. Patients who exhibited infection symptoms such as discharge, fever, pain, lymphadenopathy (LAP) and itching after the catheterization procedure were included in the study. Patients with known infection source (fever, pneumonia, urinary tract infection, cellulitis and septicemia) confirmed with history, clinical

examination, blood culture, chest X-ray, urinalysis and other investigations; immunocompromised patients, those with infective endocarditis and whose catheter were inserted in another center were excluded from the study.

Patients' demographic data such as age and gender, biochemical laboratory outcomes, catheter type, catheter insertion site, total catheter weeks in situ, comorbidities, infection symptoms, culture results, and sensitivity and resistance of pathogens against antimicrobial drugs were recorded and analyzed.

Sample Collection and Analysis: Catheters removed because of no need anymore or occlusion were not included in the analysis and only the catheters suspected to be infected in patients who exhibited symptoms were included. In all patients, first catheter sites were meticulously cleaned. Each catheter was carefully removed using sterile forceps and attention was given to not contact with the skin. Four to five cm of the catheter tip was cut with a sterile scissor and put into a sterile container. The samples were then sent to the laboratory for analysis within one hour.

All catheter tips were processed in thioglycollate medium for 24 hours. Subculture was then performed in four media as two blood agars for aerobic and anaerobic conditions, MacConkey agar and chocolate agar. A colony number >15 on each plate was considered significant and taken to further process.

Swabs were prepared from the plates showing growth and stained with Gram method. Gram positive cocci were analyzed in the clusters with catalase and tube coagulase tests, and catalase and coagulase positive tubes were defined as *staphylococci*. Whereas, Gram negative bacilli were determined up to the species level according to the protocol described by Duguid et al.⁷

Blood samples were simultaneously collected from the peripheral vascular system of the patients and analyzed. In conclusion, a number of colonies ≥ 15 in the semi-quantitative method (catheter tip) and $\geq 10^3$ cfu/mL in the quantitative method (blood culture) were considered positive. Antimicrobial susceptibility of the isolates was tested with the automated identification system (VITEK® 2, bioMérieux, France). Isolated pathogens showing intermediate susceptibility were considered resistant. The blood cultures that were taken from inside the catheter and from the peripheral vascular system were then compared to determine whether the same type of pathogen and antibiotic susceptibility was

present. Antibiotic susceptibility testing was performed using the disk-agar diffusion method described by the European Union Committee on Antimicrobial Susceptibility Testing (EUCAST), depending on the isolated microorganism.⁸

Statistical Analysis: Statistical analysis was performed using SPSS 20.0 (Statistical Package for Social Sciences, SPSS, IBM Inc, Chicago, IL, USA) statistical package software. Normality of the data was analyzed with the Kolmogorov Smirnov test. Since the data were normally distributed; continuous variables are expressed as mean \pm standard deviation and categorical variables as frequency and percentage. A p value less than 0.05 was considered as statistically significant.

RESULTS

A total of 86 patients who underwent catheterization due to various indications in the cardiovascular surgery clinic of our hospital were included in the study. Of all patients, 49 (56.98%) were male and 37 (43.02%) were female. The mean age of the patients was 52.70 ± 17.82 years, and the mean age was found as 55.35 ± 17.82 years in male and 49.20 ± 17.87 years in female patients.

When comorbidities of the patients were reviewed; no additional disease was found in 55 (63.95%), hypertension in 11 (12.79%), diabetes mellitus in 2 (2.33%), hypertension plus diabetes mellitus in 15 (17.44%), morbid obesity in one (1.16%) and postpartum hemorrhage in 2 (2.33%) patients. Biochemical laboratory analysis outcomes of the patients are given in [Table 1](#).

Patients were examined in terms of catheterization and catheter type was found as temporary in 70 (81.40%) patients and permanent in 16 (18.60%) patients. Catheter insertion site was found as the right subclavian vein in 37 patients, left subclavian in 10 patients, right jugular vein in 20 patients, left jugular vein in 2 patients, right femoral vein in 11 patients and left femoral vein in 6 patients ([Figure 1](#)). The mean catheter duration in situ was found as 6.90 ± 6.78 weeks.

Among infection symptoms; discharge was found in 61 (70.93%), fever in 67 (77.91%), pain in 78 (90.70%), itching in 62 (72.09%) and lymphadenopathy (LAP) in 16 (18.60%) patients. According to blood culture laboratory outcomes, bacterial growth was found in 54 (62.79%) patients. More than one pathogen was isolated in 15 (17.44%) patients. When culture outcomes were examined; the most commonly isolated microorganism was *S.*

aureus (25.58%) followed by *E. coli* (6.98%), *S. haemolyticus* (5.81%) and *K. pneumonia* (5.81%). Distribution of the pathogens isolated from cultures of the patients is shown in [Table 2](#). Sensitivity and resistance of the microorganisms isolated from the cultures are given in [Table 3](#).

DISCUSSION AND CONCLUSION

Catheter related bloodstream infections (CRBSIs) are among rare, but significant complications of catheterization procedure that is performed during or after cardiovascular interventions. CRBSIs significantly affect length of stay in the hospital and patients' quality of life. The most common cause of CRBSIs is the contamination of the catheter hub and entry of the skin flora during/after insertion of venous catheters.^{9,10} Early diagnosis and treatment of these infections is the mainstay of the prevention of morbidity, mortality and increased costs.¹¹ Detection of the responsible pathogens and their pattern of susceptibility to antimicrobial medications is critical for a successful treatment. In a study by Mozaffari et al., the rate of catheter colonization was found as 73% in cardiac patients.¹² In our study, this rate was found as 62.79%. We think that the lower rate of catheter colonization found in our study was resulted from the experience of medical staff who performed catheterization and the meticulous technique used.

Studies have reported the factors affecting the rates of CRBSI complications as selection of catheters, insertion site (location, insertion techniques, care), skill of the person who inserts the catheter, emergency vs elective insertion, underlying disease and duration of catheterization.¹³ In our study, the most common catheter insertion site was the right subclavian vein by 43% followed by the right jugular vein by 23%. In a study by Turken et al., catheter insertion sites were reported as internal jugular vein by 42.6%, subclavian vein by 41.6% and femoral vein by 15.8%.¹⁴ Catheter colonization is reported to be higher in the catheters inserted into the jugular vein compared to those inserted into the subclavian vein.¹⁵ In the present study, the rate of growth was 49.12% in the patients with catheters inserted into the right or left subclavian vein, while this rate was 63.64% in those with catheters inserted into the right or left jugular vein. This can be partly explained by the probability of the jugular site to be contaminated by the secretions from endotracheal/tracheostomy tube or saliva dribbling from the mouth.

Microbiological diagnosis of CRBSI is very important, because infection treatment primarily depends on the isolated microorganism and its resistance pattern. Microorganisms causing catheter infections often come either from the catheter tip or the skin around the catheter.¹⁶ The most commonly isolated pathogens from catheters were reported as Coagulase-negative *staphylococci*, *S. aureus*, aerobic gram-negative bacilli and *C. Albicans*.¹⁷ In a study by Jin et al. about CRBSIs, the most commonly isolated pathogen was *S. aureus* followed by *Candida*, coagulase negative staphylococci, *Pseudomonas*, *Klebsiella* species and *E. coli*.¹⁸ In a study by Mjalawi et al. investigating the pathogens isolated in patients who underwent diagnostic or therapeutic catheterization, the most commonly detected organism was *S. aureus* followed by *K. pneumoniae*, *E. coli* and *S. pneumoniae*; respectively.¹⁹ In another study by Gecgel and Demircan investigating the predominant pathogens in hospitalized cardiology and cardiovascular patients, the most commonly isolated pathogen was *S. aureus*, followed by *A. baumannii*, acinetobacter species and *E. faecalis*.²⁰ In the present study, the most commonly identified microorganism was *S. aureus* followed by *E. coli*, *S. haemolyticus* and *Klebsiella* species. Although distribution of the isolated pathogens differs between our study and the other studies, the most commonly isolated microorganism was *S. aureus*.

S. aureus is a Gram-positive coccus with a diameter differing between 0.5 and 1.5 μm in diameter, with or without a polysaccharide capsule. Resistance of *S. aureus* is resistant against multiple classes of antimicrobial agents in the hospital setting is a challenge for clinicians when treating *S. aureus* infections.²¹ In a study by Mozaffari et al., *staphylococci* species were found to be sensitive against vancomycin and linezolid.¹² Phatak et al. and Goel et al. reported similar results.^{22,23} Similarly, in our study *S. aureus* was sensitive to vancomycin and linezolid. *S. aureus* is a harmful human pathogen associated with nosocomial infections, and it is increasingly becoming resistant to most antibiotics. Therefore, new therapeutic strategies should be developed in order to treat catheter related infections, especially those caused by *S. aureus*.

In conclusion, catheterization-related infections are among rare, but significant complications of cardiovascular procedures. Early diagnosis and treatment are of paramount importance in the prevention of these infections. Factors affecting the

incidence of these infections include catheter insertion site, catheterization duration, selection of catheters and skills of the practitioners. In our study, the most commonly isolated pathogen from the catheters was *S. aureus*. Data in the literature about the pathogens isolated in catheter-related infections and their sensitivity and resistance to antimicrobial agents are mostly old. Further comprehensive, multicenter studies are needed on this issue. This study has some limitations. The study has a retrospective design and included a relatively small number of patients. In addition, this study was conducted in a single center. Therefore, generalization of our results may not be appropriate. In future studies, we plan to divide the patients into groups with and without bacterial growth due to catheterization and to compare the results between the groups.

Ethics Committee Approval: Our study was approved by the Mogadishu Somali Turkey Recep Tayyip Erdogan Training and Research Hospital Ethics Committee (Date: 07.08.2019, decision no: 132).

Conflict of Interest: No conflict of interest was declared by the author.

Author Contributions: Concept – UTKK; Supervision – UTKK, BG; Materials – UTKK, BG; Data Collection and/or Processing – UTKK, BG; Analysis and/ or Interpretation – UTKK, BG; Writing – UTKK.

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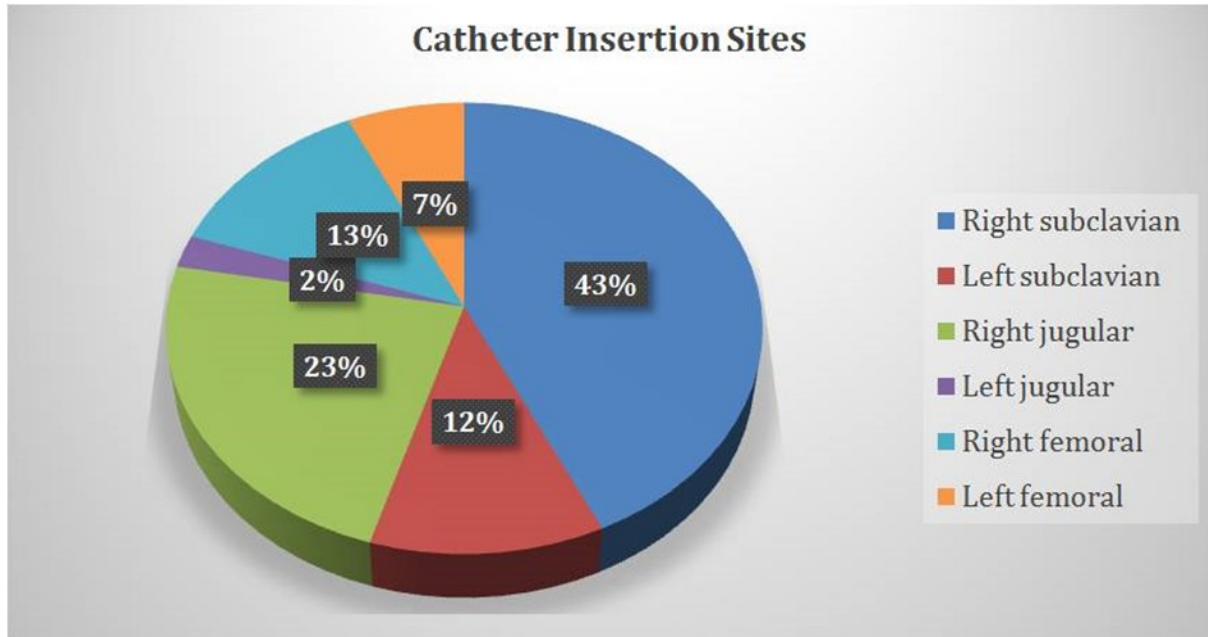


Figure 1. Distribution of the catheterization sites.

Table 1. Biochemical laboratory analysis outcomes.

Parameter	Mean±SD
WBC ($10^3/\mu\text{L}$)	9.62±6.80
RBC ($10^6/\mu\text{L}$)	3.10±0.59
HGB (g/dL)	8.85±1.75
HCT (%)	25.98±5.07
PLT (k/mm^3)	250.62±111.66
NE ($10^3/\mu\text{L}$)	7.12±6.47
LYM ($10^3/\mu\text{L}$)	1.48±0.65
MONO ($10^3/\mu\text{L}$)	0.75±0.55
EOS ($10^3/\mu\text{L}$)	0.38±1.40
BASO ($10^3/\mu\text{L}$)	0.05±0.05
MCV (fL)	84.50±5.25
MCH (pg)	28.76±2.01
MCHC (g/dL)	34.16±1.79
MPV (fL)	9.67±1.40
PDW (%)	13.24±3.00
PCT (%)	0.24±0.11

WBC: white blood cell; RBC: red blood cell; HGB: hemoglobin; HCT: hematokrit; PLT: platelets; NE: neutrophils; LYM: lymphocytes; MONO: monocytes; EOS: eosinophils; BASO: basophils; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; MPV: mean platelet volume; PDW: platelet distribution width; PCT: plateletcrit.

Table 2. Distribution of the isolated organisms.

Isolated Organisms	No	%
No Growth	32	37.21
Gram positive pathogens		
<i>Staphylococcus aureus</i>	22	25.58
<i>Staphylococcus haemolyticus</i>	5	5.81
<i>Enterococcus faecalis</i>	3	3.49
<i>Staphylococcus epidermidis</i>	3	3.49
<i>Staphylococcus lentus</i>	1	1.16
<i>Staphylococcus intermedius</i>	1	1.16
Gram negative pathogens		
<i>Escherichia coli</i>	6	6.98
<i>Klebsiella pneumoniae</i>	5	5.81
<i>Pseudomonas aeruginosa</i>	2	2.33
<i>Acinetobacter baumannii</i>	2	2.33
<i>Enterobacter cloacae</i>	2	2.33
<i>Providencia alcalifaciens</i>	1	1.16
<i>Aeromonas hydrophila</i>	1	1.16
TOTAL	86	100.00

Table 3. Sensitivity and resistance of the most commonly isolated pathogens against some antibiotics in the patients.

Antibiotic	Isolated Organisms							
	<i>S. aureus</i>		<i>E. coli</i>		<i>S. haemolyticus</i>		<i>K. pneumoniae</i>	
	S	R	S	R	S	R	S	R
Clindamycin	17	5			4	1		
Levofloxacin	11	7			-	3	1	-
Vancomycin	22	-			5	-		
Cefoxitin	15	6	3	1	3	1	3	1
Ciprofloxacin	12	9	3	2	1	4	3	2
Fusidic acid	11	2			1	1		
Teicoplanin	10	-			1	-		
Trimethoprim-Sulfamethoxazole	5	17	3	3	-	5	1	4
Daptomycin	14	-			3	-		
Gentamicin	18	4	4	2	1	4	3	2
Penicillin G	1	21			-	5		
Tigecycline	18	-			2	1		
Tetracycline	14	8			3	1		
Linezolid	21	-			5	-		
Oxacillin	6	5			-	2		
Ceftazidime							-	3
Piperacillin + Tazobactam			2	-			3	1
Imipenem			6	-			5	-
Amikacin			5	-			4	-
Meropenem			3	-			4	-
Ampicillin			-	4			-	4
Ceftriaxone			2	3			-	4
Amoxicillin + Klavulonic acid			3	3			3	2
Ertapenem			2	1			3	-
Cefixime			2	1			-	2
Cefuroxime			2	4			1	3
Telithromycin	1	-			1	-		
Rifampicin	-	1			1	-		
Ampicillin + Sulbactam					-	1		
Erythromycin	4	1			1	1		
Cefoperazone + Sulbactam			1	-				
Cefazolin			2	1			-	1
Chloramphenicol			-	1				
Quinupristin / Dalfopristin	3	-			1	-		

S: Sensitivity; R: Resistance.