Evaluation of Nosocomial Infections and Related Hospital Mortality in Coronary Intensive Care Unit

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ABSTRACT

Introduction: Mechanical/therapeutic technologies have resulted in an increased risk of infections including ventilator-associated pneumonia, central line-associated bloodstream infections, and potentially increased the risk of care process complications such as anesthesia/intubation/sedation complications; central line infections, stress ulcers, delirium, and the use of inappropriate or false medications in coronary intensive care units. These complications are associated with significantly increased in-hospital mortality, morbidity, length of stay, and/or healthcare costs and are potentially preventable. We aimed to evaluate the nosocomial infections developed in the coronary intensive care unit and the relationship between coronary intensive care unit infections and in-hospital mortality.

Patients and Methods: The data of 500 patients followed in the coronary intensive care unit more than 48 hours between 01.01.2019 and 31.12.2020 were retrospectively analyzed. Patient records were obtained from surveillance data obtained by infectious diseases and clinical microbiology specialists and infection control nurses through daily visits. The criteria determined by the Centers for Disease Control and Prevention were used in the diagnosis of nosocomial infections. Various clinical samples (blood, urine, endotracheal aspiration fluid) taken from the patients were processed in the microbiology laboratory using qualitative or quantitative methods.

Results: The most common detected infection type was catheter-related bloodstream infection (79.1%), followed by catheter-associated urinary tract infection (18.7%) and ventilator-associated pneumonia (6.25%) respectively. Gram-negative bacillus infections accounted for 70.8% of the causative agents, gram-positive cocci for 20.18%, and fungal infections for 12.5%. The most frequently detected microorganism species were *Klebsiella pneumoniae* (*K. pneumoniae*) and *Escherichia coli* (*E. coli*) [7 (14.5%), 6 (12.5%)] respectively. Central venous catheter use was more common in non-infected group than infected group [45.0 (93.8%), 50.0 (73.5%) p= 0.005]. Continuous renal replacement therapy was more common in infected group compared to non-infected group [32 (66.7%), 21 (30.9%) p< 0.001]. The numbers of intubated days were higher in the infected group than in the non-infected group and this was statistically significant [mean (SD) 9.9 ± 9.2, 2.3 ± 2.9, P< 0.001]. In-hospital mortality rates were higher in infected group compared to non-infected group [28 (58.3%), 19 (27.9%), p= 0.001].

Conclusion: We found a significant relationship between nosocomial infections and in-hospital mortality in patients who were followed in coronary intensive care unit more than 48 hours [OR= 3.52 (1.30-9.53 CI= 95%) P= 0.01]. The most common sites of nosocomial infections are catheter-related bloodstream infections followed by catheter-associated urinary tract infections and ventilator-associated pneumonia. In multidisciplinary coronary intensive care units, daily visits with infectious diseases and clinical microbiology specialists and infection control nurses, close clinical and laboratory follow-up (detection of fever, elevation in procalcitonin and C-reactive protein (CRP) levels) are indispensable and more importantly nosocomial infections and infection-related mortality are preventable.

Key Words: Nosocomial infections; coronary care unit; catheter related infections

Koroner Yoğun Bakım Ünitesinde Hastane Enfeksiyonları ve Bununla İlişkili Mortalitenin Değerlendirilmesi

ÖZET

Giriş: Mekanik/terapötik teknolojiler ventilatör ilişkili pnömoni ve santral hat ilişkili kan akımı enfeksiyonları riskinde artışa neden olmakta ve hasta bakım süreci komplikasyonları riskini potansiyel olarak arttırmaktadır. Anestezi/entübasyon/sedasyon komplikasyonları, merkezi hat enfeksiyonları, stres ülserleri, deliryum ve koroner yoğun bakım ünitelerinde uygunsuz ilaç kullanımı gibi komplikasyonlar, önemli ölçüde artan hastane içi mortalite, morbidite, kalış süresi ve/veya sağlık hizmetleri maliyetleri ile ilişkilidir ve potansiyel olarak önlenebilirdir. Koroner yoğun bakım ünitesinde gelişen hastane enfeksiyonları ve enfeksiyonlar ile hastane mortalitesi arasındaki ilişkiyi değerlendirmeyi amaçladık.

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Hastalar ve Yöntem: 01.01.2019-31.12.2020 tarihleri arasında 48 saatten fazla yoğun bakım ünitesinde takip edilen 500 hastanın verileri geriye dönük olarak incelendi. Hasta verileri enfeksiyon hastalıkları ve klinik mikrobiyoloji uzmanları ve enfeksiyon kontrol hemşireleri tarafından günlük ziyaretlerle gerçekleştirilen sürveyans verilerinden elde edildi. Hastane enfeksiyonu tanısında "Hastalık Kontrol ve Önleme Merkezleri" tarafından belirlenen kriterler kullanıldı. Hastalardan alınan çeşitli klinik örnekler (kan, idrar, endotrakeal aspirasyon sıvısı) mikrobiyoloji laboratuvarında kalitatif ya da kantitatif yöntemlerle gerekli işleme alındı.

Bulgular: En sık saptanan enfeksiyon tipi santral hat ilişkili kan dolaşım enfeksiyonları (%79.1) iken, bunu sırasıyla kateter ilişkili üriner sistem enfeksiyonları (%18.7) ve ventilatör ilişkili pnömoni (%6.25) izledi. Etkenlerin %70.8'ini gram-negatif basiller; %20.18'ini gram-pozitif koklar ve %12.5'ini mantar enfeksiyonları oluşturmaktaydı. En sık saptanan mikroorganizma türleri *K. pneumoniae* ve *E. coli* idi [sırasıyla 7 (%14.5), 6 (%12.5)]. Santral venöz kateter kullanımı enfekte olmayan grupta enfekte gruba göre daha yaygındı [45.0 (%93.8), 50.0 (%73.5) p= 0.005] Sürekli renal replasman tedavisi, enfekte grupta enfekte olmayan gruba göre daha yaygındı [32 (%66.7), 21 (%30.9) p< 0.001]. Entübe gün sayısı enfekte hastalarda daha yüksekti ve enfekte olmayan gruba göre istatistiksel olarak anlamlıydı (ortalama (SD) 9.9 ± 9.2, 2.3 ± 2.9; p< 0.001). Hastanede ölüm oranları, enfekte grupta enfekte olmayan gruba göre daha yüksekti [28 (%58.3), 19 (%27.9), p= 0.001].

Sonuç: Multidisipliner YBÜ'lerde enfeksiyon hastalıkları ve klinik mikrobiyoloji uzmanları ve enfeksiyon kontrol hemşireleri ile günlük sürveyans vizitleri; yakın klinik ve laboratuvar takip (ateş, prokalsitonin ve CRP düzeylerinin yüksekliği) vazgeçilmezdir ve daha da önemlisi hastane enfeksiyonları ve enfeksiyona bağlı ölümler büyük ölçüde önlenebilirdir.

Anahtar Kelimeler: Hastane enfeksiyonları; koroner bakım ünitesi; kateter ilişkili enfeksiyonlar

INTRODUCTION

Although coronary intensive care units (CICUs) are mainly designed for close monitoring and treatment of patients with acute coronary syndrome (ACS), malignant arrhythmia, and decompensated right and/or left heart failure (HF), these units have been established especially in the last twenty years. Due to systemic diseases that increasingly require vasoactive infusion, non-invasive or invasive mechanical ventilation (MV), renal replacement therapy, and mechanical circulatory support such as intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation (ECMO); the CICUs transformed from centers focused solely on cardiac diseases to multidisciplinary intensive care units.

On the other hand, this temporal increase in the number of patients and mechanical/therapeutic technologies has resulted in an increased risk of infections including ventilator-associated pneumonia (VAP), central line-associated bloodstream infections (CLABSI), and potentially increased the risk of care process complications such as anesthesia/intubation/sedation complications, central line infections, stress ulcers, delirium, and the use of inappropriate or false medications. These complications are associated with significantly increased in-hospital mortality, morbidity, length of stay, and/or healthcare costs and are potentially preventable.

To the best of our knowledge, there is no data on such intensive device use in terms of infection and mortality in the CICUs, and we aimed to evaluate the nosocomial infections developed in the CICU related to device use and the relationship between CICU infections and in-hospital mortality.

PATIENTS and METHODS

Our hospital is a tertiary referral center with a 60-bed capacity coronary intensive care unit. The data of the patients who stayed more than 48 hours in CICU, 500 patients followed in the CICU between 01.01.2019 and 31.12.2020 were retrospectively analyzed. The criteria determined by the Centers for Disease Control and Prevention were used in the diagnosis of hospital infections. Patient data were obtained from surveillance data obtained by Infectious Diseases and Clinical Microbiology specialists and Infection Control Nurses through daily visits.

Forty-eight patients not in the incubation period at the time of admission had proven infection 48-72 hours after hospitalization with clinical and laboratory findings (fever that cannot be attributed to any other cause and procalcitonin, CRP, WBC levels) consistent with nosocomial infection and 68 patients who were not found to have nosocomial infections during hospitalization were included in the study. The algorithm for patient evaluation and inclusion in the study is shown in Figure 1.

Ethics committee approval was obtained from Kartal Koşuyolu High Specialization Training and Research Hospital Clinical Research Local Ethics Committee (on 24.08.2021 and numbered 2021/10/519) in accordance with the Declaration of Helsinki.

Data collection: Patient data were obtained from surveillance data (National Health Service Associated Infections Surveillance System) obtained by Infectious Diseases Specialists and Infection Control Nurses through daily visits and hospital data management unit.

Definitions and outcome: Centers for Disease Control and Prevention criteria that were used in the diagnosis of nosocomial infections are as follows:

Central line-associated bloodstream infection (CLABSI): Recovery of a pathogen from blood culture (a single blood culture for organisms not commonly present on the skin, and two or more blood cultures for organisms commonly present on the skin) in a patient who had a central line at the time of

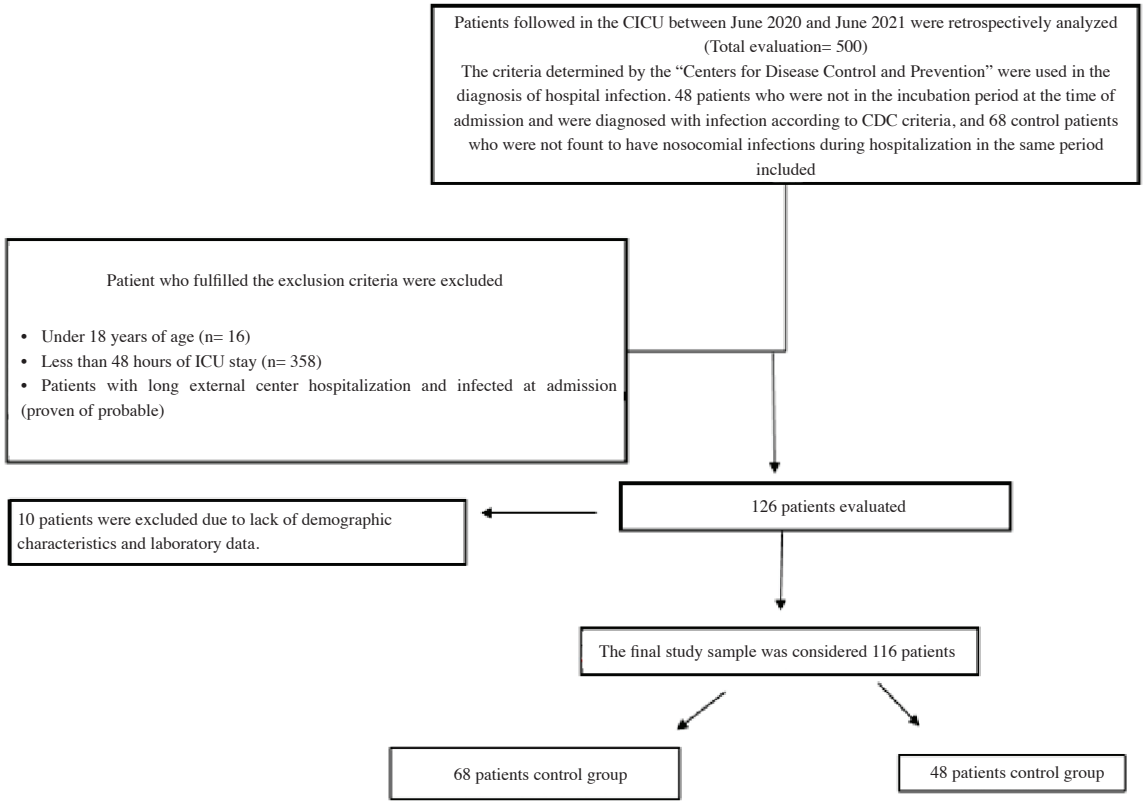

Figure 1. Consort flow diagram.

infection or within 48 hours before the development of infection. The infection cannot be related to any other infection the patient might have and must not have been present or incubating when the patient was admitted to the facility[1].

Ventilator-associated pneumonia (VAP): This is identified by using a combination of objective criteria: deterioration in respiratory status after a period of stability or improvement on the ventilator, evidence of infection or inflammation, and laboratory evidence of respiratory infection[2].

Catheter-associated urinary tract infection (CAUTI): Presence of fever, suprapubic tenderness, or costovertebral angle pain in the setting of urine culture with bacterial counts $\geq 10^5$ cfu/mL of no more than two organism species (and does not include fungal isolates or minor pathogens)[2].

Microbiologic evaluation: Various clinical samples (blood, urine, endotracheal aspiration fluid) taken from the patients were sent to the microbiology laboratory. Urine and endotracheal aspiration samples were cultivated on solid medium using a quantitative method. Blood or other sterile body fluid samples placed in blood culture medium were incubated at 37°C for five days in BD BACTEC™ (Becton Dickinson, Diagnostic Instrument System, Sparks, USA), automated blood culture system. Identification and antibiotic susceptibility testings were performed with VITEK® 2 Compact (bioMérieux, France) in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST)[3].

Primary outcome: The primary outcome of this study is in-hospital mortality.

Statistical Analysis

Numerical variables were expressed as mean and standard deviation (SD). Discrete data were shown as percentages and absolute numbers. Patient and control group comparisons for numerical variables were made with the unpaired t-test. Discrete variables were compared with Chi-square or Fisher exact test, as appropriate. Logistic regression was used to predict the in-hospital mortality (primary outcome), multivariable logistic regression variables were chosen according to univariable screening with a p-value lower than 0.10 included in the multivariable model. Regression output is presented with an odds ratio (OR) and confidence interval (CI).

RESULTS

The most commonly detected infection type was CLABSI (79.1%), followed by CAUTI (18.7%) and VAP (6.25%) respectively. Some patients had both CLABSI and CAUTI or VAP and CAUTI concurrently (Table 1). Gram-negative ba-

Table 1. Diagnosis of patients with nosocomial infections in CICU and causative microorganisms

Infection site	N (%)
CLABSI	36 (75)
VAP	12 (25)
CAUTI	5 (10.4)
Causative agent	
Klebsiella pneumoniae	7 (14.5)
Escherichia coli	6 (12.5)
Pseudomonas aeruginosa	6 (12.5)
Candida spp.	5 (10.4)
Staphylococcus aureus	4 (8.3)
Enterococcus spp.	4 (8.3)
Acinetobacter baumanii	3 (6.2)
Others	12 (25)

CICU: Coronary intensive care unit, CLABSI: Central line-associated bloodstream infections, VAP: Ventilator-associated pneumonia, CAUTI: Catheter-associated urinary tract infection. Others: *Sphingomonas*, *Proteus*, *Serratia* spp.

cillus (GNB) infections accounted for 70.8% of the causative agents, gram-positive cocci (GPC) for 20.18%, and fungal infections for 12.5%. The most frequently detected microorganism species were *Klebsiella pneumoniae* (*K. pneumoniae*) and *Escherichia coli* (*E. coli*) [7 (14.5%), 6 (12.5%) respectively].

The mean age was 63.1 ± 14.4 in the infected group and 63.7 ± 15.1 in the non-infected group (P= 0.820). In addition; diabetes mellitus (DM) was more common in the infected group compared to the non-infected group [38 (79.2%), 30 (44.1%) p< 0.001]. The proportion of patients with glomerular filtration rate (GFR)< 60 was higher in the infected group compared to the non-infected group [32 (66.7%), 29 (42.6%), P= 0.01)]. Other clinical and demographic variables are presented in Table 2.

Central venous catheter (CVC) use was more common in the non-infected group than the infected group [45.0 (93.8%), 50.0 (73.5%) p= 0.005]. Coronary angiography (CAG) and/or percutaneous coronary intervention (PCI) rates were higher in the non-infected group than the infected group [41 (60.3%), 22.0 (45.8%) p= 0.124]. Continuous renal replacement therapy (CRRT) was more common in the infected group compared to the non-infected group [32 (66.7%), 21(30.9%) P< 0.001]. The numbers of intubated days were higher in the infected group than the non-infected group and this was statistically significant [mean (SD) 9.9 ± 9.2, 2.3 ± 2.9, P< 0.001]. In-hospital mortality rates were higher in the infected group compared to the non-infected group [28 (58.3%), 19 (27.9%), P= 0.001]. Other types of invasive procedures are shown in Table 3.

Univariable logistic regression analysis showed an association between infection status and creatinine with mortality [(OR= 3.26 (1.51-7.04 CI 95%) P= 0.003), (2.06 (1.36-3.10 CI 95%) P< 0.001) respectively]. Univariable analysis demonstrated that hemoglobin was not associated with mortality [0.87 (0.73-1.02 CI= 95%) P= 0.08]. Multivariable logistic regression analysis showed association between infection, admission creatinine with mortality [(OR= 3.52 (1.30-9.53 CI 95%) P= 0.01), (1.96 (1.25-3.10 CI 95%) P= 0.003) respectively]. Multivariable analysis demonstrated that hemoglobin was not associated with mortality [1.04 (0.84-1.30 CI= 95%) P= 0.68] (Table 4).

DISCUSSION

We found a significant relationship between nosocomial infections and in-hospital mortality in patients who stayed in CICU for more than 48 hours [OR= 3.52 (1.30-9.53 CI= 95%) p= 0.01]. The most common sites of nosocomial infections were CLABSI followed by CAUTI and VAP.

Although CICUs constitute 5 to 10% of all hospitalizations, they have a higher probability and rate of nosocomial infections. With the increase in life expectancy, easier access

Table 2. Baseline clinical and demographic characteristics of patients and control group

	Infected (N= 48)	Non-infected (N= 68)	Total (N= 116)	p
Age, mean (SD)	63.1 ± 14.4	63.7 ± 15.1	63.5 ± 14.8	0.820
Male, n (%)	26 (54.2)	44 (64.7)	70 (60.3)	0.25
CAD, n (%)	25 (52.1)	32 (47.1)	57 (49.1)	0.59
DM, n (%)	38 (79.2)	30 (44.1)	68 (58.6)	<0.001
HT, n (%)	35 (72.9)	50 (73.5)	85 (73.3)	0.94
GFR (45-60) (%)	32 (66.7)	29 (42.6)	61 (52.6)	0.011
CHF n (%)	25 (52.1)	47 (69.1)	72 (62.1)	0.06
EF, mean (SD)	43.9 ± 18	40.3 ± 14.6	41.8 ± 16.1	0.24

CAD: Coronary artery disease, DM: Diabetes mellitus, HT: Hypertension, GFR: Glomeruler filtration rate, CHF: Congestive heart failure, EF: Ejection fraction.

Table 3. Types of invasive procedures

	Infected (n= 48)	Non-infected (n= 68)	Total (n= 116)	p
CVC, n (%)	45.0 (93.8)	50.0 (73.5)	95 (81.9)	0.005
V-A ECMO, n (%)	9 (18.8)	7 (10.3)	16 (13.8)	0.193
IABP, n (%)	25 (52.1)	32 (47.1)	57 (49.1)	0.103
CAG and/or PCI, n (%)	22.0 (45.8)	41 (60.3)	63 (54.3)	0.124
CRRT, n (%)	32 (66.7)	21 (30.9)	53 (45.7)	<0.001
Intubation, n (%)	41 (85.4)	41 (60.3)	82 (70.7)	0.003
Numbers of day intubated, mean (SD)	9.9 ± 9.2	2.3 ± 2.9	5.5 ± 7.3	<0.001
Drain, n (%)	7 (14.6)	9 (13.2)	16 (13.8)	0.06
TPN, n (%)	43.9 (18)	40.3 (14.6)	41.8 (16.1)	0.24
Foley catheter, n (%)	47 (97.9)	66 (97.1)	113 (97.4)	0.77
Arrest on admission, n (%)	29.0 (60.4)	28.0 (41.2)	57 (49.1)	0.04
In-hospital mortality, n (%)	28 (58.3)	19 (27.9)	47 (40.5)	0.001

CVC: Central venous catheter, V-A ECMO: Veno-arterial extra-corporeal membrane oxygenation, IABP: Intra-aortic balloon pump, CAG: Coronary angiography, PCI: Percutan coronary intervention, CRRT: Continuous renal replacement theraphy, TPN: Total parenteral nutrition SD: Standart deviation.

Table 4. Univariable and multivariable logistic regression analysis for predicting hospital mortality

	OR (%95 CI)	p	OR (%95 CI)	p
Age	0.99 (0.96-1.01)	0.37	0.99 (0.96-1.01)	0.4
Gender (male)	0.75 (0.36-1.60)	0.46		
Infection status	3.26 (1.51-7.04)	0.003	3.52 (1.30-9.53)	0.01
CAD	1.75 (0.82-3.71)	0.14		
DM	1.28 (0.60-2.72)	0.23		
EF	0.97 (0.95-0.99)	0.02	0.96 (0.93-0.99)	0.01
Admission creatinin	2.06 (1.36-3.10)	<0.001	1.96 (1.25-3.10)	0.003
WBC	1.04 (0.98-1.09)	0.14		
Hb	0.87 (0.73-1.02)	0.08	1.04 (0.84-1.3)	0.68

CAD: Coronary artery disease, DM: Diabetes mellitus, EF: Ejection fraction, WBC: White blood cell, Hb: Hemoglobine.

to health services, and developments in medical interventions/device technologies, both the number and co-morbidity of patients hospitalized in CICUs have increased and their length of stay has been prolonged. Likewise, conditions such as the need for intubation/ventilator at a higher rate, renal replacement therapy, invasive arterial monitoring, use of central venous catheters due to emergency interventions or peripheral incompatibility in patients with prolonged hospitalization increase the frequency of CLABSI and VAP, which have a significant rate in hospital infections.

In a study analyzing 6698 nosocomial infections in 227 451 patients, it was found that urinary tract infections (UTI) (35%), pneumonia (24%), and primary bloodstream infections (BSI) (17%) were almost always associated with the use of an invasive device (93% with a urinary catheter, 82% with a ventilator, 82% with a central line, respectively)[4]. In an ICU study from Turkey BSI was the most commonly detected nosocomial infection followed by UTI and pneumonia[5]. These are consistent with our findings.

On the other hand, in EPIC II study, the most common infection sites were the respiratory tract (63.5%), abdomen (19.6%), bloodstream (15.1%), and urinary tract (14.3%) respectively[6]. Since these studies mostly involved surgery or general ICU stay, the detected infection rates and locations may differ from those of our center. Although we are a tertiary center, and the number and duration of inpatients and the use of catheters and/or medical devices seem to be higher in CICU, our nosocomial infection rates overlap with Turkey's data.

Critically ill patients are inherently susceptible to a multitude of complications related to both the severity of underlying disease and the need for intensive care therapies. Many of these complications are associated with increased morbidity and mortality and often result in greater resource use, healthcare expenses, and longer intensive care unit (ICU) lengths of stay[7,8]. A number of these complications are potentially preventable, and their incidence rates are used as quality metrics within modern-day ICU settings.

Contemporary CICUs have an increasing prevalence of non-cardiovascular comorbidities and multi-system organ dysfunction. Thus, it stands to reason that patients admitted to contemporary CICUs will be susceptible to similar preventable complications associated with both their multisystem critical illness and the resources required to treat their complex conditions. At the same time, there is a need among CICU providers to understand those complications that are most applicable to critically ill cardiovascular patients, who may not be well represented in the general ICU. As a result, there may be opportunities to improve CICU outcomes through the implementation of evidence-based preventive practices. However, good practice recommendations specific to CICU are currently scarce[9].

Infections and sepsis are prevalent in CICU populations, both on admission and as acquired complications during hospitalization[10,11]. Patients in the CICU increasingly receive therapies such as invasive medical devices for hemodynamic monitoring, short-term mechanical support, and CRRTs which are associated with an increased risk of healthcare-associated infections (HAIs) [12]. HAIs include CAUTI, CLABSI, VAP infections with multidrug resistant (MDR) pathogens, and surgical site infections occurring with mechanical circulatory support (MCS).

Although there are no CICU-specific guidelines available to inform best practices for HAI prevention, guidance on the prevention of HAIs is reviewed here in with a focus on CICU populations[13,14]. Hand hygiene is critically important, and improved compliance reduces the incidence of HAIs. Hands should be washed with either alcohol-based hand sanitizers or soap and water before and after any patient contact. Alcohol-based hand sanitizers are effective for preventing the spread of most MDR pathogens; soap and water may be more effective for preventing the spread of diarrheal pathogens[15,16].

Despite the common use of central lines, invasive arterial monitorization, MCS, and other intensive treatment modalities, and the fact that our hospital is a tertiary referral center, our nosocomial infection rates are similar to nation-wide data.

CONCLUSION

In multidisciplinary CICUs, daily visits with infectious diseases and clinical microbiology specialists and infection control nurses, close clinical and laboratory follow-up (detection of fever, elevation in procalcitonin and CRP levels) are indispensable, and more importantly, nosocomial infections and infection-related mortality are preventable.

Ethics Committee Approval: The approval for this study was obtained from Kartal Koşuyolu High Training and Research Hospital Clinical Research Ethics Committee (Decision no: 2021/10/519, Date: 24.08.2021).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

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Author Contributions: Concept/Design - YUK; Analysis/Interpretation - ŞK, ÖYA; Data Collection - ŞK; Writing - YUK, AK; Critical Revision - AK; Final Approval - ŞK; Statistical Analysis - AK; Overall Responsibility - ÖYA.

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