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Omar Chehab

Rami Z. Morsi

Amjad Kanj

Rayan Jo Rachwan

Mohit Pahuja

See next page for additional authors

Authors

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Incidence and clinical outcomes of nosocomial infections in patients presenting with STEMI complicated by cardiogenic shock in the United States

Omar Chehab, MD, MSc[a,1], Rami Z. Morsi, MD[b,1], Amjad Kanj, MD, MPH[c], Rayan Jo Rachwan, MD[d], Mohit Pahuja, MD[a], Shareef Mansour, MD[e], Hussam Tabaja, MD[a], Usman Ahmad, DO[a], Said El Zein, MD[a], Mohammad Raad, MD[f], Ali Saker, MD[a], Paulino Alvarez, MD[e], Alexandros Briasoulis, MD, PHD[e,*]

[a] Department of Medicine, Detroit Medical Center/Wayne State University School of Medicine, Detroit, Michigan, USA
[b] Department of Neurology, University of Chicago, Chicago, Illinois, USA
[c] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA
[d] Department of Cardiovascular Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA
[e] Division of Cardiovascular Medicine, Department of Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA
[f] Division of Cardiology, Department of Medicine, Henry Ford Hospital, Detroit, Michigan, USA

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ABSTRACT

Objectives: This study addresses the incidence, trends, and impact of nosocomial infections (NI) on the outcomes of patients admitted with ST-segment elevation myocardial infarction (STEMI) and cardiogenic shock (STEMI-CS) using the United States National Inpatient Sample (NIS) database.

Methods: We analyzed data from 105,184 STEMI-CS patients using the NIS database from the years 2005-2014. NI was defined as infections of more than or equal to three days, comprising of central line-associated bloodstream infection (CLABSI), urinary tract infection (UTI), hospital-acquired pneumonia (HAP), *Clostridium difficile* infection (CDI), bacteremia, and skin related infections. Outcomes of the impact of NI on STEMI-CS included in-hospital mortality, length of hospital stay (LOS) and costs. Significant associations of NI in patients admitted with STEMI-CS were also identified.

Results: Overall, 19.1% (20,137) of patients admitted with STEMI-CS developed NI. Trends of NI have decreased from 2005-2014. The most common NI were UTI (9.2%), followed by HAP (6.8%), CLABSI (1.5%), bacteremia (1.5%), skin related infections (1.5%), and CDI (1.3%). The strongest association of developing a NI was increasing LOS (7-9 days; OR: 1.99; 95% CI: 1.75-2.26; >9 days; OR: 4.51; 95% CI: 4.04-5.04 compared to 4-6 days as reference). Increased mortality risk among patients with NI was significant, especially those with sepsis-associated NI compared to those without sepsis (OR: 2.95; 95% CI: 2.72-3.20). Patients with NI were found to be associated with significantly longer LOS and higher costs, irrespective of percutaneous mechanical circulatory support placement.

Conclusions: NI were common among patients with STEMI-CS. Those who developed NI were at a greater risk of in-hospital mortality, increased LOS and costs.

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Abbreviations and Acronyms: STEMI, ST-elevated myocardial infarction; STEMI-CS, cardiogenic shock following ST-elevated myocardial infarction; pMCS, percutaneous mechanical circulatory support; NIS, National Inpatient Sample; AHRQ, Agency of Healthcare Research and Quality; ICD-9-CM, International Classification of Diseases - 9th Clinical Modification; IABP, Intra-aortic balloon pump; PVAD, percutaneous ventricular assist device; ECMO, extracorporeal membrane oxygenation

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* Corresponding author at: Division of Cardiovascular Medicine, Department of Medicine, University of Iowa Hospitals and Clinics, 200 Hawkins Drive E318 Iowa City, IA 52242.
E-mail addresses: omar.chehab@wayne.edu (O. Chehab), alexandros-briasoulis@uiowa.edu (A. Briasoulis).

[1] These authors contributed equally to this study.

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Introduction

Nosocomial infections (NI) complicating hospitalizations for cardiovascular diseases are associated with increased healthcare costs, length of stay and in-hospital mortality.[1,2] Cardiogenic shock (CS) following ST-elevation myocardial infarction (STEMI-CS) is frequently accompanied by a noninfectious systemic inflammatory response.[1,3] The degree of overlap of this response with an early infectious complication is unclear, thus making the detection of a coexisting infection difficult.[1] Rates of infections in non-CS patients with STEMI following cardiac interventions such as cardiac catheterization and percutaneous coronary interventions have been reported to be <1%.[4,5] However, these rates are probably higher in patients with CS, in particular those requiring percutaneous mechanical circulatory support (pMCS).[2,6,7] Furthermore, despite the major advances in device technology and caring for critically ill patients, the overall in-hospital mortality rates among patients with CS are still elevated (27%-51%).[8] While the cause of mortality in these patients is likely multifactorial, NI have been reported to play a major role. In fact, a recent analysis of observational US data showed that having only one NI increased the absolute risk of in-hospital mortality by 8.9% in patients with CS. In addition, CS has been identified as the most common diagnosis linked to NI (4%) in the same study.[2] CS has also been previously identified as a predisposing factor for NI.[3,9] Moreover, sepsis has been described as the most common non-cardiac cause of death in patients hospitalized with CS.[10]

To date, only few large studies have evaluated the incidence and impact of NI on outcomes of patients with STEMI-CS. The objectives of this study are to: (1) assess the incidence of NI in STEMI-CS patients; and (2) compare the healthcare costs, length of stay, and in-hospital mortality related to NI between pMCS and non-pMCS STEMI-CS patients.

Materials and methods

Study database

The National Inpatient Sample (NIS) database was established by the Agency of Healthcare Research and Quality (AHRQ). It presents a sample of 20% of all inpatient discharges across different hospitals in the United States.[11] It provides the public with data on individual hospitalizations. The data includes patient's age and gender, length of hospital stay, cost of hospitalization, mortality rates, comorbidities, in-hospital complications, in-hospital procedures and type of admission (i.e. emergency or elective). The data used in this retrospective cohort were from the years 2005 to 2014, inclusive. Recently, the AHRQ issued a change in the NIS design and how patient discharges are weighed to provide closer national estimates when performing trend analysis.[11,12] The new variable "Trend Weights" was developed for years 2012 and beyond. It is also well-adjusted for previous years. This method ensured the same level of patient analysis across all the years.[11,12]

Study population, variables, and outcomes

Patients with STEMI and CS were identified using the international classification of diseases, ninth revision, clinical modification (ICD-9-CM) of "410.x1" for STEMI as the primary reason of admission and 785.51 for CS as secondary diagnosis. Patients who were admitted for non-STEMI using the diagnostic code of 410.7x were excluded so that our analysis is limited to patients admitted with STEMI. The ICD-9 codes for STEMI and CS have been validated in using administrative databases.[13–16] Online Fig. 1 summarizes our sample selection methodology. The ICD-9 code for STEMI had a sensitivity, specificity, negative and positive predictive value of 72.4%, 99.5%, 96.1% and 95.9%, respectively.[17] On the other hand, the ICD-9 code for CS was found to have a sensitivity, specificity, negative and positive predictive value of 59.8%, 99.3%, 98.1%, and 78.8%, respectively.[14] Patients with pMCS, such as the intra-aortic balloon pump (IABP), percutaneous ventricular assist device (PVAD) (eg, Impella and TandemHeart), and extracorporeal membrane oxygenation (ECMO) were identified. NI are defined as infections that occur during a patient's hospital stay duration of at least two days, with hospital-acquired pneumonia (HAP) up to three days since admission.[18,19] In our analysis, patients who had a length of hospital stay of less than three days were excluded. We identified patients with NI as having any of the following infections during hospitalization: central line-associated bloodstream infection (CLABSI), urinary tract infection (UTI), HAP, *Clostridium difficile* infection (CDI), bacteremia, and skin related infections. To ensure that placement of pMCS was done prior to development of a NI, time to procedure analysis was performed (Fig. 1). Moreover, patients whose hospital stay was complicated by sepsis were identified using the ICD-9-CM/clinical classification of diseases (CCS) codes as highlighted in Online Tables 1 and 2. Patients younger than 18 years of age, transferred to a different facility, those with missing outcomes, age, or gender, were excluded from the analysis. Demographic characteristics (ie, age, gender, and race), along with comorbidities and procedures, were included in our analysis. Chronic comorbidities, such as hypertension, liver disease, and obesity, were obtained using the CCS software and Elixhauser comorbidity classification (Online Tables 1 and 2). Patients were then grouped as shown in Table 1 along with other details of the ICD-9-CM/CCS codes that were used according to Online Tables 1 and 2.

Statistical analysis

For our analysis, we adhered to the main practices proposed by Khera et al. on statistical and research methodologies using the NIS

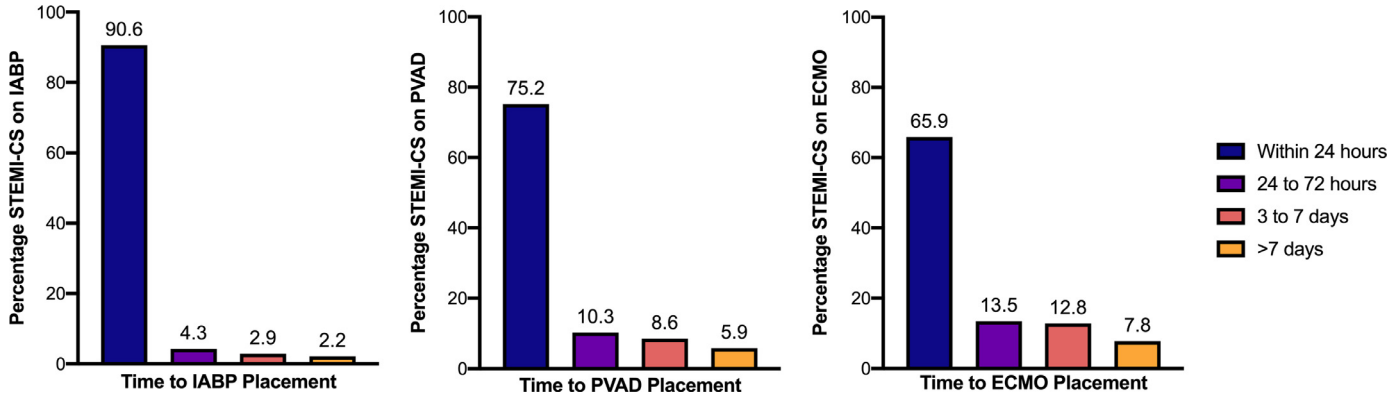

Fig. 1. Timing of pMCS placement in STEMI-CS.

Table 1
Baseline characteristics of STEMI-CS patients with and without nosocomial infections.

		Nosocomial infections		
	Total	No infection	Infection	*p*-value*
No. of observations (weighted) (%)	105184	85046 (80.9)	20137 (19.1)	
Demographic characteristic				
Age, yrs (mean±SE)	65.1±12.9	64.8±12.9	66.9±13.1	<0.001
Males	69293 (65.9)	57877 (68.1)	11416 (56.7)	<0.001
Females	35890 (34.1)	27169 (31.9)	8721 (43.3)	
Race				
White	66113 (62.9)	53575 (63.0)	12538 (62.3)	<0.001
Black	5870 (5.6)	4638 (5.5)	1232 (6.1)	
Hispanic	7018 (6.7)	5545 (6.5)	1473 (7.3)	
Length of hospital stay				
4-6 days	36230 (34.4)	33242 (39.1)	2988 (14.8)	
7-9 days	24891 (23.7)	21083 (24.8)	3808 (18.9)	<0.001
>9 days	44062 (41.9)	30721 (36.1)	13341 (66.3)	
Comorbidities (%)				
Anemia	21129 (20.1)	16226 (19.1)	4903 (24.3)	<0.001
Hypertension	52111(49.5)	42795 (50.3)	9316 (46.3)	<0.001
Diabetes	30836 (29.3)	24402 (28.7)	6434 (32.0)	<0.001
Chronic liver disease	1293 (1.2)	976 (1.1)	317 (1.6)	<0.001
Obesity	10254 (9.7)	8389 (9.9)	1865 (9.3)	<0.001
Chronic pulmonary disease	22991 (21.9)	18603 (21.9)	4388 (21.8)	0.08
History of CVA	3543 (3.4)	2887 (3.4)	656 (3.3)	0.3
History of paralysis	1684 (1.6)	1189 (1.4)	495 (2.5)	<0.001
Pulmonary circulation disorders	262(0.2)	111(0.1)	151(0.7)	<0.001
Congestive heart failure	3090 (2.9)	1649 (1.9)	1441 (7.2)	<0.001
Valvular disease	864 (0.8)	486 (0.6)	378 (1.9)	<0.001
Cardiac arrhythmia	50858 (48.4)	40621 (47.8)	10237 (50.8)	<0.001
Coagulopathy	15652 (14.9)	11810 (13.9)	3842 (19.1)	<0.001
Chronic kidney disease	14454 (13.7)	11050 (13.0)	3404 (16.9)	<0.001
Fluid and electrolyte disorders	42760 (40.7)	32688 (38.4)	10072 (50.0)	<0.001
Peripheral vascular disease	9806 (9.3)	7782 (9.2)	2024 (10.1)	0.001
Alcohol abuse	4754 (4.5)	3849 (4.5)	905 (4.5)	0.9
Malignancy	2487 (2.4)	2031 (2.4)	456 (2.3)	0.2
Acquired immune deficiency syndrome	149 (0.1)	101 (0.1)	48 (0.2)	<0.001
Rheumatoid arthritis/collagen vascular disease	1937(1.8)	1520 (1.8)	417 (2.1)	<0.001
Hypothyroidism	6938 (6.6)	5567 (6.5)	1371 (6.8)	0.002
Weight loss	6409 (6.1)	4315 (5.1)	2094 (10.4)	<0.001
Elixhauser comorbidity index (%)				
0	34759 (33.0)	29341 (34.5)	5418 (26.9)	<0.001
1-3	46065 (43.8)	37582 (44.2)	8483 (42.1)	
≥4	24360 (23.2)	18123 (21.3)	6237 (31.0)	
Revascularization methods (%)				
CABG	20789 (19.8)	16992 (20.0)	3797 (18.9)	<0.001
PCI	72223 (68.7)	59088 (69.5)	13135 (65.2)	<0.001
Fibrinolytic therapy	2095 (2.0)	1762 (2.1)	333 (1.7)	0.003
Vasopressor use (%)	6027 (5.7)	4738 (5.6)	1289 (6.4)	<0.001

CVA: cerebrovascular accident.
CABG: coronary artery bypass graft surgery.
PCI: percutaneous coronary intervention.
* *p*-value <0.05 considered significant.

database.[20] Trend weights were used to estimate national hospitalizations. Stratification and clustering data were done to provide national estimates. For trend analysis, we reported hospitalizations and outcomes as absolute values for each calendar year and compared means using one-way ANOVA. First, we looked at the baseline characteristics of STEMI-CS patients with and without NI. Subsequently, we compared baseline demographics and comorbidities between groups using the Pearson $\chi 2$ test for categorical variables and one-way linear regression for continuous variables. We reported categorical and continuous variables as percentages and mean ± standard error (SE), respectively. Incidence of NI and mortality based on each subtype of NI and use of pMCS were then identified. We then performed multivariable logistic regression analysis to identify variables that were highly associated with developing NI after controlling for age, gender, race, hospital demographics and comorbidities. Furthermore, to assess the impact of NI as a significant risk factor for mortality, increased length of hospital stay and hospital costs across patients admitted with STEMI-CS, multivariable logistic and linear regression were done with NI as an independent predictor. Moreover, similar subgroup analysis was performed amongst those with NI with and without sepsis. Finally, trends of the incidence of NI in patients admitted with STEMI-CS with and without pMCS were computed using a Poisson regression model with a robust error variance to evaluate for changes in the number of outcomes (incidence of NI) per year stratified by use of pMCS while inserting the year variable into the model assuming the association to be linear. All data extraction and analyses were performed using SPSS (Version 25.0 Armonk, NY). Two-sided p-value <0.05 was used for statistical significance.

Results

A total of 172,490 patients with STEMI-CS were identified, with 28.9% and 71.1% had hospital stays of less than or equal to three days and more than three days from the years 2005 to 2014, respectively. The mortality rate of patients who were admitted with less than or equal to three days and more than three days was 61.6% and 17.4%,

Table 2
Incidence of nosocomial infections and mortality based on use of pMCS.

Type of infection	Number of infections (%)				Number of deceased (%)			
	STEMI-CS	*STEMI-CS without pMCS*	*STEMI-CS with any pMCS*	*p*-value*	*STEMI-CS*	*STEMI-CS without pMCS*	*STEMI-CS with any pMCS*	*p*-value*
Total infections	20137 (19.1)	8052 (18.9)	12085 (19.3)	0.2	16245 (21.8)	7459 (23.5)	8786 (20.6)	<0.0001
CLABSI	1314 (1.2)	397 (0.6)	931 (1.2)	<0.001	353 (26.9)	102 (26.0)	251 (27.3)	0.6
UTI	10744 (10.2)	6282 (9.0)	6123 (7.7)	<0.001	2310 (21.5)	1176 (23.4)	1134 (19.8)	<0.001
HAP	6326 (6.0)	1968 (2.8)	4449 (5.6)	<0.001	1700 (26.9)	488 (25.7)	1212 (27.4)	0.2
CDI	1387 (1.3)	596 (0.9)	863 (1.1)	0.4	373 (26.9)	143 (26.2)	230 (27.3)	0.7
Bacteremia	1494 (1.4)	518 (1.2)	976 (1.6)	<0.001	261 (17.5)	105 (20.3)	156 (16.0)	0.04
Skin-related wound infections	1502 (1.4)	577 (1.4)	925 (1.5)	0.1	177 (11.8)	85 (14.7)	92 (9.9)	0.005

STEMI-CS: cardiogenic shock associated with ST-elevated myocardial infarction.
pMCS: percutaneous mechanical circulatory support.
IABP: intra-aortic balloon pump.
PVAD: percutaneous assist ventricular device.
ECMO: extracorporeal membrane oxygenation.
CLABSI: central line-associated bloodstream infection.
UTI: urinary tract infection.
HAP: Hospital-associated pneumonia.
CDI: *C. difficile* infection.
* *p*-value <0.05 considered significant.

respectively. After excluding patients with less than or equal to three days, 105,184 hospitalizations for STEMI-CS were identified. Among those, 20,137 had a NI (19.1%), with a mean age of 65.1 years (± 12.9 years). Those admitted for STEMI-CS found to have a NI were predominantly males (56.7% vs 43.3%, $p<0.001$) and Whites (62.9%). STEMI-CS patients who developed a NI were more likely to have other comorbidities such as anemia (24.6% vs 16.6%, $p<0.001$), diabetes mellitus (32.3% vs 28.7%, $p<0.001$), fluid and electrolyte disorders (50.5% vs 38.7%, $p<0.001$), and chronic kidney disease (18.0% vs 13.8%, $p<0.001$).

Nosocomial infections among STEMI-CS patients

No significant difference was observed in the incidence of total NI among patients admitted with STEMI-CS with and without pMCS (19.3% vs 18.9%, $p = 0.2$) (Table 2, Fig. 2). Among those with pMCS, the incidence of NI in patients with IABP, PVAD, and ECMO was 19.1%, 22.5%, and 28.7%, respectively. Those with more than one pMCS had a 23.8% rate of NI. The most common NI among patients with STEMI-CS was UTI (9.2%) followed by HAP (6.8%), CLABSI (1.5%), bacteremia (1.5%), skin related infections (1.5%), and CDI (1.3%) (Table 2, Fig. 2). Moreover, HAP (18.0%), CDI (5.5%), CLABSI (5.1%), and skin related infections (3.7%) were highest among patients placed on ECMO, whereas UTI (9.7%) and bacteremia (2.8%) were highest among those on PVAD (Table 3). The incidence of NI among admissions for STEMI-CS decreased from the year 2005 to 2014, irrespective of pMCS use ($p<0.001$) (Fig. 3). Fig. 4 presents the factors that were highly associated with greater odds of NI among STEMI-CS admissions. These were: female gender (OR: 1.82; 95% CI: 1.75-1.86); increasing length of hospital stay (7-9 days; OR: 1.99; 95% CI: 1.75-2.26; >9 days; OR: 4.51; 95% CI: 4.04-5.04 compared to 4-6 days as reference); history of chronic liver disease (OR: 1.44; 95% CI: 1.06-1.98), pulmonary circulation disorders (OR: 1.94; 95% CI: 1.04-3.61), fluid and electrolyte disorders (OR: 1.27; 95% CI: 1.16-1.40); history of congestive heart failure (OR: 2.19; 95% CI: 1.75-2.73); and chronic kidney disease (OR: 1.16; 95% CI: 1.03-1.31).

Incidence of mortality by type of nosocomial infection and mechanical circulatory support

Tables 3 and 4 present the incidence of mortality among patients with STEMI-CS with different NI, stratified by use of different pMCS.

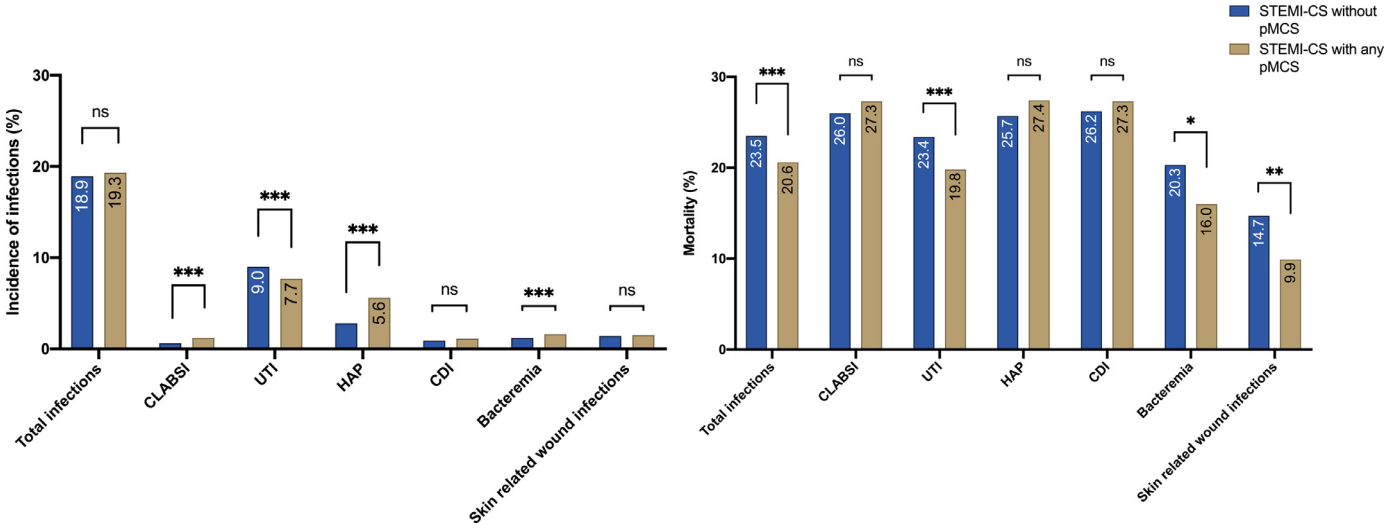

Fig. 2. Difference in the incidence of nosocomial infections and mortality associated with nosocomial infections between STEMI-CS patients without pMCS and with any pMCS.

Table 3
Incidence of nosocomial infections and mortality by subtype of pMCS used.

Type of infection	Number of infections (%)					Number of deceased (%)				
	STEMI-CS with IABP	*STEMI-CS with PVAD*	*STEMI-CS with ECMO*	*STEMI-CS with combined pMCS*	*p*-value*	*STEMI-CS with IABP*	*STEMI-CS with PVAD*	*STEMI-CS with ECMO*	*STEMI-CS with combined pMCS*	*p*-value*
Total infections	11501 (19.1)	237 (22.5)	78 (28.7)	240 (23.8)	<0.001	8022(19.5)	227 (32.0)	122 (71.8)	361 (62.8)	<0.001
CLABSI	875 (1.5)	5 (0.5)	14 (5.1)	27 (2.7)		223 (25.5)	0 (0.0)	14 (100.0)	13 (48.1)	<0.001
UTI	5536 (9.2)	102 (9.7)	19 (7.0)	72 (7.1)		1051 (19.0)	29 (28.4)	5 (26.3)	49 (68.1)	<0.001
HAP	4106 (6.8)	124 (11.8)	49 (18.0)	121 (12.0)		1061 (25.8)	55 (44.4)	20 (40.8)	62 (51.7)	<0.001
CDI	780 (1.3)	5 (0.5)	15 (5.5)	43 (4.3)		197 (25.3)	0 (0.0)	15 (100.0)	18 (41.9)	<0.001
Bacteremia	913 (1.5)	30 (2.8)	5 (1.8)	24 (2.4)		137 (15.0)	10 (33.3)	0 (0.0)	9 (37.5)	0.001
Skin related wound infections	876 (1.5)	26 (2.5)	10 (3.7)	14 (1.4)		77 (8.8)	5 (19.2)	5 (50.0)	5 (35.7)	<0.001

STEMI-CS: cardiogenic shock associated with ST-elevated myocardial infarction.
pMCS: percutaneous mechanical circulatory support.
IABP: intra-aortic balloon pump.
PVAD: percutaneous assist ventricular device.
ECMO: extracorporeal membrane oxygenation.
CLABSI: central line-associated bloodstream infection.
UTI: urinary tract infection.
HAP: Hospital-associated pneumonia.
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* *p*-value <0.05 considered significant.

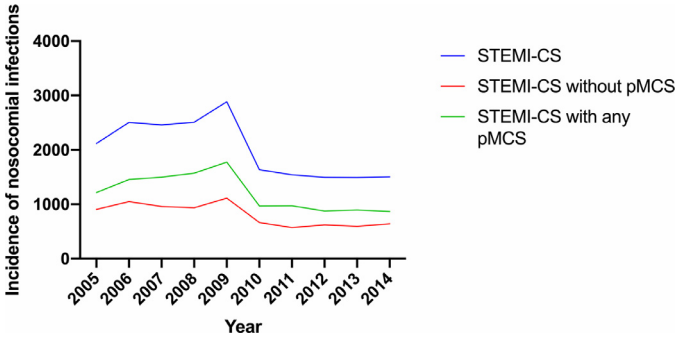

Fig. 3. Trends of nosocomial infection based on use of pMCS.

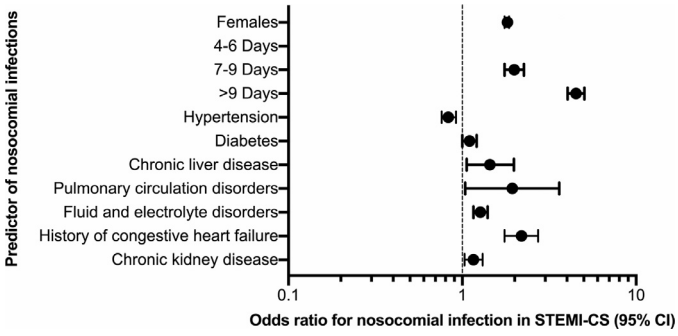

Fig. 4. Variables highly associated with nosocomial infection in STEMI-CS.

The mortality rate was 21.8% among those who developed a NI. The incidence of death was lower in patients on pMCS compared to those not on any pMCS (20.6% vs 23.5%, $p<0.001$).

Impact of nosocomial infections on mortality, length of hospital stay, and average cost of hospitalization

NI were associated with higher risk of in-hospital mortality (adjusted OR: 1.11, 95% CI: 1.07-1.16) and increased length of hospital stay (17 vs 10 days, $p<0.001$) and cost ($216,540 vs $151,932, $p<0.001$). When stratified by pMCS, the incidence of NI was found to be an independent predictor of mortality among those with IABP (adjusted OR: 1.19, 95% CI: 1.13-1.26) and those with more than one pMCS (adjusted OR: 2.20, 95% CI: 1.50-3.33). No increased risk of mortality was found in patients who were not on any pMCS, PVAD, or ECMO (Table 3).

Moreover, average length of hospital stay was higher in those who developed a NI, especially among those on ECMO (38 days vs 13 days, $p<0.001$) and more than one pMCS (33 vs 15 days, $p<0.001$). Similarly, a higher average cost of hospitalization was found among those who developed a NI, irrespective of pMCS.

Table 4
Impact of nosocomial infections on mortality, length of hospital stay, and average cost stratified by use of pMCS.

Type of population	In-hospital mortality		Length of hospital stay			Average cost of hospitalization		
	Unadjusted odds ratio (95% CI)	Adjusted[a] odds ratio (95% CI)	No infection	Infection	*p*-value	No infection	Infection	*p*-value
STEMI-CS	1.21 [1.16-1.25]	1.11 [1.07-1.16]	10	17	<0.001	151,932	216,540	<0.001
No pMCS	1.13 [1.06-1.19]	1.05 [0.99-1.12]	9	15	<0.001	124,244	168,456	<0.001
IABP	1.27 [1.21-1.34]	1.19 [1.13-1.26]	10	18	<0.001	163,044	231,394	<0.001
PVAD	1.18 [0.87-1.61]	0.92 [0.59-1.45]	10	21	<0.001	278,499	444,062	<0.001
ECMO	0.20 [0.12-0.36]	0.10 [0.02-0.33]	13	38	<0.001	481,860	636,704	0.003
Combined pMCS	1.16 [0.87-1.55]	2.20 [1.50-3.33]	15	33	<0.001	466,580	774,809	<0.001

STEMI-CS: cardiogenic shock associated with ST-elevated myocardial infarction.
pMCS: percutaneous mechanical circulatory support.
IABP: intra-aortic balloon pump.
PVAD: percutaneous assist ventricular device.
ECMO: extracorporeal membrane oxygenation.
[a] After adjusting for age, gender, race, comorbidities, hospital characteristics, and nosocomial infections.

Sepsis in admitted STEMI-CS patients

We performed a subgroup analysis to further investigate the role of sepsis in STEMI-CS patients admitted with a NI. During the 10-year period from 2005 to 2014, 3,987 STEMI-CS hospitalizations with NI-associated sepsis were identified, accounting for 19.8% among STEMI-CS hospitalizations with NI (Online Table 3). The mean age for STEMI-CS patients hospitalized with NI-associated with sepsis was 66.7 years (± 13.3 years). Those who developed NI-associated sepsis were predominantly males (61.7% vs 38.3%, $p < 0.001$) and Whites (59.4%). STEMI-CS patients who developed NI-associated sepsis were more likely to have the following comorbidities: diabetes (34.9% vs 31.3%, $p<0.001$), pulmonary circulation disorders (1.2% vs 0.6%, $p<0.001$), congestive heart failure (13.1% vs 5.7%, $p < 0.001$), valvular disease (3.4% vs 1.5%, $p < 0.001$), coagulopathy (25.2% vs 17.6, $p<0.001$), fluid and electrolyte disorders (58.8% vs 47.8%, $p<0.001$), and weight loss (14.5% vs 9.4%, $p < 0.001$).

Compared to those who did not develop sepsis, those who developed NI-associated sepsis had greater odds of in-hospital mortality (OR: 2.95; 95% CI: 2.62-3.05), increased length of hospital stay (23 days vs 16 days, $p<0.001$), and a higher average cost of hospitalization ($p<0.001$) (Online Table 4). There was no difference in the incidence of NI-associated sepsis between patients on pMCS and without pMCS ($p = 0.05$), however mortality rates were higher among patients on pMCS (41% vs 36.8%, $p = 0.009$) (Online Table 5). Moreover, among deceased patients, the incidence of sepsis was highest in those with more than one pMCS (61.5%), followed by PVAD (47.4%), ECMO (50.0%), IABP (39.6%), and without pMCS (36.8%) (Online Table 6). Baseline characteristics of STEMI-CS patients with and without NI were then stratified by subtype of pMCS used as highlighted in Online Table 7.

Discussion

In this study, we used the NIS database to investigate the role of NIs in the context of STEMI-CS. In a study by Miller et al., CS was the most common cardiovascular condition associated with healthcare-acquired infection (HAI) accounting for 4% of admitted patients.[2] In our study, the most common NI were UTI, HAP, and CLABSI followed by bloodstream infection, skin related infections and CDI in admitted STEMI-CS patients. In contrast, in Miller et al.'s study, the most common HAI, among patients with heart failure, acute myocardial infarction, CS, CABG, and atrial fibrillation or flutter, were CDI followed by catheter-associated UTI, ventilator-associated pneumonia, and CLABSI.[2] However, these were not stratified according to each cardiovascular condition. Another reason includes using lesser codes for defining hospital acquired pneumonia. For example, in our study, we defined HAP using codes for ventilator-associated pneumonia and other codes specific for HAP as previously done in a study by Giuliano et al.[21] In a study by Nash et al., UTIs, pneumonia and bloodstream infections have also been found to be prevalent HAI in ST-segment elevated myocardial infarction (STEMI) patients, accounting for 6.0%, 4.6%, and 2.6% of STEMI patients aged older than 18 years, respectively.[22]

Another observation made in our study was that the incidence of NI has been decreasing in patients admitted with STEMI-CS over 10 years from 2005 to 2014. On the other hand, the incidence of HAI has been increasing for patients with CS since 2008 according to Miller et al..[23] The incidence of HAI, however, did not change for patients admitted with acute myocardial infarction or CABG. These differences highlight the increasing need for studies focusing on NI susceptibility and prevention for both acute myocardial infarction and CS.

Truffa et al. explored the incidence and outcomes of infections in patients with STEMI treated with PCI and found that the main location of the infection was in the bloodstream. Additionally, compared to those without infection, STEMI patients with infection had more comorbidities.[24] Our study comparing STEMI-CS patients with NI and those without NI also showed that STEMI-CS patients with NI were likely to have more comorbidities than those without. Moreover, in our study, increasing length of hospital stay was found to be associated with NI. This was consistent with previous studies highlighting the significance of hospital stay as a risk factor for developing infections.[25,26] A retrospective cohort by Jeon et al. found that among 113,893 admissions, there was a nonlinear increase in the incidence of bloodstream related infection. This increase was found to be higher among sicker patients who required higher level of care.[27]

In our analysis, patients admitted with STEMI-CS whose hospital stay was complicated with a NI had an 11% independent increase risk of mortality. This increase is magnified when patients were diagnosed with sepsis during their admission (OR: 2.95; 95% CI: 2.72-3.20). This finding was also highlighted in a study by Kohsaka et al. where culture-positive patients with acute myocardial infarction complicated by CS were at higher risk of mortality.[28] Moreover, a large prospective study by Vught et al. found that sepsis-associated nosocomial infections were associated with 15-21% increased risk of mortality; however, only 2% were specifically attributable to NI. This showed that the difference in mortality was more related to an advanced illness severity since admission.[29] In the NIS database, patients with STEMI-CS whose hospital stay was complicated with sepsis are considered of a higher severity illness compared to those without sepsis and thus explains the higher mortality rates among those with NI and sepsis. Because different types of pMCS have been used in the setting of CS,[30] we also sought to investigate the association between NI and type of pMCS used in STEMI-CS patients. The incidence of death was lower in patients on pMCS compared to those not on any pMCS (20.6% vs 23.5%, $p < 0.001$); however, higher mortality rates were observed among those with sepsis and on any pMCS (41.0% vs 36.8%, $p = 0.009$). A similar observation by Paoli et al. found that increasing sepsis severity was associated with higher mortality and increasing cost of hospitalization.[31] A retrospective study by Schmidt et al. explored how NI impacted adult patients receiving venoarterial ECMO (VA-ECMO) for refractory CS. They defined patients with acute refractory CS if the following signs were present: "evidence of tissue hypoxia concomitant with adequate intravascular volume and sustained hypotension and reduced cardiac index ($<2.2 L/min/m^2$) despite infusion of high-dose catecholamines (epinephrine $>0.2\mu g/kg/min$ or dobutamine $>20\mu g/kg/$ min ± norepinephrine $>0.2\ \mu g/kg/min$)."[6] The definition of a NI set by Schmidt et al. complied with the definition set by the Centers for Disease Control and Prevention National Nosocomial Infections Surveillance System. In this study by Schmidt el al., infected patients had longer hospital stays, which was also shown in our study. The authors also found that a NI with severe sepsis or septic shock was an independent predictor of mortality in patients receiving peripheral VA-ECMO.[32] NI-associated sepsis was also evident among 61.5% of deceased STEMI-CS patients placed on ECMO in our study after subgroup analysis. However, in our analysis, NI were not found to be independent predictors of mortality among patients on ECMO. This can be attributed to an already elevated mortality rate among ECMO patients. Sepsis was also reported in patients with CS complicating acute myocardial infarction, particularly in those who were placed on prolonged IABP.[32] This finding was consistent with findings from our study demonstrating that NI-associated sepsis was found in 38.6% of deceased STEMI-CS patients placed on IABP.

Study limitations

This study has several limitations, particularly because this was a retrospective analysis of a large database. One of the main limitations of this study is the inability to draw conclusions related to the time to event of a NI. Therefore, this study used ICD-9 codes to identify NI,

allowing for potential coding errors. Another reason why coding errors are a potential limitation in this study is because of the inability to distinguish between infections that were nosocomial in origin and those that were not nosocomial. However, to fulfill the definition of NI, we excluded patients who stayed less than three days in the hospital.

Other limitations include inability to determine causality for length of hospital stay and NI, and lack of hospitals reporting NI. Bond et al. explores two missions that were started by the United States government, the "2009 HHS Action Plan to Prevent Healthcare-Associated Infections" and the "2011 Partnership for Patients" to prevent NI-related infections.[33-35] One of these plans included preventing reimbursement to hospitals with higher rates of NIs as a sign of low quality of care.[36] This might decrease hospital incentives in reporting NI and thus could explain the low sensitivity of NI-related ICD-9/10 coding as highlighted by various literature.[33,34,36] Moreover, in a study by Meier et al., the authors examined the mandatory reporting of healthcare-associated infections (HAI) by different states. Different states have different laws for reporting HAI. This discrepancy further allows a hospital, for which these laws do not apply, to underreport NI and mitigate any financial impact NI may have on the hospital itself.[37] Another limitation of this study is that the NIS database does not provide objective measures, such as vital signs, ejection fraction reports, cardiac catheterization and angiographic results, as well as laboratory data (ie, troponin, brain natriuretic peptide, etc.). Because data used for this study only captured STEMI-CS admissions from 2005 to 2014, we may have missed admissions outside this period. Despite these limitations, the analysis was performed on a large sample size from the NIS database. Lack of reporting bias found in retrospective studies also strengthens our analysis. The NIS also uses internal and external quality control measures to reduce coding errors. Additionally, the ICD-9 codes have been previously validated to encompass CS patients in the setting of myocardial infarction,[38,39] and specifically in STEMI-CS patients.[40]

Conclusions

To the best of our knowledge, this is the largest study to date demonstrating the association between NI and STEMI-CS. This study provided insight into how mortality in STEMI-CS patients who developed NI varied depending on the type of pMCS used. Of noteworthy importance, STEMI-CS patients who developed NI were at greater odds of in-hospital mortality. Increasing length of hospital stay was the strongest association with developing a NI. The significant impact of NI on mortality, length of hospital stay, and hospitalization costs in STEMI-CS should prompt hospitals to develop system-based algorithms to rapidly detect, document, manage, and prevent NI in patients with STEMI-CS.

Declaration of Competing Interest

The authors have no relationships relevant to the contents of this paper to disclose.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2020.08.008.

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