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Serious Infection After Acute Myocardial Infarction

Incidence, Clinical Features, and Outcomes

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Objectives The aim of this study was to address the knowledge gap using the APEX-AMI (Assessment of Pexelizumab in Acute Myocardial Infarction) trial database. We also assessed the association between serious infections and 90-day death or death/myocardial infarction (MI).

Background Little is known about the incidence, location, etiological organisms, and outcomes of infection in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention.

Methods We analyzed data from 5,745 STEMI patients enrolled in the APEX-AMI trial. Detailed information on infection was collected for all patients. We described characteristics of patients according to infection and details of infection. Cox proportional hazards models were used to assess 90-day outcomes among patients with and without infections after adjusting for associated clinical variables and with infection as a time-dependent covariate.

Results Overall, 138 patients developed a serious infection (2.4%), most of whom presented with a single-site infection. The median (25th, 75th percentile) time until diagnosis of infection was 3 (1, 6) days. The most commonly identified organism was *Staphylococcus aureus*, and the main location of infection was the bloodstream. These patients had more comorbidities and lower procedural success at index percutaneous coronary intervention than those without infections. Serious infection was associated with significantly higher rates of 90-day death (adjusted hazard ratio: 5.6; 95% confidence interval: 3.8 to 8.4) and death or MI (adjusted hazard ratio: 4.9; 95% confidence interval: 3.4 to 7.1).

Conclusions Infections complicating the course of patients with STEMI were uncommon but associated with markedly worse 90-day clinical outcomes. Mechanisms for early identification of these high-risk patients as well as design of strategies to reduce their risk of infection are warranted. (Pexelizumab in Conjunction With Angioplasty in Acute Myocardial Infarction [APEX-AMI]; NCT00091637) (J Am Coll Cardiol Intv 2012;5:769–76) © 2012 by the American College of Cardiology Foundation

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Rates of infection complicating percutaneous coronary intervention (PCI) are very low (1–9), and reported rates of infection in patients undergoing cardiac catheterization are <1% (10–12). Cardiogenic shock complicating acute myocardial infarction (MI) is often accompanied by a systemic inflammatory response, manifested by high levels of interleukin-6 and associated with multi organ failure and high mortality rates (13–15). The extent of overlap between cardiogenic shock and other conditions leading to a systemic inflammatory state, including serious infection, is unclear. In 1 report, among patients with cardiogenic shock complicating ST-segment elevation myocardial infarction (STEMI), 21% died of noncardiac causes, and the cause of death was sepsis in 29% (13).

Little is known about the incidence, location, demographic data, and etiological organisms of serious infection in patients with acute MI, particularly STEMI, who are treated with primary PCI in the contemporary era. Thus, the primary objective of our study was to address this knowledge gap with the database of the APEX-AMI (Assessment of Pexelizumab in Acute Myocardial Infarction) trial. We also assessed the association between serious infection and 90-day death or death/MI.

Abbreviations and Acronyms

ACE = angiotensin-converting enzyme
BP = blood pressure
CABG = coronary artery bypass grafting
CAD = coronary artery disease
CHF = congestive heart failure
CI = confidence interval
COPD = chronic obstructive pulmonary disease
ECG = electrocardiograph
HR = hazard ratio
ICH = intracerebral hemorrhage
MI = myocardial infarction
MRI = magnetic resonance imaging
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

Methods

We analyzed data from the APEX-AMI trial, a randomized clinical trial of 5,745 STEMI patients treated with primary PCI. Briefly, the APEX-AMI trial was a multicenter (17 countries and 296 hospitals), randomized, double-blind trial of pexelizumab versus placebo in conjunction with primary PCI in STEMI. The trial was approved by the institutional ethics committee or institutional review board of each participating site, and all enrolled patients provided written informed consent. The present analyses were approved by the institutional review board of Duke University Medical Center. The primary outcome of the APEX-AMI trial was 30-day mortality. Secondary outcomes were 90-day mortality and the composite of death, cardiogenic shock, and congestive heart failure at 30 days. Additional outcomes included stroke, recurrent MI, and sepsis. In this large clinical trial, no difference in 30-day mortality was observed between the 2 randomized treatment groups (16).

Because pexelizumab is an inhibitor of C5 complement activation, resulting in formation of C5a (anaphylatoxin and proinflammatory substance) and C5b-9 or the membrane attack complex, patients with known or suspected active serious infection were excluded from the trial before randomization, and detailed information about the occurrence of infection during and after treatment was collected (16). Data on serious infections were categorized in the case report form as follows: sepsis with and without shock, pneumonia, cellulitis, sternal wound, puncture site, and other. If a culture was obtained, the site of the culture (blood, urine, sputum, or wound), type of organism detected by the culture, date of infection, whether the investigator determined the infection was related to the study drug, and outcome were recorded. Infections were also collected as adverse events (serious or non serious). These were categorized by the *Medical Dictionary for Regulatory Activities* system organ class, high-level, and preferred term. Both sources of infection diagnosis were used for our analysis.

"Serious infection" was determined by the investigator and was not centrally adjudicated. However, all in-hospital data from the case report forms were source data verified. Discrepant data with regard to infection were reconciled, and extensive data queries were performed to verify the data.

Although analysis of infection was not part of the formal statistical plan, we did plan to investigate events, such as serious infections that were prospectively collected as "yes" or "no" variables on the case report form.

Statistical analysis. Continuous variables were presented as median (25th, 75th percentile). Nonparametric p values were given for comparing continuous variables. Categorical variables were presented as percentages and were compared using chi-square or exact p values. A frequency table was provided for number of infections, time from randomization to infection (in days), infection site (e.g., urine, bloodstream, and others), and infectious organism.

Tables of outcomes and concomitant medications were also provided. The p values were omitted from these tables because they included time-dependent covariates with unrecorded times, and it was unclear whether infection strictly preceded the outcome/medication dosing. A Cox proportional hazards model was fit for 90-day death and 90-day death or MI with infection as a time-dependent covariate. The model was adjusted for "sheath time" (the time a patient was undergoing catheterization/PCI and had an in-dwelling catheter) and other variables previously determined to be significant predictors of death in the APEX-AMI trial: age, baseline Killip class III or IV, baseline systolic blood pressure, baseline heart rate, and baseline creatinine level (17). Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) were reported. The model was fit both including and excluding early deaths

(i.e., patients who died in the first 24 h) to address survival bias such that a patient who died early had less opportunity to develop an infection.

A sensitivity analysis was performed, dividing our infection patients into 2 groups: infection within 48 h and infection after 48 h of hospital admission. This analysis was done to assess eventual differences in clinical outcomes between early infection and nosocomial infection (or hospital-acquired infection), defined as any infection that occurred 48 h after hospital admission.

All analyses were conducted with SAS (version 9.2, SAS Institute, Cary, North Carolina). The significance level was set at 0.05. No adjustments were made for multiple comparisons.

Results

Baseline characteristics. Of 5,745 patients enrolled in the APEX-AMI trial, 138 (2.4%) developed at least 1 serious infection. The median (25th, 75th percentile) time until diagnosis of infection was 3 (1, 6) days, and 80% of the infections had already occurred by day 8 after hospital admission (Fig. 1). Most patients (n = 96, 69.6%) developed a serious infection 48 h after hospital admission, and only 30.4% (n = 42) developed infection before 48 h. The rates of serious infections were similar between patients treated with pexelizumab (2.3%) and placebo (2.5%).

Baseline characteristics of patients with and without infections are shown in Table 1. Patients with serious infections were older; more often had a history of a chronic inflammatory condition, chronic obstructive pulmonary disease, and diabetes; and more often had anterior MI, Killip class III or IV, higher heart rate, higher creatinine value, higher levels of peak creatine kinase, and creatine kinase myocardial band levels with greater ST-segment deviation than patients without infections. In addition, they had lower success rates than those patients who did not develop serious infections (post-intervention Thrombolysis In Myocardial Infarction [TIMI] flow grade 3, 75.4% vs. 90.3%, respectively).

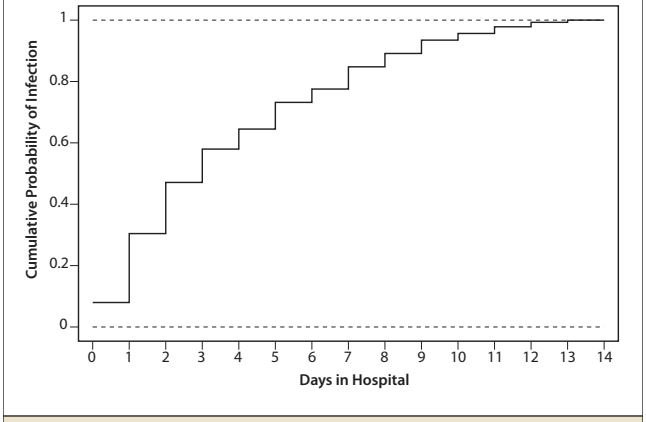

Figure 1. Rates of Serious Infection by Days in the Hospital

Infections were recorded to the day. Infections from randomization to day 1 (exclusive) were considered as occurring at day 0.

In-hospital medications. In-hospital medications are listed in Table 2. Patients with serious infection had numerically less use of statins, angiotensin-converting enzyme inhibitors, beta-blockers, aspirin, and abciximab than patients without serious infection.

In-hospital procedures. In-hospital procedures are described in Table 3. In general, patients with serious infections had numerically more in-hospital procedures than patients without serious infections, including repeat diagnostic catheterization, additional PCI, cardiac surgery (coronary artery bypass grafting), automatic implantable cardiac defibrillator placement, use of mechanical support (intra-aortic balloon pump or left ventricular assist device), permanent pacemaker placement, mechanical ventilation, echocardiography, red blood cell transfusion, and dialysis. Similar results were observed when only serious infections that occurred after the procedures were analyzed (data not shown).

In-hospital complications. In-hospital complications are shown in Table 4. Patients with serious infections had numerically more in-hospital complications than patients without serious infections, including recurrent ischemia, atrial fibrillation, ventricular tachycardia, ventricular fibrillation, cardiac arrest, deep venous thrombosis, renal failure, and bleeding. Similar results were seen when only complications that occurred after a serious infection were considered (data not shown). Patients with versus without serious infection had longer length of hospital stay (12 vs. 5 days) and longer length of intensive care unit stay (7 vs. 2 days).

Serious infection features. Table 5 contains data about the location of infections, number of infections per patient, and organisms associated with infections. Most patients had only 1 type of infection, the most common location being the bloodstream, and the most common organism being *Staphylococcus aureus*.

Clinical outcomes. Clinical outcomes are described in Table 6. Rates of death, congestive heart failure, shock, MI, and stroke were higher among patients with serious infection compared with those without serious infection. Similar results were observed when only clinical outcomes that occurred after a serious infection were analyzed. Among patients with serious infections, there was no difference in clinical outcomes between patients treated with placebo or pexelizumab.

After multivariable adjustment, serious infection was significantly associated with 90-day death (adjusted HR: 5.3; 95% CI: 3.5 to 7.8, $p \leq 0.001$) and death or MI (adjusted HR: 4.6; 95% CI: 3.2 to 6.6, $p \leq 0.001$). After the exclusion of deaths that occurred in the first 24 h after acute MI presentation (n = 0 in the infection group and n = 60 in the no infection group), serious infection remained significantly associated with 90-day death (adjusted HR:

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Table 1. Baseline Demographic Data and Other Characteristics

	Serious Infection (n = 138)	No Serious Infection (n = 5,606)*	p Value
Age, yrs	65 (57, 75)	61 (52, 71)	<0.001
Female, %	26.1	23.0	0.394
Enrolled in the U.S. (yes), %	32.6	30.4	0.583
Transfer patient (yes), %	37.0	36.1	0.841
Anterior MI, %	70.3	58.9	0.007
Time from symptoms to hospital admission, h	2.3 (1.3, 3.8)	2.2 (1.3, 3.3)	0.581
Time from symptoms to randomization, h	3.1 (2.1, 4.2)	2.8 (2.0, 3.9)	0.116
Time from hospital admission to randomization, h	0.6 (0.3, 0.9)	0.5 (0.2, 0.9)	0.197
Systolic BP, mm Hg	129 (110, 148)	133 (117, 150)	0.017
Heart rate, beats/min	80 (65, 96)	75 (65, 86)	0.004
Diastolic BP, mm Hg	74.5 (65, 90)	80 (70, 90)	0.016
Height, cm	173 (165, 178)	172.7 (166, 178)	0.776
Weight, kg	80 (68, 90)	80 (70, 91)	0.436
Body mass index	26.7 (24.5, 29.6)	27.1 (24.5, 30.1)	0.683
CK value	140 (87, 361.2)	143.7 (90, 277)	0.794
Peak CK value	3,463 (1,525.8, 5,850)	1,771.1 (843, 3,261.5)	<0.001
Creatinine value	97.2 (79.6, 114.9)	88.4 (79.6, 106.1)	0.001
CK-MB value	6.8 (3.3, 84)	4.6 (2.2, 14.8)	0.016
Peak CK-MB value	268.9 (147.3, 430)	157.8 (68, 292.1)	0.001
ST deviation, mm	15.5 (10, 21.3)	13 (9, 18.5)	0.004
Race, %			
White vs. non-White	92.8	94.4	0.416
Smoking status, %			0.407
Never	37.0	33.2	
Current	37.7	43.4	
Past	25.4	23.4	
Killip class, %			
Class III or IV vs. I or II	10.1	1.6	<0.001
Medical history, %			
Atrial fibrillation	6.5	4.1	0.156
Angina	26.1	24.0	0.568
CABG	2.2	2.2	1.000
CAD	21.7	16.3	0.087
CHF	9.4	3.5	0.001
Chronic inflammatory condition	6.5	1.7	0.001
Chronic liver disease	1.4	0.7	0.259
COPD	11.6	4.7	<0.001
Current renal dialysis	0.7	0.3	0.323
Diabetes	22.5	15.7	0.033
Family history of CAD	16.2	19.0	0.411
ICH stroke	0.0	0.3	1.000
Hyperlipidemia	48.6	49.7	0.820
Hypertension	57.2	49.3	0.063
Post-intervention TIMI grade, %			<0.001
Grade 0	4.8	2.5	
Grade 1	3.2	0.9	
Grade 2	16.7	6.4	
Grade 3	75.4	90.3	

Values are median (25th, 75th percentile) or %. *One patient developed an infection before the randomization and thus is excluded from the denominator.

BP = blood pressure; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CHF = congestive heart failure; CK = creatine kinase; CK-MB = creatine kinase myocardial band; COPD = chronic obstructive pulmonary disease; ECG = electrocardiograph; ICH = intracerebral hemorrhage; TIMI = Thrombolysis In Myocardial Infarction.

Table 2. In-Hospital Medications Used by Patients With and Without Serious Infections

Medications	Serious Infection	No Serious Infection
Antibiotics	123/138 (89.1%)	662/5,606 (11.8%)
Aspirin	128/138 (92.8%)	5,444/5,601 (97.2%)
Thienopyridines	115/117 (98.3%)	5,206/5,249 (99.2%)
Abciximab	50/84 (59.5%)	2,527/3,903 (64.7%)
Eptifibatide	25/84 (29.8%)	1,121/3,903 (28.7%)
Tirofiban	9/84 (10.7%)	255/3,903 (6.5%)
Statins	109/138 (79%)	5,118/5,602 (91.4%)
ACE inhibitors	98/138 (71%)	4,459/5,600 (79.6%)
Beta-blockers	97/138 (70.3%)	4,770/5,600 (85.2%)

Values are n/N (%).
ACE = angiotensin-converting enzyme.

5.6; 95% CI: 3.8 to 8.4, $p \leq 0.001$) and death or MI (adjusted HR: 4.9; 95% CI: 3.4 to 7.1, $p \leq 0.001$). Similar results were observed in patients who developed a serious infection within 48 h of (n = 42, 30.4%) and 48 h after (n = 96, 69.6%) hospital admission (data not shown).

Patients who presented in hospital with serious infection were also more likely to be readmitted within 90 days for another serious infection compared with patients who did not develop a serious infection during index hospital stay for acute MI (5.1% vs. 0.7%, respectively). Overall, when compared with patients who did not have an infection, those with any serious infection were also more likely to die or be readmitted for any cause within 30 days (23.0% vs. 11.0%) and within 90 days (41.0% vs. 20.4%).

Table 3. In-Hospital Procedures in Patients With and Without Serious Infections

Procedures	Serious Infection	No Serious Infection
Repeat diagnostic catheterization	18/138 (13.0%)	319/5,598 (5.7%)
Additional PCI (does not include primary PCI for the qualifying MI)	12/138 (8.7%)	383/5,598 (6.8%)
Cardiac surgery (CABG)	23/138 (16.7%)	181/5,599 (3.2%)
Automatic implantable cardioverter-defibrillator	1/138 (0.7%)	28/5,599 (0.5%)
Intra-aortic balloon pump	55/138 (39.9%)	389/5,599 (7.0%)
Left ventricular assist device	3/138 (2.2%)	22/5,599 (0.4%)
Dialysis	6/138 (4.4%)	21/5,598 (0.4%)
Multi-uptake gated acquisition	0/138 (0%)	51/5,598 (0.9%)
Stress test	5/138 (3.6%)	191/5,598 (3.4%)
Cardiac MRI	2/138 (1.5%)	103/5,598 (1.8%)
Permanent pacemaker	2/138 (1.5%)	47/5,599 (0.8%)
Mechanical ventilation	52/138 (37.7%)	169/5,599 (3.0%)
Echocardiography	115/138 (83.3%)	3,866/5,594 (69.1%)
Red blood cell transfusion	48/138 (34.8%)	295/5,606 (5.3%)

Values are n/N (%).
CABG = coronary artery bypass grafting; MRI = magnetic resonance imaging; PCI = percutaneous coronary intervention.

Table 4. In-Hospital Complications in Patients With and Without Serious Infections

Events	Serious Infection (n = 138)	No Serious Infection (n = 5,606)
Recurrent ischemia	9.4%	4.2%
Atrial fibrillation	26.8%	6.4%
Ventricular tachycardia	12.3%	2.3%
Ventricular fibrillation	12.3%	3.7%
Complete atrioventricular block	3.6%	1.6%
Electrical mechanical dissociation	1.4%	1.0%
Asystole	7.2%	2.1%
Cardiac arrest	10.1%	2.2%
Pericarditis	2.9%	1.2%
Cardiac tamponade	0.7%	0.3%
Acute mitral regurgitation	1.4%	0.2%
Acute ventricular septal defect	2.9%	0.1%
Ventricular rupture	2.2%	0.3%
Symptomatic hypotension	36.2%	8.8%
Pulmonary embolism	2.2%	0.0%
Deep venous thrombosis	0.7%	0.1%
Renal failure	20.3%	1.3%
Bleeding	44.9%	15.4%

Discussion

We demonstrated that, in a contemporary cohort of STEMI patients who underwent primary PCI, serious infection was rare, occurred at a median of 3 days after presentation, and was more frequent among sicker patients with a history of inflammatory disease, chronic obstructive pulmonary disease, and diabetes and among those with worse prognostic markers, such as higher creatinine level at baseline, more advanced Killip class, higher heart rate, and larger infarcts. These patients also had worse angiographic results at the index PCI. Patients who underwent procedures (e.g., coronary artery bypass grafting, intra-aortic balloon pumping, dialysis) after the index PCI also more frequently developed serious infections. Patients with infection also had more in-hospital complications other than infection and had longer intensive care unit and hospital stays. The most common site of infection was the bloodstream, and the most commonly identified organism was *Staphylococcus aureus*. Finally, serious infection was associated with 5-fold higher rates of 90-day death and death or MI.

Fever and systemic inflammation in conjunction with MI. Patients with MI, particularly large MIs, can manifest fever at presentation or during their hospital course, but it is particularly common in the first 24 h after presentation and does not necessarily mean that an infection is present (18–21). However, it can often be a clinical challenge to determine whether the fever is due to the MI, to a complicating infection, or to other causes of systemic inflammation. Regardless of the etiology, because fever has a strong influence on oxygen consumption, it is important to

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Table 5. Number of Infections, Location, Main Organisms, and Distribution of Randomized Treatment for Infected Patients

Number of infections	
1	107 (77.5)
2	25 (18.1)
3	5 (3.6)
5	1 (0.7)
Location of infection	
Pleural effusion	1 (0.7)
Sputum	35 (25.4)
Tissue	1 (0.7)
Unlisted*	28 (20.3)
Urine	20 (14.5)
Blood	56 (40.6)
Wound	6 (4.3)
Organisms of infection	
Culture contaminants	2 (1.4)
E. coli	10 (7.2)
Other	50 (36.2)
P. aeruginosa	7 (5.1)
Staph aureus	13 (9.4)
Staph. epidermis	5 (3.6)
Staph. species	8 (5.8)
Strep pneumonia	3 (2.2)
Strep. species	8 (5.8)
Unlisted†	28 (20.3)
Distribution of treatment for infected patients	
Placebo	72 (52.2)
Pexelizumab	66 (47.8)

Values are n (%). *"Unlisted" is for patients who were infected but with no culture data.
†"Unlisted" is for patients who were infected but with no organism data.

recognize preventable or treatable underlying causes of fever that might predispose a patient to infarct extension and greater infarct size (19,20).

The SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial investigators explored the systemic inflammatory state in patients with cardiogenic shock complicating STEMI (22,23). They concluded that inappropriate vasodilation in patients with systemic inflammatory response syndrome might play an important role in the pathogenesis and persistence of shock, with or without infection (22). Although Ben-Dor et al. (19) found that fever was frequent after reperfusion, they concluded that it was due to infarct size and not to a nonspecific systemic inflammatory response. In their study, fever was correlated with high-sensitivity C-reactive protein but not with fibrinogen levels or white blood cell count. Subsequently, Naito et al. (20) found that fever after acute MI was associated with worse clinical outcome and with infarction expansion, suggesting a relationship between systemic inflammatory response and left ventricular remodeling in the post-infarction period. Furthermore, the rates of death due to pump failure, malignant arrhythmias, and cardiac failure increased significantly with increasing quartile of body temperature (20).

Clinical infection after MI. Although fever tends to occur most commonly in the first 24 h after MI and might be related to infarct size, serious infection as a complication of MI seems to occur later in the hospital course. Although previous literature is scarce with regard to primary PCI-treated acute MI patients, in a cooperative study involving over 12,000 cardiac catheterizations, only 0.10% of patients had serious infection complications documented (9). One case-control study in stable patients who underwent elective PCI found that, similar to our results, infection after PCI was most prevalent on day 3 after presentation and that *Staphylococcus aureus* was the most common organism (24). Another study in elective PCI found that *Staphylococcus epidermidis* was the most frequently identified organism associated with post-PCI infection. Together, these studies suggest that infection might be most related to instrumentation (25). As with our study, previous studies have suggested that congestive heart failure, multiple punctures in the same site, difficult vascular access, duration of sheath placement lasting more than 1 day, and longer duration of procedures are important risk factors for bacteremia associated with cardiac catheterization or PCI (10,24).

In a retrospective case-control study of 1,227 acute MI patients admitted during the previous 47 months, 5% had infectious complications (26). In findings similar to ours, patients with infections were older (67.5 vs. 62.6 years), had longer length of hospital stay (26.7 vs. 12 days), and had higher mortality (45% vs. 12%) compared with patients without infections. The most common site of infection was the lungs (63%), followed by the urinary tract (37%). Heart infections, such as purulent pericarditis and myocardial abscess, after acute MI have been reported but are very infrequent (2,27–34).

Association of infection with clinical outcomes and length of stay. Mortality associated with the presence of infection in patients undergoing elective PCI with drug-eluting stents has been estimated at 1% (35). However, mortality has reached over 40% in some studies of infection after MI (24,26). In 1 prior study, the most common causes of death

Table 6. Clinical Outcomes in Patients With and Without Serious Infections

Endpoints	Serious Infection	No Serious Infection
Death	40/138 (29.0%)	278/5,604 (5.0%)
CHF	32/138 (23.2%)	245/5,606 (4.4%)
Shock	28/138 (20.3%)	168/5,606 (3.0%)
MI	16/138 (11.6%)	174/5,601 (3.1%)
Stroke	9/138 (6.5%)	68/5,601 (1.2%)

Values are n/N (%).
CHF = congestive heart failure; MI = myocardial infarction.

in acute MI patients with infections were cardiogenic shock (41%) and septic shock (30%) (26).

In our study of patients with STEMI treated with primary PCI in the contemporary era, we demonstrated that serious clinical infection was independently associated with 5-fold worse clinical outcomes, including mortality and death or MI at 90 days. Importantly, these STEMI patients with serious infection during the index hospital stay were more likely to be readmitted to the hospital with another serious infection within 90 days from discharge compared with those patients who never developed an infection. Our findings illustrate the importance of serious infection as a marker of worse subsequent clinical outcomes in patients with STEMI treated with primary PCI.

In addition to increased mortality and morbidity associated with serious infection in acute MI patients, serious infections also seem to be associated with measures of resource use. Whereas the length of stay after uncomplicated STEMI in the United States is approximately 4 to 5 days, length of stay in complicated STEMI has been shown to average 11 days (36,37). In our study, we demonstrated that patients with clinically diagnosed serious infections had longer length of stay than patients without infections, mirroring previous data on uncomplicated and complicated MIs. Patients with serious infections also had lower rates of post-intervention TIMI grade 3 flow compared with patients without infection. It is possible that longer procedure times, more bleeding, and vascular access complications in these patients could have contributed to a longer length of stay. Conversely, these complications or low TIMI flow grade itself might have resulted in the use of invasive support devices like intra-aortic balloon pumps and other in-dwelling lines or catheters that might have not only increased the likelihood of developing a serious infection during the course of hospital stay but also resulted in longer hospital stay.

Another important related issue is the underlying definition of hospital infection. In general, a new infection occurring in a patient during hospital stay at least 48 h after admission is suspected to be nosocomial or hospital-acquired. The rate of nosocomial infection has been proposed as a measure of quality in patient care (38,39). In our study, 96 (69.6%) patients who presented with a serious infection did so 48 h after hospital admission. Interestingly, in our overall cohort of patients who developed serious infection, there were no differences in 90-day clinical outcomes between those patients who developed a serious infection within 48 h and those who did so after this time window. These results highlight the importance of identifying patients who are at risk for infection after PCI for STEMI as well as seeking effective strategies for prevention, both to improve clinical outcomes and to reduce resource use. In addition, vigilance for early diagnosis and treatment of those who develop infection is essential to minimize serious complications. In particular, if a patient develops a fever more than 24 h after presentation, this fever might not be due to infarct size or systemic inflammatory response to the infarction but rather might be an early sign of a serious infection that could lead to worse clinical outcomes and greater resource use.

Study limitations. First, this was an observational study; therefore, a causal relationship between serious infection and clinical outcomes cannot be established. In addition, it is likely that in our study most serious infections were hospital-acquired and related to instrumentation. Despite our efforts and extensive statistical adjustments for important confounders, we cannot fully tease out the influence of pre-existing conditions predisposing a patient to infection or of the infection itself that led to worse clinical outcomes. Second, our population with infection was small, although the larger APEX-AMI population with STEMI from which they were drawn allowed us to define the contemporary incidence of infection. Third, serious infection was determined by the investigator and was not centrally adjudicated. However, all in-hospital data from the case report forms were source data-verified. In addition, discrepant data with regard to infection were reconciled, and extensive data queries were performed to verify the accuracy of the data. Finally, we did not collect information on the specific treatments that were used for serious infection in our patient population.

Conclusions

In the contemporary era, serious infections complicating the course of patients with STEMI treated with primary PCI were uncommon (2.4%) but were associated with worse 90-day clinical outcomes and longer hospital stays. The most commonly identified organism was *Staphylococcus aureus*, and the main location was the bloodstream. Most patients developed a serious infection 48 h after hospital admission, and patients who developed any infection were more likely to be re-admitted with another serious infection within 90 days of hospital discharge. Further studies to identify these high-risk patients as well as to design strategies to reduce their risk of infection are warranted.

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Key Words: infection ■ outcomes ■ percutaneous coronary intervention ■ ST-segment elevation myocardial infarction.