In-hospital outcomes and prevalence of comorbidities in patients with ST-elevation myocardial infarction with and without infective endocarditis: insight from the National Inpatient Sample (2013–2014)

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ABSTRACT

In patients with infective endocarditis (IE), ST-elevation myocardial infarction (STEMI) is an uncommon phenomenon. Due to limited data, we intend to evaluate the clinical outcomes in hospitalized patients with STEMI with and without underlying IE. Mortality and morbidity are exponentially worse in STEMI with concomitant IE when compared with without IE. Patients with primary diagnosis of STEMI with and without IE were identified by querying the Healthcare Cost and Utilization Project database of the National Inpatient Sample for the years 2013 and 2014 based on International Classification of Diseases, Ninth Revision codes. During 2013 and 2014, a total of 117,386 patients were admitted with the principle diagnosis of STEMI, out of whom 305 had comorbid IE. There was a significantly increased in-hospital mortality (27.5% vs 10.8%), length of stay (LOS) (14 days vs 5 days), acute kidney injury (AKI; 44.9% vs 18.7%), stroke (23.6% vs 3%), aortic valve replacement (9.5% vs 0.3%), mitral valve replacement (0.2%–5.2%), sepsis (50% vs 6%) and acute respiratory failure (36.7% vs 16.7%) in patients with STEMI with IE when compared with patients with STEMI and without comorbid IE. STEMI without IE had a higher number of angiographies (58.7% vs 25.9%) and percutaneous coronary interventions (50.7% vs 14.4%) during the hospital course when compared with STEMI with IE. In conclusions, hospitalized patients with STEMI with a concurrent diagnosis of IE are at higher risk of in-hospital mortality, increased LOS, AKI, stroke, valve replacements, and acute respiratory failure.

Significance of this study

What is already known about this subject?

- STEMI with concurrent infective endocarditis is associated with increased mortality due to hemodynamic instability and relative risks for undergoing any percutaneous interventions due to concurrent systemic infection.
- There are no clear guidelines about management of ST-elevation myocardial infarction (STEMI) with infective endocarditis (IE).
- Cardiac catheterization in patients with IE can lead to dislodgment of vegetations leading to septic embolic stroke
- Use of antiplatelet and anticoagulant therapy in patients with embolic stroke in IE can lead to hemorrhagic conversions.

What are the new findings?

- STEMI with concurrent IE is associated with increased mortality as compared with IE without STEMI.
- STEMI with concurrent IE is associated with markedly decreased percutaneous interventions and diagnostic cardiac catheterizations.
- STEMI with concurrent IE is associated with increased utilization and inpatient length of stays.

How might these results change the focus of research or clinical practice?

- Our review shows increased mortality in patients with STEMI with concurrent IE. There are currently no established guidelines for the most appropriate and effective management of patients with STEMI and concurrent IE.

INTRODUCTION

Infective endocarditis (IE), which refers to the infection of a heart valve, endocardial surface, or indwelling cardiac device, is the fourth most common life-threatening infection.[1 2] A common complication of IE is septic embolism, which occurs in as many as 50% of patients with IE.[3] Septic emboli can travel to numerous organs/systems, including the central nervous system, lungs, coronary arteries, mesentery, kidneys, liver, and extremities.[3] Although septic embolization to the coronary arteries has been documented, it is relatively rare, occurring at rates of 3%–11%.[2] Information regarding the

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relationship between ST-elevation myocardial infarction (STEMI) and IE is currently lacking. We used data from the National Inpatient Sample (NIS) databases to perform a cross-sectional analysis regarding trends and outcomes in patients with STEMI as well as IE. Through this study, we hope to provide further information regarding the relationship between STEMI and IE in terms of inpatient outcomes and to determine whether there is a further need for clinical trials to determine appropriate interventions in these patients.

METHODS

Data source

The NIS has been explained in detail in prior studies.[4] For the current study, all adult patients during 2013 and 2014 with the primary diagnosis of STEMI from the NIS were included. Patients were filtered using International Classification of Diseases, Ninth Revision (ICD-9) clinical modification codes. We excluded any hospitalizations with missing demographics, that is, age, gender, admission or discharge diagnosis and mortality data. For purposes of analysis, race/ethnicity was categorized as white, black and Hispanic.

Primary and secondary outcomes

Our objective was to assess the primary and secondary outcomes in patients with the principle diagnosis of STEMI with and without IE. The primary outcomes were mortality and length of stay (LOS). Secondary outcomes were stroke, acute kidney injury (AKI; with and without new hemodialysis), aortic/mitral/pulmonic and tricuspid valve surgery, heart block, cardiac arrest, cardiogenic shock, pacemaker implantation, diagnostic coronary angiographies, percutaneous coronary interventions (PCI), coronary artery bypass graft, heart failure, cardiac arrest, cardiac tamponade, sepsis, acquired pneumonia and hematologic complications. The ICD-9 codes used to identify these outcomes are included as an online supplemental file.

Statistical analysis

SPSS software (V.26) was used to perform all statistical analyses. χ^2 tests were used to identify group differences in categorical outcomes, with 2-sample t-test for analysis of continuous outcomes. Logistic regression modeling was used to calculate the adjusted OR (aOR) for each outcome between the 2 study groups controlling for comorbidity differences between the 2 groups. A p value <0.05 was considered statistically significant. We audited the analyses using the checklist provided by the NIS to assess and make sure data analyses are as per rules recommended by the NIS (https://www.hcupus.ahrq.gov/db/nation/nis/nischecklist.jsp).

RESULTS

We identified a total of 117,081 inpatient hospitalizations for primary diagnosis of STEMI during the years 2013 and 2014 using ICD-9 codes 410.00–410.02, 410.10–410.12, 410.20–410.22, 410.30–410.32, 410.40–410.42, 410.50–410.52, 410.60–410.62, 410.70–410.72 (410.71 was excluded in codes for non-STEMI), 410.80–410.82 and 410.90–410.92. We further identified patients (n=305) with a secondary diagnosis of IE using the ICD-9 codes 4210, 4211, 4219, 03642, 09884, 11281, 11504, 11514, 11594, 4249, 42491 and 42499. Thus, our final sample had 2 study groups: STEMI without IE (n=117,081) and STEMI with concurrent IE (n=305). Table 1 shows background characteristics by study group. The patients with STEMI without IE were significantly older with mean age of 66.3±14.1 (p<0.001), and had a greater proportion of patients with hypertension, prior myocardial infarction, anemia, prior PCI, history of smoking and coronary artery disease (p<0.001). However, patients with STEMI and IE had a higher proportion of baseline atrial fibrillation (p<0.001) compared with those without IE.

Table 1 Baseline characteristics of patients with STEMI with and without comorbid IE

Characteristics	STEMI without infective endocarditis	STEMI with infective endocarditis	
Patients (n)	**117,081**	**305**	**P value**
Age, mean (SD), y	66.3±14.1	63.3±16.2	<0.001
Female	36.8%	35.4%	0.620
Race			
White	77.0%	77.0%	0.162
Black	9.3%	12.2%	
Hispanic	7.4%	6.8%	
Hypertension	51.7%	27.9%	<0.001
Diabetes mellitus	23.4%	23.3%	0.971
Chronic kidney disease	6.3%	6.2%	0.946
COPD	0.3%	0.0%	0.301
Anemia	10.2%	19.0%	<0.001
Prior MI	8.9%	3.3%	0.001
Peripheral arterial disease	6.0%	8.5%	0.062
Prior percutaneous intervention	17.1%	9.2%	<0.001
History of smoking	41.2%	30.2%	<0.001
Atrial fibrillation	18.0%	28.9%	<0.001
Dyslipidemia (no cases)			
Coronary artery disease	77.1%	48.2%	<0.001
Obesity	13.3%	11.1%	0.275
Primary payer			
Medicare/Medicaid	62.6%	71.1%	0.009
Private insurance	27.3%	21.7%	

COPD, chronic obstructive pulmonary disease; IE, infective endocarditis; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction.

Table 2 details the aORs for the 2 study groups for the primary and secondary analyses, both unadjusted, and adjusted with control for significant variables from table 1. After control for confounding, STEMI with IE had higher in-hospital mortality (aOR=2.44 (1.88–3.18)) and increased LOS (aOR=4.82 (3.77–6.16)). Additionally, patients with STEMI and IE had higher odds of stroke (aOR=7.83 (5.95–10.29)), heart block (aOR=1.98 (1.23–3.20)), AKI (aOR=2.60 (2.05–3.30)), aortic valve replacement (aOR=31.14 (20.62–47.05)), mitral valve replacement (aOR=26.09 (15.11–45.03)), acquired pneumonia (aOR=1.70 (1.22–2.36)), sepsis (aOR=10.98 (8.63–13.96)) and hematologic complications (aOR=2.97 (2.18–4.05)) compared with those without IE. Patients with STEMI and without IE had statistically significant higher

Table 2 Outcomes of STEMI with and without IE

In-hospital outcomes	STEMI without infective endocarditis (n=117,081)	STEMI with infective endocarditis (n=305)	aOR
In-hospital death	10.8%	27.5%	2.44 (1.88–3.18)
Length of stay (d)	5.2±6.8	13.7±13.4	4.82 (3.77–6.16)
Stroke	3.0%	23.6%	7.83 (5.95–10.29)
Aortic valve replacement	0.3%	9.5%	31.14 (20.62–47.05)
Mitral valve replacement	0.2%	5.2%	26.09 (15.11–45.03)
Heart block	3.3%	5.9%	1.98 (1.23–3.20)
Diagnostic coronary angiographies	58.7%	25.9%	0.31 (0.24–0.41)
Percutaneous coronary intervention	50.7%	14.4%	0.21 (0.15–0.30)
CABG	5.9%	3.3%	0.65 (0.34–1.24)
Acute kidney injury	18.7%	44.9%	2.60 (2.05–3.30)
New dialysis	3.3%	15.4%	3.12 (2.23–4.38)
Pacemaker implantation	1.4%	2.3%	1.59 (0.75–3.39)
Cardiogenic shock	9.5%	13.1%	1.27 (0.83–1.64)
Heart failure	27.8%	43.6%	1.83 (1.44–2.33)
Cardiac arrest	7.1%	8.2%	0.82 (0.54–1.25)
Acquired pneumonia	7.0%	14.8%	1.70 (1.22–2.36)
Sepsis	6.0%	48.9%	10.98 (8.63–13.96)
Acute respiratory failure	16.7%	36.7%	2.01 (1.58–2.56)
Hematologic complications	4.8%	16.4%	2.97 (2.18–4.05)

aOR, adjusted OR; CABG, coronary artery bypass graft; IE, infective endocarditis; STEMI, ST-elevation myocardial infarction.

proportion of PCIs (aOR=0.21 (0.15–0.30)) and diagnostic coronary angiographies (aOR=0.31 (0.24–0.41)). Figure 1 shows the outcomes of STEMI with and without IE.

DISCUSSION

In the current study, we found that patients with STEMI and IE had significantly higher rates of in-hospital mortality (aOR=2.44) compared with patients who had STEMI without IE. There are a number of potential reasons that could explain these findings. First, IE itself is known to have a relatively high mortality, with in-hospital mortality rates around 20% and 1-year mortality rates approaching 30%.[5] Additionally, we found that patients with STEMI and IE are significantly less likely to have had diagnostic coronary angiographies (aOR=0.31) and PCI (aOR=0.21). This is an extremely important finding, as current guidelines for the treatment of STEMI recommend prompt reperfusion therapy using PCI within 120 minutes of first medical contact to reduce mortality.[6] The lack of intervention in these patients is likely due to the fact that there are no currently established

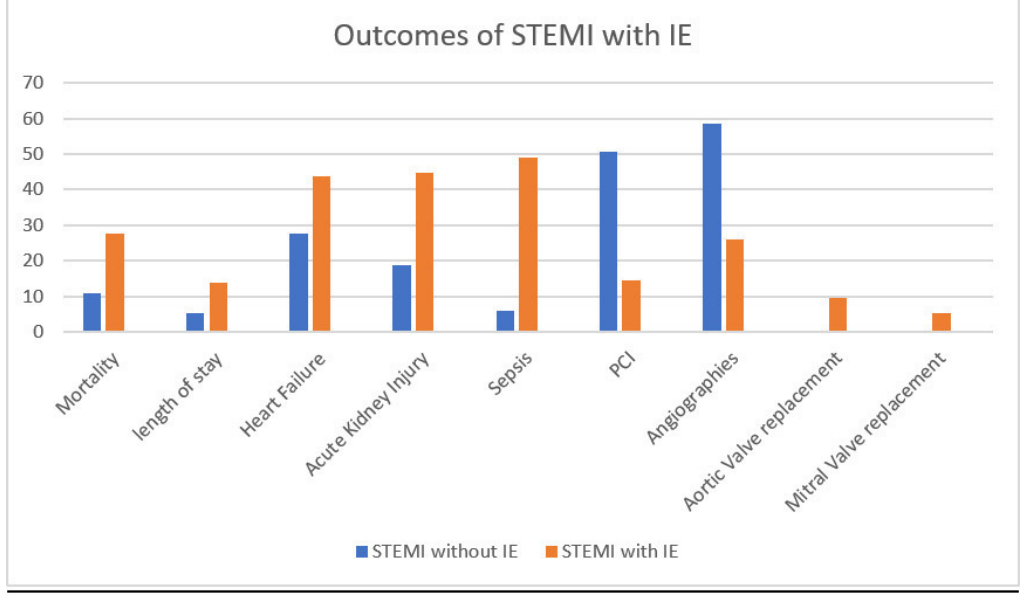

Figure 1 Outcomes of ST-elevation myocardial infarction (STEMI) with and without infective endocarditis (IE) as percentages, p values in table 2. PCI, percutaneous coronary intervention.

guidelines for the management of STEMI with concurrent IE. While PCI is the first-line treatment for STEMI in patients without IE, catheter-based interventions in IE-associated STEMI carry the risk of development of mycotic aneurysms and distal embolization.[7 8] Furthermore, thrombolytic therapy, which is considered a treatment option for patients who are unable to receive prompt PCI, is contraindicated in these patients due to the fact that these patients may have subclinical intracerebral embolism with mycotic pseudoaneurysm in the cerebral arteries.[7] In these cases, the use of thrombolytic therapy can lead to significant fatality due to massive intracranial hemorrhage, and therefore should be avoided.[7] Because the typical interventions for the treatment of STEMI with IE carry a significant risk, it is likely that less coronary interventions are being performed because of the reasons outlined above. It is also possible that patients with STEMI and IE are undergoing other procedural interventions, such as aspiration thrombectomy, for which ICD-9 codes are not available. In addition, due to a lack of existing clinical guidelines for management in these patients because of the rarity of this concurrent presentation, further clinical trials comparing intervention strategies should be employed to develop appropriate management guidelines.

It is important to mention that in the current study, the amount of patients having STEMI without IE undergoing diagnostic coronary angiography (58.7%) and PCI (50.7%) is much lower than data from the American College of Cardiology, which shows that 93.5% of patients having acute coronary syndrome in 2014 either underwent diagnostic catheterization or PCI.[9] It is possible that this discrepancy is due to errors and inconsistency with the ICD-9 coding system, especially in relation to procedural codes. Despite this, our data still demonstrate a significant finding that patients with STEMI without IE are undergoing interventions much less frequently.

Another contributing factor to the increased in-hospital mortality rate is that patients suffering from both STEMI and IE were significantly more likely to develop multiple organ failure. This includes stoke (aOR=7.83), AKI (aOR=2.60), heart failure (aOR=1.83), acquired pneumonia (aOR=1.70), acute respiratory failure (aOR=2.01), and sepsis (aOR=10.98). The majority of these complications can be explained by septic embolization from cardiac valves of left side of the heart and subsequently to the brain or kidneys, leading to stroke or renal infarction.[3] In addition to infarction, the emboli may develop into abscesses in various organs which can result in sepsis.[3] Embolization from the right side of the heart can lead to the development of pulmonary embolism or infection in the lungs, and thus resulting in complications such as pneumonia and acute respiratory failure.[3] Lastly, heart failure is known to be a complication of both STEMI and IE. In IE, the development of heart failure is often due to valvular damage such as aortic insufficiency, because of the extension of IE beyond the valve annulus.[10] Extension beyond the valve apparatus can result in both destruction of the valve and conduction abnormalities especially with aortic valve IE.[10] STEMI is known to cause heart failure due to left ventricular (LV) systolic dysfunction as a consequence of myocardial ischemia and death, as well as due to rhythm disturbances and valvular abnormalities.[11] Thus, heart failure is more severe in patients suffering from both STEMI and IE.

Another significant finding is the increased rates of both aortic (aOR=31.14) and mitral (aOR=26.09) valve replacement. The explanation for this finding likely lies in the complication rates associated with both conditions. In STEMI, valvular replacement is traditionally performed to repair mechanical complications such as papillary muscle rupture, or when LV remodeling leads to displacement of the papillary muscles and annular dilation, causing acute mitral regurgitation.[10] The use of PCI as primary reperfusion therapy has reduced the rates of mechanical complications in patients with STEMI to less than 1%.[12] Therefore, it is not surprising to see that in the current study, the rates of aortic and mitral valve replacement in patients suffering from STEMI without IE are 0.3% and 0.2%, respectively. However, valvular damage is a more common complication in IE. Data from 2011 show that valve replacement occurs in 26 out of 1000 cases of IE.[13] The damage to the valves in IE is due to bacterial adhesion to the heart valve, leading to damage and disruption of the endothelium.[14] A subsequent inflammatory response develops, with release of cytokines, integrins, and tissue factor.[14] This inflammation causes leaflet damage via the development of fistula, valve tears, or abscess leading to more value replacements.[14] Thus, valve damage is more severe in patients suffering both conditions.

Finally, LOS (aOR=4.82) was significantly increased in the patients suffering from STEMI and IE. This is explained by a number of factors mentioned previously, including increased rates of multiple organ complications and the need for surgical intervention such as aortic and mitral valve replacements. These complications will prolong hospitalization as further management is required, including the need for additional procedures (ie, valvular replacement).

Limitations

There are limitations to utilization of the Healthcare Utilization Project database, including errors in relation to the ICD-9 coding system. In order to prevent this, we have used codes that have been validated in previous studies. We have performed a retrospective analysis and given insight into an association between 2 conditions rather than attempting to prove causation between these conditions and the studied outcomes. This limitation is important, as we were unable to identify etiology of STEMI in patients with IE (eg, STEMI secondary to septic embolism or STEMI due to demand ischemia in patients with IE with sepsis and hypotension) with data from the NIS database. An additional limitation is that the ICD coding system is unable to identify when patients are readmitted with the same condition. Because of this, every admission is considered a separate case and therefore a new patient encounter.

CONCLUSION

Hospitalized patients with STEMI with concomitant diagnosis of IE are at higher risk of in-hospital mortality, increased LOS, AKI, stroke, valve replacements, and acute respiratory failure. Clinical trials that compare optimal interventions in these patients are needed.

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