ST-Elevation Myocardial Infarction Associated With Infective Endocarditis

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ST-elevation myocardial infarction (STEMI) as a complication of infective endocarditis (IE) is a rarely reported entity. No clear guidelines exist with regards to the management of this medical emergency. We sought to systematically review the clinical presentation and management of this condition. We searched relevant articles on STEMI associated with IE and extracted data on demographic variables, key clinical characteristics upon presentation, treatment strategies, and clinical outcomes. We identified 100 patients from 95 articles. The mean age at presentation was 53 ± 17 years with male preponderance (n = 63, 63%, p = 0.01). Most patients (63 of 100, 63%) presented with STEMI as their first manifestation of IE, with others occurring at 15 ± 17 days after diagnosis of IE. Findings that suggested possible septic emboli were not consistently present, including history of prosthetic valve placement (15%), presence of other embolic disease (27%), fever (42%) increased leukocyte count (80%), and presence of murmur (88%). Atherosclerotic disease was absent in 95% on cardiac catheterization. Eleven patients receiving tissue plasminogen activator fared poorly, with 9 major bleeds; balloon angioplasty was successful in 56% (9 of 16 cases), aspiration thombectomy in 68% (21 of 31 cases), and coronary stenting in 81% (14 of 16 cases). The 30-day mortality was 43%. In conclusion, patients with STEMI in the face of recent IE, new precordial murmur, fever, increased leukocyte count or other embolic events, septic emboli should be considered as a cause for STEMI. Best practices for management are not known, but thrombolytics appear to carry significant bleeding and embolic risks. **(Am J Cardiol 2019;123:1239−1243)**

Infective Endocarditis (IE) is the fourth most common life-threatening infection, accounting for 1.58 million disability life-years lost globally in 2010.[1] Although the global risk of septic embolism is very high in infective endocarditis, the incidence of coronary embolism causing myocardial infarction is relatively low, ranging from 3% to 11%.[2,3] Given the low incidence of coronary embolism, ST-elevation myocardial infarction (STEMI) as a complication of IE is a rarely reported entity. Since only case reports and small-scale studies are published to date, no clear guidelines exist with regards to the management of this medical emergency. Use of thrombolytic and interventional revascularization therapies that are well-established for the treatment of atherothrombotic STEMI may result in unfavorable consequences and be detrimental to patients with STEMI from IE.[4] We aimed to perform a systematic review of the literature on this important association to better characterize the presentation, prognosis, and outcomes related to different treatment methods utilized in the management of patients with IE and STEMI.

Methods

The review was performed according to the preferred reporting items for systematic reviews and meta-analysis guidelines for systematic reviews.[5] A systematic electronic search of MEDLINE (through PubMed), EMBASE, and the Cochrane library was performed for case reports, case series and systematic reviews on STEMI secondary to IE from inception until July 17, 2018. The search was performed using 2 broad search themes "ST-elevation myocardial infarction" and "infective endocarditis" (Supplementary file 1). These themes were combined using Boolean operator "AND." We also performed a hand search for references from included articles to identify additional publications. Abstracts from national and international meetings were also reviewed for eligibility. Only articles on human subjects and English language articles were included. The inclusion criteria for our search were: (1) age greater than 18; (2) reports in English literature delineating association of ST-elevation myocardial infarction and infective endocarditis. We excluded articles in which the endocarditis was deemed to be noninfective or in patients with coronary syndromes other than STEMI.

Screening of articles for eligibility was performed by 2 authors (SN, RL). Conflicts during screening process were resolved by third author (AD). Data extraction was performed by three authors (SN, RL, AD). Data extracted included demographic variables, key clinical characteristics

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upon presentation (including time from IE diagnosis to STEMI, fever [defined as temperature ≥38.3°C], presence of heart murmur); laboratory parameters (including white blood cell count, biomarkers); electrocardiogram (EKG) findings on admission; echocardiographic features (including vegetation size and valves involved); catheterization features (including presence of coronary disease); and treatment strategies (including thrombolytic therapy, antithrombotic therapy, thrombus aspiration, balloon angioplasty, coronary stenting, and coronary artery bypass grafting; Supplementary file 2). Individual investigators were contacted for missing information. The primary end points of the study were inpatient mortality and 30-day mortality. Secondary end points were presence of atherosclerotic coronary disease on cardiac catheterization and valvular dysfunction requiring valve replacement surgery. Categorical variables were expressed as percentage and continuous variables as mean ± SD. Chi-square testing was used for statistical analysis where applicable. Statistical analysis was carried out using Microsoft Excel 2013 (Microsoft Corporation, Redmond, Virginia) and Stata 13.1 (Stata Corporation, College Station, Texas).

Results

We identified 100 patients with STEMI associated with IE from 95 articles (Figure 1). The mean age at presentation was 53 ± 17 years with male preponderance (n = 63, 63% p = 0.01). Most patients (63 of 100, 63%) presented with STEMI as their first manifestation of IE. Eleven percent of the patients (11 of 100) were in cardiac arrest at the time of their presentation. A total of 15 (15 of 100, 15%) patients had a previous history of mechanical or bioprosthetic valve placement before presentation. In patients with previously diagnosed IE predating their STEMI, the mean time to develop STEMI from diagnosis of IE was 15 ± 17 days. Presence or absence of a precordial murmur was reported in only 68 cases, out of which 88% (60 of 68 cases) noted the presence of a murmur. Temperature on admission was reported in 31 patients, with 42% (13 of 31 cases) reporting an admission fever. Leucocyte count was mentioned in 29 cases only, and was increased (>12,000 mm^3) in 80% (23 of 29 cases). EKGs were reported in all 100 patients. Anterior distribution was the most commonly described in 42% (42 of 100 cases; Table 1).

Biomarker levels (troponin I, troponin T, creatine kinase-muscle/brain) were mentioned in 43 cases, with increased biomarkers reported in 98% (42 of 43 cases). Twenty-seven percent of the cohort had embolic events, including central nervous system (n = 16) or peripheral embolic events (n = 11) at time of presentation. However absence of these events was rarely reported. A transthoracic echocardiogram was reported in 72 cases, with a vegetation identified in 72% (52 of 72 cases). A transesophageal echocardiogram was reported in 53 cases, with a vegetation identified in all (53 of 53 cases). Intravenous tissue plasminogen activator (TPA) therapy was attempted in 11 cases at presentation for STEMI. One patient had a good outcome, whereas 9 reported intracranial bleeds and one had fatal gastrointestinal bleeding. Cardiac catheterization was performed in 71 patients. No evidence of atherosclerotic disease was noted in 95% (67 of 71 cases). Embolic events occurred more frequently in left coronary system vessels 85% (51 of 59; Table 2). Aspiration thrombectomy was attempted in 31 cases, and was reported to be successful in 68% (21 of 31 cases). Balloon angioplasty was reported in 16 cases, and was successful in 56% (9 of 16 cases). However, mycotic aneurysm was reported as a complication in 2 angioplasty cases. Coronary stenting was performed in 16 cases. Bare metal stents were placed in 8 patients, drug-eluting stents in 2 cases, bioresorbable vascular scaffolds in 1 case and unknown type (not described) in 5 cases. Stenting was reported as successful in 81% (13 of 16 cases). One patient developed a mycotic aneurysm and another experienced a septic cerebral embolism after stent placement. Antiplatelet therapy choice and duration was inconsistently mentioned in most cases after placement of stent. Coronary artery bypass grafting was successfully performed to the target vessel in 6% (6 of 100 cases). Nine patients were managed conservatively without TPA or cardiac catheterization. Of these 5 died during hospital stay. Valve dysfunction requiring surgery as a result of the endocarditis was reported in 39% (39 of 100 cases). Four patients (4 of 39 cases) died during valve replacement surgery. The in-patient mortality was 41% (41 of 100 cases) and the 30-day mortality was 43% (43 of 100 cases) in our series. No difference in mortality was observed when comparing anterior or anterior and lateral MI with other MI types (44% vs 39%, p = 0.60).

Discussion

Door-to-balloon time has become a critical quality measure for hospitals,[6] and elimination of all noncritical steps to get patients to the catheterization laboratory has been vital to improving this measure. This also means that triaging physicians and cardiologists have very little time to perform an elaborate history and physical when a STEMI is identified on EKG. Given that STEMI was the initial presentation for 63% of the patients in our series, early identification of features that might suggest a septic embolic cause is critical, since these patients may fare quite poorly with standard anticoagulation or thrombolytics that are part of typical atherosclerotic myocardial infarction management.

We found that our patients' basic demographics (53 ± 17 years old, 63% men) did not clearly distinguish them from typical demographics reported in the literature in patients with STEMI from atherosclerotic cardiovascular disease (50 to 66 years, 70% to 77% men).[7–9] We found that a history of prosthetic valve implantation (15%), a fever on admission (42%), a new precordial murmur (88%), or a significantly increased white count (80%) should raise suspicion for potential septic emboli, but none appear enough to distinguish embolic STEMI from STEMI due to atherosclerotic cardiovascular disease (ASCVD). Absence of atherosclerotic coronary disease was noted on catherization in 95% of our cohort, whereas over 90 % of patients with ASCVD-related STEMI have evidence of coronary artery disease, with more than half with multivessel disease.[10,11] Absence of plaque at site of vessel occlusion, absence of collaterals, absence of atherosclerotic disease in other vessels, and involvement of left coronary system particularly the left anterior descending artery

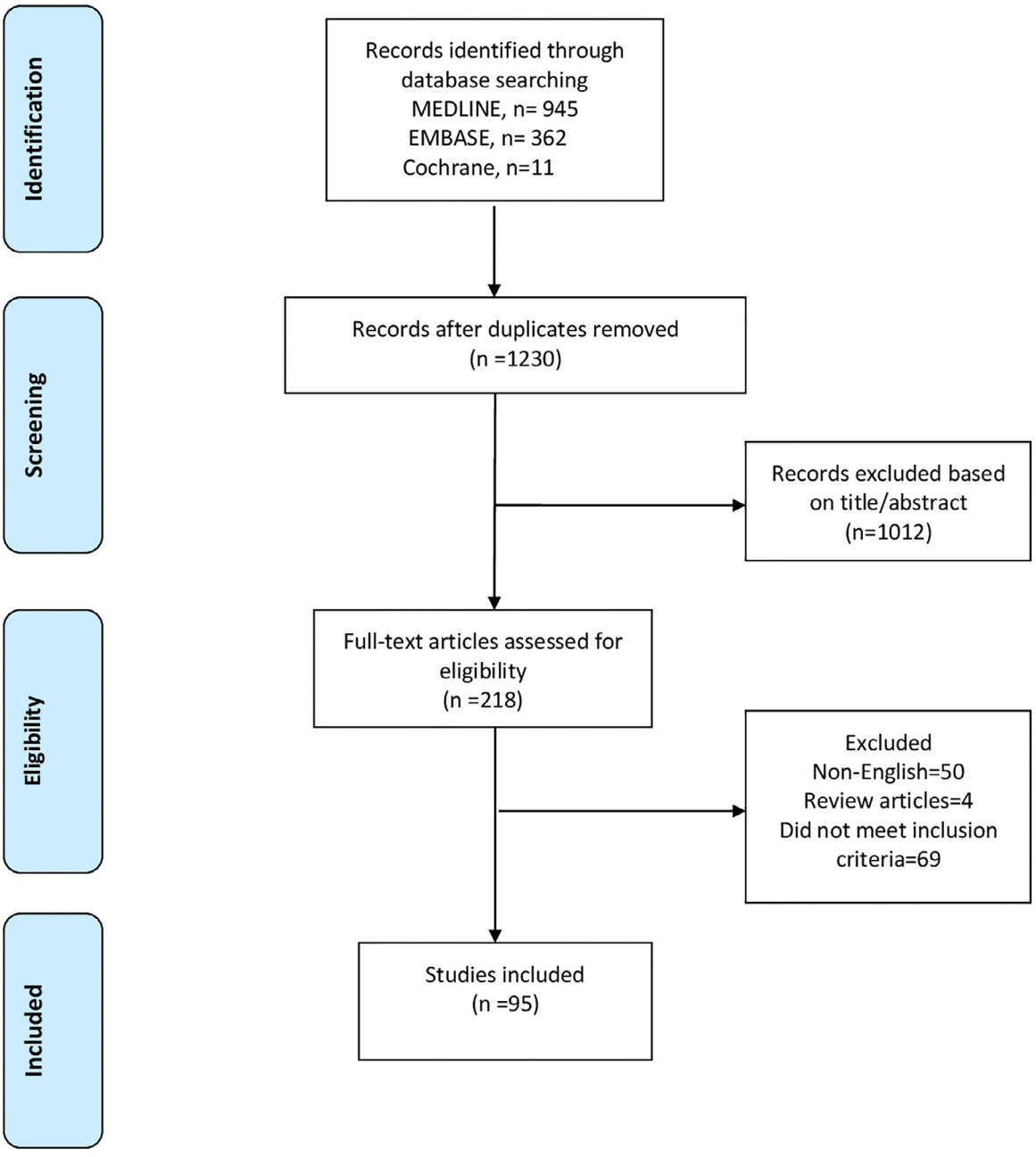

Figure 1. Flow chart describing systematic search and study selection process.

Table 1
Distribution of ST-elevation myocardial infarction on electrocardiogram upon presentation

Distribution	Number (percentage)
One territory	
Anterior	42 (42%)
Inferior	19 (19%)
Lateral	7 (7%)
More than one territory	
Anterior and lateral	25 (25%)
Anterior and inferior	3 (3%)
Inferior and lateral	3 (3%)
Inferior and posterior	1 (1%)

Table 2
Distribution of coronary embolus in 71 patients who underwent cardiac catheterization

Number of vessels involved	Number (percentage)
No embolus	4/71 (6%)
Single vessel	59/71 (83%)
Two vessel	6/71(8%)
Three vessel	2/71 (3%)
Specific single vessels involved	
Left coronary system and branches	51/59 (87%)
Left anterior descending and branches	44/59 (75%)
Left circumflex and branches	6/59 (10%)
Left main	1/59 (2%)
Right coronary system and branches	7/59 (12%)

increases likelihood of an embolic cause.[12] In those cases it may also be helpful to perform optical coherence tomography or an intravascular ultrasound to identify coronary embolism as potential cause of STEMI.[13,14] Presence of a precordial murmur appears to be very common (88%), and should lead to an urgent bedside echocardiogram to identify any underlying vegetation before proceeding for cardiac catheterization. Other embolic events were present in 27% of cases and if present, would likely distinguish this presentation from typical atherosclerotic disease and should be sought if other findings (increased WBC count, fever, absence of previous coronary disease) would make atherosclerotic disease less likely. Patients with known endocarditis who present within weeks of diagnosis with new STEMI should be strongly considered for embolic events in the face of new STEMI. In patients with known IE, the mean time to develop STEMI from diagnosis of IE was 15 days, which is consistent with other studies of IE that showed the risk of new embolism is highest during the first days after initiation of antibiotic therapy and decreases thereafter, particularly beyond 2 weeks.[15,16]

We found that in-hospital mortality (41%) as well as the 30-day mortality (43%) was significantly higher in our cohort compared with other studies of atherosclerotic STEMI (3% to 6% mortality rate in-hospital, 2% to 10% 30-day mortality).[7,9,17] Although no guidelines currently exist for this patient population, conservatively managed patients had high mortality rates in our series (55%), and thrombolytics in our cohort were associated with much higher rates of bleeding (90%) than ASCVD patients in the literature (1.8%),[18] which is postulated to be from fibrinolytic effects on previously stable vegetations.[2]

Catheter-based interventions can be successful but incur risks of mycotic aneurysm formation in IE-associated STEMI as seen in our series. Based on this limited data, an early invasive catheter-based intervention seems to be most prudent, especially in light of the desire to avoid thrombolytics. Although aspiration thrombectomy is no longer considered first line in atherosclerotic STEMI,[19] it may be a reasonable first line choice in patients with a high clinical suspicion for septic emboli in light of risks of angioplasty and stenting of an infected thrombus.

We limited our review to English-language publications and hence may have missed cases reported in the non-English literature. We were dependent on the case descriptions in the literature; many of these cases did not include information on underlying co-morbidities, presence of murmur, fever, white blood cell count, limiting our analysis of all variables in each patient in this cohort.

In conclusion, STEMI due to IE can present in three distinct forms: (1) STEMI in a patient with known endocarditis, (2) STEMI in a patient with sepsis or bacteremia but not known to have endocarditis, and (3) STEMI as initial presentation of endocarditis. For the third presentation, it is important to maintain a high index of suspicion in patients who present with no previous atherosclerotic history, history of a prosthetic valve implantation, new fever, increased WBC count, and evidence of peripheral embolization or presence of a new precordial murmur. An urgent bedside echocardiogram may be helpful to identify underlying vegetation that could suggest need for urgent antibiotic therapy and possibly avoidance of thrombolytic therapy. Aspiration thrombectomy should be considered first line. TPA should be avoided in these patients given the high risk of bleeding complications. The role of balloon angioplasty and coronary stents in these patients requires further study. Since STEMI in IE is a rare entity, the next steps may include creation of a patient registry for data synthesis and potential future treatment trials.

Disclosures

The investigators have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.01.033.

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