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Original Research Article

Trends and outcomes of thrombolytics in patients with STEMI

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ABSTRACT

Background: In ST-segment elevation myocardial infarction (STEMI) percutaneous coronary intervention (PCI) is the gold standard, but the time/resource constraints can necessitate alternative approaches. This study aimed to analyze outcomes and predictors of in-hospital mortality in STEMI patients undergoing thrombolysis.
Methods: A retrospective analysis of national inpatient sample data (2016-2020) included adult patients admitted with STEMI. Using ICD-10 procedural codes, patients undergoing thrombolysis or PCI were identified. Elixhauser's comorbidity index identified comorbidities, and univariate and multivariate analyses adjusted for confounders. The primary outcome was mortality rates in STEMI patients undergoing thrombolysis versus PCI. Secondary outcomes were factors influencing mortality rates and major complications associated with thrombolysis.
Results: Out of 819,979 patients diagnosed with STEMI, 0.2% (2349 patient's) received thrombolysis as their primary treatment upon admission. The mortality rate among patients undergoing thrombolysis was 12.34% versus 4.09% with PCI. Additionally, a higher proportion of patients undergoing thrombolysis required left ventricular assist device (LVAD) (4.8% versus 0.89% in the PCI group), and the incidence of cardiogenic shock was significantly elevated in this cohort (10.8% versus 6.68% in the PCI group). Factors influencing in-hospital mortality among patients undergoing thrombolysis included age (with a 3% increase in mortality observed with each year of age), LVAD placement (patients with LVADs had 3.6 times higher odds of mortality compared to those without, with aOR 3.69, p=0.029, 95% CI 1.14-11.89), and the use of mechanical ventilation, which independently predicted mortality outcomes.
Conclusions: Thrombolysis in STEMI patients is a vital alternative to PCI. It is associated with higher mortality and complications compared to PCI. Age, LVAD placement, and mechanical ventilation independently predict mortality. Identifying these factors can help us improve the outcomes of thrombolysis. Further prospective research is warranted to optimize outcomes in thrombolysis for STEMI.

Keywords: In-hospital mortality, STEMI, Thrombolysis

INTRODUCTION

ST-elevation myocardial infarction (STEMI) is a form of acute coronary syndrome characterized by total blockage of coronary arteries. The name STEMI comes from the electrocardiogram (ECG) findings, specifically an elevation in the ST segment, indicating a significant portion of the heart myocardium is at risk of necrosis if blood flow is not quickly restored.[1] It is associated with significantly high morbidity and mortality. To treat STEMI, rapid restoration of blood flow is critical.

Two primary methods are used: percutaneous coronary intervention (PCI) and thrombolytic therapy. PCI, often referred to as angioplasty, involves mechanically opening the blocked artery using a balloon and usually placing a

stent to keep it open.[2] Primary percutaneous coronary intervention (pPCI) is widely favored over thrombolytic therapy for managing ST-elevation myocardial infarction (STEMI), as it aims to achieve effective reperfusion of coronary arteries and has demonstrated significant efficacy in minimizing infarct size.[3] Percutaneous coronary intervention (PCI) surpasses thrombolytic therapy in reducing short-term mortality, non-fatal reinfarction, and stroke. Moreover, these advantages persist regardless of the specific thrombolytic agent used.[4]

However, in situations where PCI cannot be performed within the recommended time frame from the initial medical contact, there is a significant increase in mortality. This issue becomes particularly critical in resource-limited areas or low-income countries where PCI is not readily available.[5] Even in affluent nations, meeting the time goals recommended by the American College of Cardiology/American Heart Association and the European Society of Cardiology for STEMI patients transferred for primary PCI (pPCI) is often challenging, with only 25% to 50% achieving a medical contact-to-balloon time of ≤120 minutes.[6,7] In such cases where prompt pPCI is unachievable, the importance of fibrinolytic therapy, which can expedite reperfusion, should not be underestimated.[8]

The objective of this study was to thoroughly investigate the clinical outcomes of STEMI (ST-elevation myocardial infarction) patients who have undergone PCI versus thrombolytic therapy. Specifically, the study aimed to determine the in-hospital mortality rate among these patients and to identify the various factors that may predict this outcome. The goal was to enhance understanding of the effectiveness and risks of thrombolysis in STEMI patients, thereby contributing to improved clinical decision-making and patient management strategies.

METHODS

We conducted a retrospective study utilizing the national inpatient sample (NIS) database. The NIS, the largest publicly available database managed by the healthcare cost and utilization project (HCUP), covers over 97% of US hospitals. It includes data from 20% of randomly stratified inpatient hospitalizations, applying discharge weights to each encounter to estimate the national inpatient population. The NIS data was de-identified and publicly accessible, making studies using this data exempt from institutional review board (IRB) approval.[9]

Inclusion criteria were adult patients (>18 years) and non-elective admission to the hospital with primary or secondary diagnosis of STEMI. All patients with elective admissions who were diagnosed with STEMI were excluded. These patients were identified using the International Classification of Diseases, 10th revision, Clinical Modification (ICD-10 CM) codes.

We utilized the Elixhauser comorbidity index (ECI), a well-known tool in medical research that includes 31 broad categories of comorbidities, to assess baseline comorbidity and its impact on in-hospital mortality and 30-day readmission risk. The ECI uses ICD-10 CM codes to identify comorbidities, with higher scores indicating higher in-hospital mortality and an increased risk of 30-day readmission.

Also, certain diagnoses like cardiogenic shock were identified using ICD-10 CM codes. Procedures such as PCI and thrombolysis were identified using ICD-10 procedural codes (ICD-10 PCS). Other procedures like LVAD placements and mechanical ventilation were also identified using the ICD-10 PCS code.

After identification of the pool of patients, their co-morbidities, other relevant diagnoses like cardiogenic shock, and the procedures they underwent, we proceeded with statistical analysis. Stata 18 BE software was used for the statistical analysis. We used logistic regression analysis for categorical variables like mortality and whether they underwent a certain procedure or not (LVAD placement, mechanical ventilation). To identify potential confounders in our study, univariate analyses were conducted and to adjust them multivariate analyses were used. A 5% alpha risk was set to determine statistical significance.

The primary outcome of this study was to evaluate mortality rates in STEMI patients undergoing thrombolysis compared to PCI. Secondary outcomes included identifying factors influencing these mortality rates and complication rates in patients who underwent thrombolysis as their primary treatment.

RESULTS

Between 2016 and 2020, a total of 819,980 patients were diagnosed with STEMI, and only 2,350 (0.2%) received thrombolysis as their primary treatment. Among those who underwent thrombolysis, 29.36% were female, and the average age was 63.31 years. There were no significant differences in gender or race distribution between patients receiving thrombolysis or PCI. About 75% of all STEMI patients were Caucasian, while African Americans, Hispanics, Asians, Native Americans, and others constituted 8.91%, 8.64%, 3.02%, 0.5%, and 3.6%, respectively This distribution of patients remained more or less the same whether they underwent thrombolysis or PCI.

Table 1: Demographic characteristics of STEMI patients.

	STEMI (%)	STEMI + Thrombolysis (%)	STEMI + PCI (%)
Females,	30.53	29.36	28
Age, years	63.55	63.31	62.14
Race			
White	75.3	75.28	75.67
Blacks	8.91	9.66	8.8.78
Hispanics	8.64	8.99	8.51
Asians	3.02	2.7	2.9
Native Americans	0.5	0	0.5
Others	3.6	3.37	3.63
Location			
Rural	6.12	7.23	5.7
Urban	93.88	92.77	94.3
Teaching facility			
Non-teaching	27.93	35.32	28.21
Teaching	72.07	64.68	71.79
Region			
Northeast	17.14	16.6	16.63
Midwest	22.78	20.64	22.68
South	39.89	38.72	40.75
West	20.2	24.04	19.93
Insurance			
Medicare	46.7	44.44	42.64
Medicare	11.07	13.94	11.4
Private	35.13	32.68	38.33
Selfpay	7.1	8.93	7.62
Hospital bed size			
Small	16.01	12.98	15.86
Medium	29.82	29.36	30.19
Large	54.17	57.66	53.95

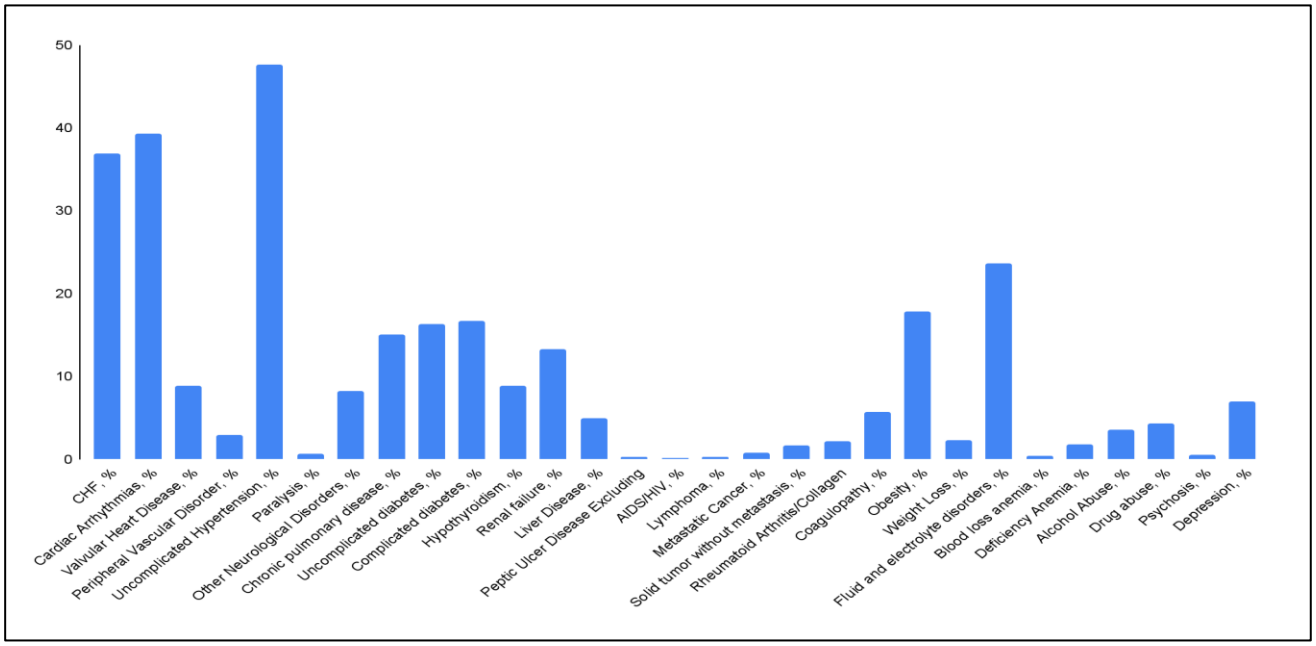

Figure 1: Comorbidity distribution chart among patients with STEMI.

Hypertension was the most common associated co-morbidity, present in 47.64%, whereas congestive heart failure (CHF) and cardiac arrhythmias were the other major co-morbidities present in 36.91% and 39.34% of the patients. Complicated diabetes was present in 16.69% of the patients and approximately 17.86% of the patients were obese. Depression also emerged as a significant co-morbidity present in 7.02%.

Approximately 93% of all STEMI patients were in urban areas, and 72% were admitted to teaching hospitals. Regionally, 39.89% of STEMI cases were from the south, 17.14% from the northeast, 22.78% from the midwest, and 20.2% from the west. Medicare covered 46.7% of the patients, Medicaid 11.07%, private insurance 35.13%, and 7.1% were self-paying.

Mortality rates differed significantly between thrombolysis and PCI patients: 12% of thrombolysis patients died compared to only 4% of PCI patients, indicating better survival outcomes with PCI.

Factors impacting in-hospital mortality among thrombolysis patients included age (with a 3% increase in mortality per year of age), LVAD placement (which increased the odds of mortality by 3.6 times compared to those without LVAD, aOR 3.69, p=0.029, 95% CI 1.14-11.89), and the use of mechanical ventilation, which independently predicted higher mortality.

Table 2: Comorbidity distribution of STEMI patients.

Distribution	%
Year	
2016	20.54
2017	20.3
2018	19.87
2019	20.39
2020	18.91
Elixhauser's comorbidities	
Congestive heart failure	36.91
Cardiac arrhythmias	39.34
Valvular heart disease	8.91
Peripheral vascular disorder	2.95
Uncomplicated hypertension	47.64
Paralysis	0.7
Other neurological disorders	8.31
Chronic pulmonary disease	15.04
Uncomplicated diabetes	16.32
Complicated diabetes	16.69
Hypothyroidism	8.92
Renal failure	13.35
Liver disease	4.91
Peptic ulcer disease excluding bleeding	0.3
AIDS/HIV	0.2
Lymphoma	0.33
Metastatic cancer	0.75
Solid tumor without metastasis	1.7
Rheumatoid arthritis/collagen vascular disease	2.14
Coagulopathy	5.67
Obesity	17.86
Weight loss	2.37
Fluid and electrolyte disorders	23.66
Blood loss anemia	0.41
Deficiency anemia	1.75
Alcohol abuse	3.59
Drug abuse	4.39
Psychosis	0.56
Depression	7.02

Notably, there were no significant gender, racial, or socioeconomic disparities in mortality outcomes due to established STEMI care protocols. Additionally, LVAD placement was more common among thrombolysis patients (4.89%) than PCI patients (0.8%). Incidences of cardiogenic shock were higher in thrombolysis patients (10.8%) compared to PCI patients (6.6%). Mechanical ventilation was used more frequently in thrombolysis-treated STEMI patients (11.91%) than in those treated with PCI (3%).

DISCUSSION

Coronary artery disease is the leading cause of death worldwide.[10] In western countries, mortality from ischemic heart disease (IHD) has significantly decreased in recent decades due to increased emphasis on prevention, improved diagnosis, and better treatment. However, there is an anticipated increase in non-communicable disease (NCD) mortality in the future, largely due to worsening metabolic risk factors.[11] ST-segment elevation myocardial infarction (STEMI) represents a critical medical emergency marked by total occlusion of a coronary artery, resulting in myocardial ischemia and eventual necrosis.[12] This sudden interruption of blood flow typically arises from factors such as plaque rupture, erosion, fissuring, or dissection of the coronary arteries, leading to the formation of an obstructive thrombus.[13] It has consistently posed a substantial global burden of morbidity and mortality in the setting of coronary artery disease, underscoring the importance of in-depth comprehension of its pathophysiology, precise diagnostic methods, and efficient treatment modalities. Two primary modalities to treat STEMI are pPCI and use of thrombolytics.

Percutaneous coronary intervention (PCI) is a minimally invasive procedure aimed at alleviating the narrowing or blockage of coronary arteries to enhance blood flow to ischemic tissues. This is typically achieved through various techniques, most commonly by inflating a balloon to widen the narrowed segment or placing a stent to maintain artery patency.[14] Primary PCI is the preferred method of restoring blood flow promptly in acute ST-elevation myocardial infarction (STEMI) with ischemic symptoms lasting less than 12 hours, STEMI with ischemic symptoms lasting less than 12 hours and when fibrinolytic therapy is contraindicated.[15] Patients should ideally undergo percutaneous coronary intervention (PCI) within 90 minutes of arriving at a PCI-capable hospital, or within 120 minutes if transfer to a PCI-capable hospital is necessary. These guidelines underscore the critical role of PCI in managing acute myocardial infarction and improving outcomes for individuals with substantial coronary artery disease.

If PCI cannot be initiated within the first 120 minutes after initial medical contact, ESC and ACC/AHA guidelines recommend the commencement of fibrinolysis within 30 minutes of the patient's hospital arrival.[3] Fibrinolytic therapy offers significant mortality benefits when administered within 12 hours of STEMI symptom onset, with maximal benefit within 2 hours. Time-to-treatment impacts mortality rates, as shown in studies like GUSTO and others, emphasizing the importance of rapid intervention. Successful fibrinolysis warrants transfer to a PCI-capable facility for angiography, as supported by GRACIA and TRANSFER AMI trials.[16,17] Fibrinolysis can be performed as a standalone therapy or followed by PCI in various strategies such as rescue PCI, facilitated PCI, or early (pharmaco-invasive) PCI. Facilitated PCI refers to immediate PCI following pharmacological therapy, which may involve full-dose fibrinolysis or a combination of half-dose fibrinolysis with a platelet glycoprotein IIb/IIIa inhibitor. Recent trials have defined early PCI or a pharmaco-invasive approach as fibrinolysis administered at non-PCI centers followed by transfer to a PCI-capable facility for catheterization within 24 hours when primary PCI is not feasible. Rescue PCI, on the other hand, entails performing PCI after failed fibrinolysis.[18]

Given the principle that "time is muscle", the primary objective was to achieve reperfusion as swiftly as possible in all scenarios of STEMI. It is understood that each 30-minute delay in reperfusion may potentially increase 1-year mortality by up to 7.5%. Only 25% of patients experiencing STEMI receive primary PCI in acute care hospitals in the United States.[19] STEMI patients arriving at non-PCI-capable centers may still face delayed door-to-balloon times, thereby making fibrinolysis a potentially preferable initial option for many STEMI patients unable to be promptly transferred to a PCI-capable facility. Hence, thrombolytic therapy, while less common than pPCI, remains a crucial treatment option for STEMI (ST-elevation myocardial infarction) for several reasons. Firstly, thrombolytics are essential in settings where timely access to PCI is not feasible. For patients in remote or rural areas, where the nearest catheterization lab may be hours away, thrombolytic therapy can be life-saving. Secondly, thrombolytic therapy can be administered quickly and with relatively straightforward logistics. In emergencies where time is of the essence, thrombolytics can be given in pre-hospital settings or small hospitals without advanced cardiac facilities. This rapid administration helps restore blood flow to the heart muscle, reducing the extent of myocardial damage and improving survival rates. Additionally, thrombolytic therapy is a cost-effective option compared to PCI. In healthcare systems with limited resources, thrombolytics offer a practical solution to manage acute STEMI. This economic advantage can be particularly significant in low- and middle-income countries where healthcare budgets are constrained. In the United States, four fibrinolytic agents are approved for STEMI treatment: streptokinase, alteplase, reteplase, and tenecteplase. Numerous studies have highlighted the beneficial impact of these therapies in reducing mortality rates among patients with suspected acute myocardial infarction. Streptokinase, due to its lack of fibrin specificity, is not

commonly used today. It has a high antigenic potential and is contraindicated in individuals who have been exposed to it within the past six months. Alteplase is administered via intravenous infusion. Reteplase and tenecteplase, with their longer half-lives, allow for bolus administration, which can be more convenient and less time-consuming. Reteplase is given as a double bolus and does not require dosing adjustment based on the patient's weight, whereas tenecteplase is administered as a single bolus with weight-based dosing.[20]

Despite the higher in-hospital mortality rates associated with thrombolysis compared to PCI, the therapy plays a pivotal role when PCI is delayed or unavailable. For instance, the study indicates that thrombolysis had a 12% mortality rate compared to 4% for PCI. However, these figures underscore the importance of timely PCI rather than diminishing the value of thrombolysis. The increased use of thrombolytics is also associated with higher incidences of complications like LVAD placement and cardiogenic shock, which further emphasizes the need for careful patient selection and management when using this therapy. It is worth keeping in mind that, Fibrinolysis often leads to incomplete revascularization of the infarct-related artery, with less than 60% of patients achieving Thrombolysis in myocardial infarction flow grade 3 (TIMI 3), potentially increasing the risk of recurrent ischemia, re-occlusion, or reinfarction following treatment.[21]

The study's reliance on ICD-10 codes for identifying STEMI cases introduces several limitations. The potential misclassification of STEMI as broader acute coronary syndrome can lead to underestimation of case numbers. Furthermore, coding inaccuracies and the inability to track individual patient trajectories within the NIS database can compromise data reliability. The NIS database limitations further hinder this study. Individual patient-level data was absent, preventing analysis of treatment selection factors between thrombolysis and PCI. Moreover, recurrent hospitalizations were recorded as separate instances, potentially leading to duplicate patient entries. Lastly, differentiating comorbidities from complications arising during hospitalization is challenging due to the lack of present-on-admission flags for secondary diagnoses.[22]

CONCLUSION

While PCI is now considered the standard treatment for patients experiencing ST-elevation myocardial infarction (STEMI), there are situations where alternative treatments like thrombolysis remain crucial. These include cases where PCI access is unavailable, the primary site lacks PCI capability, or weather conditions prevent timely transfer to a PCI-capable facility. Thrombolysis has been extensively documented as life-saving in such circumstances. It ensures that patients in areas with limited access to advanced cardiac care still receive timely and effective treatment. Its ease of administration and cost-effectiveness make it an indispensable option in the global fight against STEMI. In summary, thrombolytic therapy remains a vital part of the STEMI treatment arsenal. However, understanding potential complications post-thrombolysis is essential for optimal patient management. Patients treated with thrombolysis face increased risks of complications such as cardiogenic shock, potentially leading to the need for left ventricular assist device (LVAD) placement.

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