ORIGINAL RESEARCH ARTICLE

Fibrinolysis vs. primary percutaneous coronary intervention for ST-segment elevation myocardial infarction cardiogenic shock

Saraschandra Vallabhajosyula[1,2,3,4,5]* ⓘD, Dhiran Verghese[4,5], Malcolm R. Bell[1], Dennis H. Murphree[6], Wisit Cheungpasitporn[7], Paul Elliott Miller[8], Shannon M. Dunlay[1,6], Abhiram Prasad[1], Gurpreet S. Sandhu[1], Rajiv Gulati[1], Mandeep Singh[1], Amir Lerman[1], Bernard J. Gersh[1], David R. HolmesJr[1] and Gregory W. Barsness[1]

[1]*Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA;* [2]*Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, MN, USA;* [3]*Center for Clinical and Translational Science, Mayo Clinic Graduate School of Biomedical Sciences, Rochester, MN, USA;* [4]*Section of Interventional Cardiology, Division of Cardiovascular Medicine, Department of Medicine, Emory University School of Medicine, 1364 Clifton Road NE, Atlanta, GA 30322, USA;* [5]*Department of Medicine, Amita Health Saint Joseph Hospital, Chicago, IL, USA;* [6]*Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA;* [7]*Division of Nephrology, Department of Medicine, University of Mississippi School of Medicine, Jackson, MS, USA;* and [8]*Division of Cardiovascular Medicine, Department of Medicine, Yale University School of Medicine, New Haven, CT, USA*

Abstract

Aims   There are limited contemporary data on the use of initial fibrinolysis in ST-segment elevation myocardial infarction cardiogenic shock (STEMI-CS). This study sought to compare the outcomes of STEMI-CS receiving initial fibrinolysis vs. primary percutaneous coronary intervention (PPCI).

Methods   Using the National (Nationwide) Inpatient Sample from 2009 to 2017, a comparative effectiveness study of adult (>18 years) STEMI-CS admissions receiving pre-hospital/in-hospital fibrinolysis were compared with those receiving PPCI. Admissions with alternate indications for fibrinolysis and STEMI-CS managed medically or with surgical revascularization (without fibrinolysis) were excluded. Outcomes of interest included in-hospital mortality, development of non-cardiac organ failure, complications, hospital length of stay, hospitalization costs, use of palliative care, and do-not-resuscitate status.

Results   During 2009–2017, 5297 and 110 452 admissions received initial fibrinolysis and PPCI, respectively. Compared with those receiving PPCI, the fibrinolysis group was more often non-White, with lower co-morbidity, and admitted on weekends and to small rural hospitals (all $P < 0.001$). In the fibrinolysis group, 95.3%, 77.4%, and 15.7% received angiography, PCI, and coronary artery bypass grafting, respectively. The fibrinolysis group had higher rates of haemorrhagic complications (13.5% vs. 9.9%; $P < 0.001$). The fibrinolysis group had comparable all-cause in-hospital mortality [logistic regression analysis: 28.8% vs. 28.5%; propensity-matched analysis: 30.8% vs. 30.3%; adjusted odds ratio 0.97 (95% confidence interval 0.90–1.05); $P = 0.50$]. The fibrinolysis group had comparable rates of acute organ failure, hospital length of stay, rates of palliative care referrals, do-not-resuscitate status use, and lesser hospitalization costs.

Conclusions   The use of initial fibrinolysis had comparable in-hospital mortality than those receiving PPCI in STEMI-CS in the contemporary era in this large national observational study.

Introduction

Cardiogenic shock (CS) is a complication that is observed in about 10% of all ST-segment elevation myocardial infarction (STEMI) and is associated with high morbidity and mortality.[1–6] Coronary reperfusion is the mainstay of therapy for patients with STEMI-CS with primary percutaneous coronary intervention (PPCI) being preferred.[7] The current societal guidelines recommend PPCI for revascularization in patients with STEMI-CS irrespective of time delay from STEMI onset (Grade of Recommendation Class I, Level of Evidence B).[7,8] When PPCI is not available, a pharmaco-invasive strategy is recommended for patients with STEMI and haemodynamic instability (Grade of Recommendation Class I, Level of Evidence C) and urgent revascularization, by either PCI or coronary artery bypass grafting (CABG) (Grade of Recommendation Class I, Level of Evidence B).[7,8]

Despite robust evidence for PPCI, only 39% of US hospitals have catheterization facilities, and as a consequence, fibrinolysis with subsequent early coronary angiography with PCI continues to be used as first-line therapy in >25% of STEMI patients.[9] These numbers are even higher in resource-poor countries, where fibrinolysis continues to be the first choice of therapy.[10] Time from symptom onset to restoration and magnitude of coronary flow correlate with short-term and long-term outcomes in STEMI-CS.[11–13] The relative benefit of PPCI over fibrinolytic therapy is time dependent. In randomized clinical trials, door-to-balloon times are relatively rapid; however, in the routine clinical practice, only 5% of transferred patients meet guideline recommendations for PPCI.[14–16] Very few studies of fibrinolysis have included patients with CS and were mostly completed in the era of coronary angioplasty and first-generation stents.[17,18]

Contemporary studies assessing trends, utilization, and outcomes associated with fibrinolysis in STEMI-CS are lacking. Using a nationally representative population treated from 2009 to 2017, we sought to assess the contemporary utilization of fibrinolytics in STEMI-CS. We hypothesized that admissions with STEMI-CS undergoing initial fibrinolytic therapy would have comparable in-hospital mortality than those receiving PPCI. We sought to assess the temporal trends of fibrinolytic therapy, resource utilization, and development of multiorgan failure in this population.

Material and methods

Study population, variables, and outcomes

The National (Nationwide) Inpatient Sample (NIS) is the largest all-payer database of hospital inpatient stays in the USA. NIS contains discharge data from a 20% stratified sample of community hospitals and is a part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality.[19] Information regarding each discharge includes patient demographics, primary payer, hospital characteristics, principal diagnosis, up to 24 secondary diagnoses, and procedural diagnoses. These data are available to other authors via the HCUP-NIS database with the Agency for Healthcare Research and Quality.[19] Institutional review board approval was not sought because of the publicly available nature of the de-identified data.

A comparative effectiveness study was performed within a retrospective cohort identified using the HCUP-NIS database. Adult (>18 years) admissions with a primary diagnosis of STEMI [International Classification of Diseases-9 Clinical Modification (ICD-9CM) 410.1x-410.6x, 410.8x, and 410.9x and International Classification of Diseases-10 Clinical Modification (ICD-10CM) I21.x-22.x except I21.4, I 32.Ax, I22.2, and I21.9] and a secondary diagnosis of CS (ICD-9CM 785.51; ICD-10CM R57.0) were identified.[20] Fibrinolytic therapy was classified as that received either prior to transfer within the previous 24 h (ICD-9CM V45.88; ICD-10CM Z92.82) or on Hospital Day 0 during the index admission (ICD-9CM 99.10; ICD-10PCS 3E03317, 3E04317).[21,22] The initial fibrinolysis cohort was compared with STEMI-CS admissions receiving PPCI. Because the ICD-9CM for fibrinolysis prior to transfer was introduced in October 2008, we excluded all admissions before 1 January 2009. We also excluded admissions without information on timing of fibrinolysis or fibrinolysis received after Hospital Day 0, with alternate indications to receive fibrinolysis (pulmonary embolism and ischaemic stroke) and admissions managed medically or with CABG in the non-fibrinolysis group.[21,23] Demographic characteristics, hospital characteristics, concomitant cardiac arrest, co-morbidities, coronary angiography, PCI, CABG, mechanical circulatory support, and non-cardiac organ support use were identified for all admissions using previously used methodologies from our group.[2,24–27] Deyo's modification of the Charlson Comorbidity Index was used to identify the burden of co-morbid diseases (Supporting Information, *Table S1*).[28] The day of the procedure was used to time the procedure with respect to hospitalization day. Acute non-cardiac organ failure was divided into respiratory, renal, hepatic, haematological, and neurological domains.[2,24–27] Complications were classified as vascular (arterial injury, acquired arteriovenous fistula, lower limb amputation, and vascular complications requiring surgery), haemorrhagic (haemorrhage and red blood cell transfusion), intracranial haemorrhage, and mechanical (acquired ventricular septal defect, papillary muscle rupture, and haemopericardium) complications (Supporting Information, *Table S1*).

This primary outcome was the in-hospital mortality of STEMI-CS admissions receiving fibrinolysis as a primary treatment strategy as compared with those receiving PPCI. The secondary outcomes included development of non-cardiac organ failure, development of complications (vascular,

haemorrhagic, and mechanical), length of hospital stay, hospitalization costs, use of palliative care referral and do-not-resuscitate (DNR) status, and discharge disposition between these two groups. The temporal trends of fibrinolytic use, use of post-fibrinolytic procedures such as coronary angiography, PCI, and CABG, and trends of in-hospital mortality between the two groups were evaluated.

Statistical analysis

As recommended by HCUP-NIS, survey procedures using discharge weights provided with HCUP-NIS database were used to generate national estimates. Using the trend weights provided by the HCUP-NIS, samples from 2009 to 2011 were re-weighted to adjust for the 2012 HCUP-NIS redesign.[29] χ^2 test and t-test were used to compare categorical and continuous variables, respectively. Logistic regression was used to analyse trends over time (referent year 2009). Univariable analysis for trends and outcomes was performed and was represented as odds ratio (OR) with 95% confidence interval (CI). Multivariable logistic regression analysis incorporating age, sex, race, primary payer status, socio-economic status, hospital characteristics, co-morbidities, out-of-hospital cardiac arrest, acute organ failure, complications, DNR status, palliative care referral, pulmonary artery catheterization, mechanical circulatory support, invasive mechanical ventilation, and haemodialysis use was performed for in-hospital mortality. For the multivariable modelling, regression analysis with purposeful selection of statistically (liberal threshold of $P < 0.20$ in univariate analysis) and clinically relevant variables was conducted. Subgroup analyses for the primary outcome were performed in the cohorts stratified by age ($\leq 75/>75$ years), sex, race (White/non-White), concomitant cardiac arrest, hospital location (rural/urban), STEMI location (anterior, inferior, and other), use of DNR status, and palliative care referral.

Additionally, we performed a propensity-matched analysis for age, sex, race, primary payer, weekend admission, socio-economic status, co-morbidity, STEMI location, prior CABG, out-of-hospital cardiac arrest, and hospital characteristics between the two cohorts. For the propensity matching, due to low rates of missing variables, admissions with missing observations were omitted. Using 1:1 nearest neighbour matching, 526 matching pairs (1052 individual admissions) were developed for further use.

The inherent restrictions of the HCUP-NIS database related to research design, data interpretation, and data analysis were reviewed and addressed.[29] Pertinent considerations include not assessing individual hospital-level volumes (due to changes to sampling design detailed earlier), treating each entry as an 'admission' as opposed to individual patients, restricting the study details to inpatient factors because the HCUP-NIS does not include outpatient data, and limiting

administrative codes to those previously validated and used for similar studies. Two-tailed $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS v25.0 (IBM Corp., Armonk, NY).

Results

From 1 January 2009 to 31 December 2017, there were over 1.6 million STEMI admissions, of which 11.5% had CS. The final groups compared 5297 (2.9%) admissions that received fibrinolysis with 110 452 (59.6%) admissions that received PPCI (Figure 1). Compared with those receiving PPCI, the initial fibrinolysis cohort was more often non-White, bearing Medicare insurance, admitted more frequently on weekends, from a lower socio-economic status, had higher rates of prior CABG and lower co-morbidity, presented with an anterior STEMI, and more frequently admitted to small and rural hospitals (all $P < 0.001$) (Table 1). The unadjusted and adjusted temporal trends of fibrinolysis and primary revascularization use in the overall STEMI-CS cohort showed a steady increase in PPCI use with a concomitant decrease in fibrinolysis use (Figure 2A and 2B). In admissions that received fibrinolysis, 95.3%, 77.4%, and 15.7% received angiography, PCI, and CABG, respectively, with a relatively stable temporal trend (Figure 2C). In the admissions receiving fibrinolysis, early (Hospital Day 0) coronary angiography and PCI were performed in 84% and 77%, respectively. The fibrinolysis group had slightly lower rates of acute organ failure compared with those receiving PPCI (all $P < 0.05$) (Table 2). The fibrinolysis group had lower use of intravascular ultrasound, coronary thrombectomy, and mechanical circulatory support devices (Table 2). The fibrinolysis group had higher rates of haemorrhagic complications, acquired ventricular septal defect, and haemopericardium and lower rates of vascular complications (Table 2).

Compared with those receiving PPCI, the fibrinolysis group had comparable all-cause in-hospital mortality [28.8% vs. 28.5%; OR 1.02 (95% CI 0.96–1.08); $P = 0.57$]. The temporal trends of in-hospital mortality in two groups showed relatively stable trends during the study period (Figure 3A and 3B). In a multivariable logistic regression analysis, the fibrinolytic group had comparable all-cause in-hospital mortality than those receiving PPCI [OR 0.97 (95% CI 0.90–1.05); $P = 0.50$] (Supporting Information, Table S2). The group receiving fibrinolysis had comparable hospital stay, use of DNR status, and palliative care referrals but had lower hospitalization costs and less frequent discharges to skilled nursing facilities (Table 3). To confirm the primary results, multiple subgroup analyses were performed. Compared with the group receiving PPCI, the group receiving initial fibrinolysis had comparable in-hospital mortality across all demographics

Figure 1 Study population. Comparative effectiveness study design using retrospective cohort of ST-segment elevation myocardial infarction (STEMI) cardiogenic shock admissions. *Medically managed admissions were defined as those not receiving coronary angiography, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG).
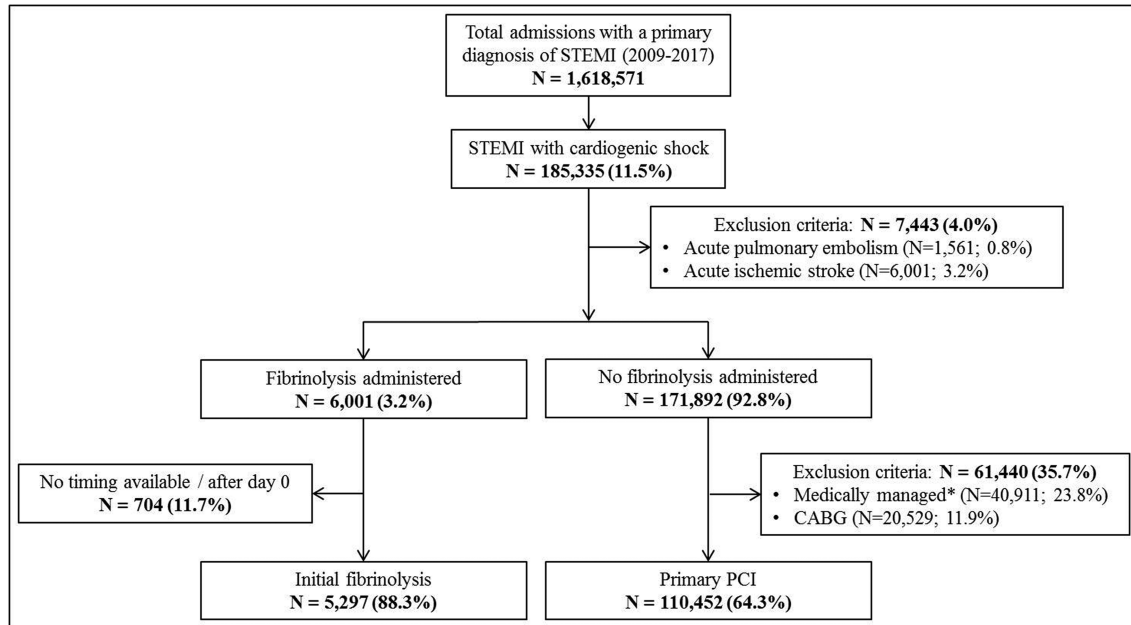
except in those admitted to rural hospitals or those with DNR status/palliative care referral (*Figure 4*).

Using propensity matching, we generated 1052 pairs of admissions. The baseline characteristics were comparable between the two groups (*Table 1*). In these propensity-matched pairs, the admissions receiving initial fibrinolysis had higher rates of acute respiratory failure, mechanical ventilation use, and haemorrhagic complications but lower rates of PCI (*Table 2*). In the propensity-matched pairs, the group receiving fibrinolysis had comparable in-hospital mortality, use of palliative care referral, DNR status use, hospital length of stay, hospitalization costs, and discharge disposition (*Table 3*).

Discussion

In this nationally representative study, we noted admissions receiving fibrinolysis to have comparable in-hospital mortality, use of palliative care referral, and DNR use than those receiving PPCI. The fibrinolysis group was more often of non-White race, with lower co-morbidity, admitted to rural hospitals, and presenting on weekends. Over 90% of all admissions receiving fibrinolysis received subsequent revascularization with PCI or CABG. The fibrinolysis group had higher rates of bleeding and mechanical complications.

In our study, consistent with prior studies, we demonstrated a steady increase in PPCI use with a concomitant decrease in fibrinolysis over the study period. In a 15 year analysis of 10 610 AMI-CS in France, Aissaoui *et al.* noted that the use of fibrinolysis decreased from 14% in 1995 to 8% in 2010 and PPCI increased from 7% to 51%.[30] In this study, 30 day mortality significantly decreased from 83.5% to 46.9%; however, the mortality from 30 days to 1 year remained unchanged.[30] Similarly, the Acute Coronary Syndrome Israeli Surveys that compared 224 patients with AMI-CS between the years 2000–2004 to patients with AMI-CS between 2006 and 2013 demonstrated increased use of PPCI in later years, and the use of fibrinolysis significantly decreased over time.[31]

There are limited contemporary data looking at the role of fibrinolysis in STEMI-CS. The GUSTO-I (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) trial in 1995 demonstrated that CS was less common in STEMI patients treated with tissue plasminogen activator.[17] However, there was no observed mortality benefit with treatment of tissue plasminogen activator in patients that presented with CS.[17] Observation from the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial and registry noted that patients with STEMI-CS treated with thrombolysis had a lower in-hospital mortality than those who did not receive thrombolysis (54% vs. 64%, *P* = 0.005).[18] In the DANAMI-2 (Danish Multicenter Randomized Study of Fibrinolytic Therapy versus Acute Coronary Angioplasty in Acute Myocardial Infarction) trial, 103 patients developed in-hospital CS. Angioplasty did not protect against development of

Table 1 Baseline characteristics of STEMI-CS admissions

Characteristic	Unmatched groups			Propensity-matched groups		
	Initial fibrinolysis (N = 5297)	Primary PCI (N = 110 452)	P	Initial fibrinolysis (N = 526)	Primary PCI (N = 526)	P
Age (years)	64.8 ± 13.0	65.7 ± 12.7	<0.001	65.1 ± 13.1	65.0 ± 12.6	0.86
Female sex	32.1	33.9	0.007	33.1	30.7	0.23
Race						
White	67.7	70.2	<0.001	66.7	73.3	0.06
Black	4.8	6.7		4.9	4.8	
Others[a]	27.4	23.1		28.3	21.8	
Primary payer						
Medicare	48.1	51.0	<0.001	49.8	49.4	0.18
Medicaid	9.6	8.9		8.0	5.5	
Private	29.4	29.4		28.7	30.0	
Others[b]	12.9	10.8		13.5	15.1	
Weekend admission	30.5	29.3	0.05	30.8	29.2	0.32
Quartile of median household income for zip code						
0th–25th	33.5	28.1	<0.001	34.4	41.0	0.11
26th–50th	29.9	26.5		29.3	24.2	
51st–75th	19.9	24.5		20.3	21.0	
75th–100th	16.7	20.9		16.0	13.9	
Charlson Comorbidity Index						
0–3	39.5	37.1	0.002	38.6	40.3	0.72
4–6	44.6	46.3		45.8	43.3	
≥7	16.0	16.6		15.6	16.4	
STEMI location[c]						
Anterior	44.1	43.6	<0.001	45.4	45.8	0.06
Inferior	43.9	42.3		46.8	48.5	
Other	12.0	14.1		11.4	7.6	
Prior coronary artery bypass grafting	3.8	2.7	<0.001	3.6	2.1	0.19
Out-of-hospital cardiac arrest	33.5	36.1	<0.001	32.1	31.1	0.73
Hospital teaching status and location						
Rural	6.8	5.7	0.001	7.2	8.6	0.41
Urban non-teaching	34.3	33.9		36.7	39.3	
Urban teaching	58.9	60.4		56.1	52.1	
Hospital bed size						
Small	9.9	9.6	0.16	10.8	8.2	0.06
Medium	23.8	24.9		23.6	19.3	
Large	66.3	65.5		65.6	72.5	
Hospital region						
Northeast	12.1	15.6	<0.001	15.4	7.1	0.09
Midwest	20.3	24.2		20.2	22.7	
South	36.9	39.0		36.7	46.2	
West	30.7	21.3		27.8	23.9	

PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; STEMI-CS, ST-segment elevation myocardial infarction cardiogenic shock.
Represented as percentage or mean ± standard deviation.
[a]Hispanic, Asian, Native American, and others.
[b]Uninsured, no charge, and others.
[c]The categories are not mutually exclusive as each admission may have had more than one STEMI location involved.

in-hospital CS compared with fibrinolysis. Interestingly, there was no difference seen with regard to 3 year mortality in CS patients treated with angioplasty vs. fibrinolysis [hazard ratio 1.05 (95% CI 0.67–1.64); P = 0.25].[11] In comparison with these studies, our contemporary data did not show any differences in in-hospital mortality with upfront use of fibrinolysis followed by PCI as compared with PPCI in STEMI-CS.

Patients who present to non-PCI-capable facilities benefit from thrombolysis and prompt transfer to a PCI-capable centre for angiography and subsequent management.[15,32–34] These initial receiving facilities are likely to be situated in rural areas and cater to patients from a lower socio-economic status.[1] Small community hospitals in rural USA attempt to have an interventional cardiologist on at least few days a week for elective procedures, if not able to have a 24/7 dedicated PCI-capable catheterization lab.[35,36] These factors are what likely led to our finding of the initial fibrinolysis cohort to be more often noted in admissions over the weekends, at small and rural hospitals and from a lower socio-economic status.

Given these limitations, there should be a strong consideration for two important healthcare delivery aspects—(i)

Figure 2 Trends in the use of fibrinolytics and primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction cardiogenic shock (STEMI-CS). (A) Unadjusted temporal trends of fibrinolytics and primary PCI use in the retrospective cohort of all STEMI-CS admissions between 2009 and 2017 ($P < 0.001$ for trend over time)*. (B) Adjusted odds ratio for fibrinolytics and primary PCI use in the retrospective cohort of all STEMI-CS admissions between 2009 and 2017 (with 2009 as the referent); adjusted for age, sex, race, co-morbidity, out-of-hospital cardiac arrest, primary payer, socio-economic status, hospital region, hospital location and teaching status, and hospital bed size ($P < 0.001$ for trend over time)*. (C) Unadjusted temporal trends of subsequent coronary angiography, PCI, and coronary artery bypass grafting (CABG) use in the STEMI-CS admissions receiving initial fibrinolysis between 2009 and 2017 ($P < 0.001$ for trend over time). *The temporal trends were generated using the retrospective cohort of all STEMI-CS admissions.
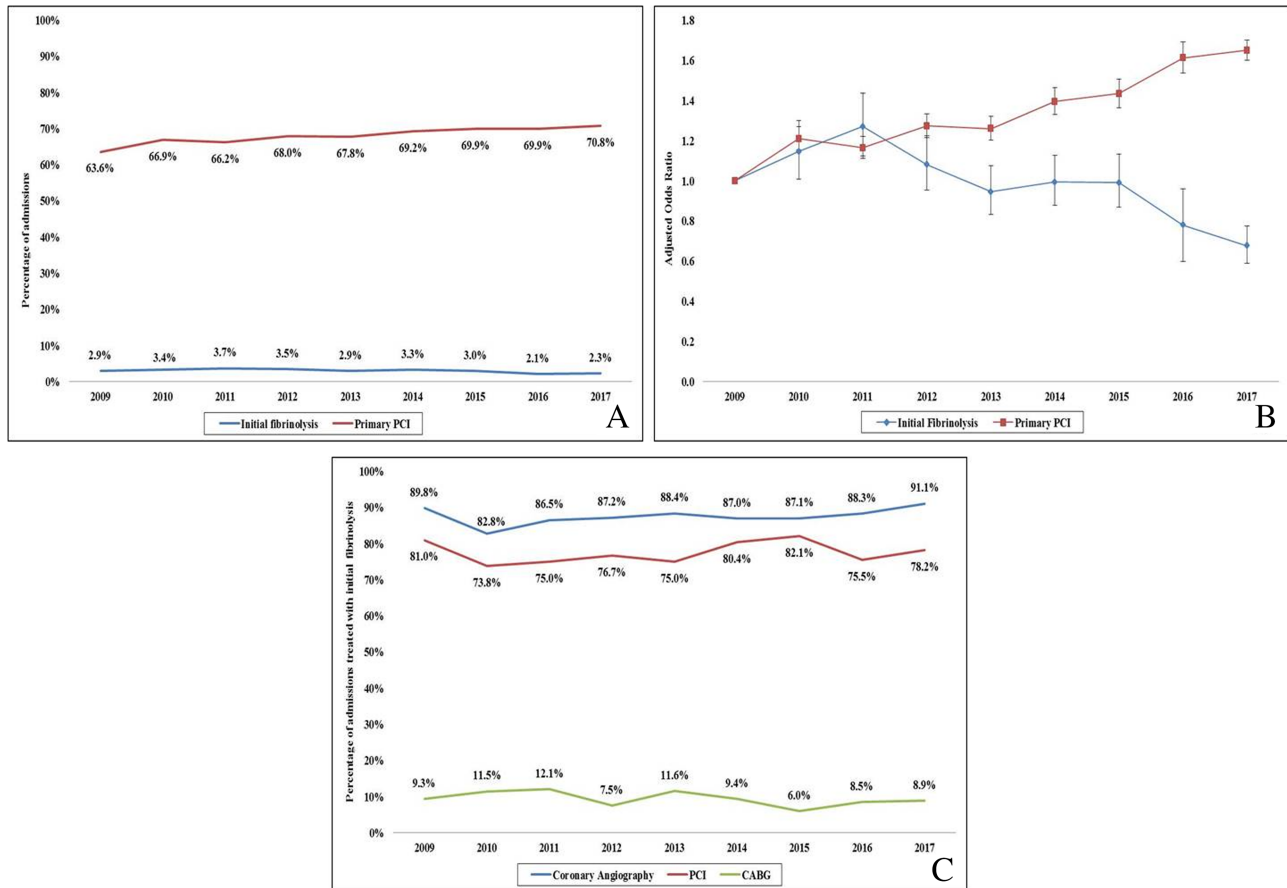
development of a pharmaco-invasive network for the management of STEMI with/without CS and (ii) development of a hub-and-spoke model for STEMI-CS care.[34] In this contemporary study, we found high rates of coronary angiography (95.3%) and PCI (77.4%) in admissions receiving fibrinolysis suggestive of greater adoption of the pharmaco-invasive strategy. In STEMI, pre-hospital fibrinolysis was associated with lower rates of CS in the CAPTIM (Comparison of Angioplasty and Pre-hospital Thrombolysis in Acute Myocardial Infarction) trial, STREAM (Strategic Reperfusion Early after Myocardial Infarction) trial, and WEST (Which Early ST-elevation myocardial infarction Therapy) study, suggesting that the additional delay in the PPCI cohort compared with pre-hospital fibrinolysis may be responsible for the

higher CS rates.[37–39] A meta-analysis of randomized control trials by Roule et al. reported a reduction in rates of STEMI-CS in association with pre-hospital fibrinolysis compared with PPCI.[12] Our study demonstrated that complication rates were low in both cohorts, which further advocates the use of thrombolysis in patients with a potential delay to PPCI. It is important to restore coronary flow irrespective of the strategy used, and therefore, an early pharmaco-invasive approach should be considered in patients who might have potential delays in reaching a PCI-capable facility.[40,41] A structured hub-and-spoke model with immediate transfers to tertiary care centres with multidisciplinary CS teams capable of advanced mechanical circulatory support and transplant evaluation should be adopted.[1,3,42,43]

Table 2 In-hospital characteristics and complications of STEMI-CS admissions

Characteristic	Unmatched groups			Propensity-matched groups		
	Initial fibrinolysis (N = 5297)	Primary PCI (N = 110 452)	P	Initial fibrinolysis (N = 526)	Primary PCI (N = 526)	P
Non-cardiac organ failure						
Respiratory	53.2	53.0	0.82	43.3	36.1	0.02
Renal	35.4	36.9	0.03	27.8	26.5	0.67
Hepatic	11.9	12.3	0.43	7.6	7.8	>0.99
Haematological	10.7	10.5	0.68	7.4	7.1	0.90
Neurological	18.5	19.7	0.05	14.3	12.4	0.40
Cardiac procedures						
Coronary angiography	87.4	100.0	<0.001	84.0	100.0	<0.001
PCI	77.4	100.0	<0.001	75.5	100.0	<0.001
CABG	10.1	—	<0.001	4.6	—	<0.001
IVUS	3.5	4.3	0.003	2.5	2.5	>0.99
Coronary thrombectomy	3.7	5.5	<0.001	1.0	0.4	0.46
PAC	4.5	4.8	0.29	3.0	4.0	0.49
Mechanical circulatory support						
Total	50.6	56.2	<0.001	46.0	49.4	0.31
IABP	48.0	50.8	<0.001	45.6	47.5	0.57
pLVAD	3.3	6.7	<0.001	1.0	1.9	0.28
ECMO	0.8	1.0	0.05	0.0	0.4	0.23
Non-cardiac organ support						
Mechanical ventilation	43.1	38.0	<0.001	41.8	29.6	<0.001
Acute haemodialysis	2.5	2.1	0.08	1.3	1.3	>0.99
Complications						
Vascular complications	0.9	1.6	<0.001	0.8	0.8	>0.99
Haemorrhagic	13.5	9.9	<0.001	8.4	4.6	0.02
Intracranial haemorrhage	0.7	0.6	0.13	0.4	0.4	>0.99
Acquired VSD	2.0	1.1	<0.001	2.1	0.6	0.04
Papillary muscle rupture	0.3	0.2	0.34	0.0	0.0	—
Haemopericardium	0.4	0.2	0.008	0.4	0.0	0.50

CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; IVUS, intravascular ultrasound; PAC, pulmonary artery catheterization; PCI, percutaneous coronary intervention; pLVAD, percutaneous left ventricular assist device; STEMI-CS, ST-segment elevation myocardial infarction cardiogenic shock; VSD, ventricular septal defect.

Figure 3 Trends in in-hospital mortality in admissions receiving fibrinolytics vs. primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction cardiogenic shock (STEMI-CS). (A) Unadjusted temporal trends of in-hospital mortality in admissions receiving initial fibrinolysis vs. primary PCI in STEMI-CS admissions between 2009 and 2017 ($P < 0.001$ for trend over time). (B) Adjusted odds ratio for of in-hospital mortality in admissions receiving initial fibrinolysis vs. primary revascularization in STEMI-CS admissions between 2009 and 2017 (with 2009 as the referent); adjusted for age, sex, race, weekend admission, co-morbidity, primary payer, socio-economic status, hospital region, hospital location and teaching status, hospital bed size, out-of-hospital cardiac arrest, acute organ failure, complications (vascular, haemorrhagic, and mechanical), pulmonary artery catheterization, mechanical circulatory support, invasive mechanical ventilation, acute haemodialysis, do-not-resuscitate status, and palliative care referral ($P < 0.001$ for trend over time).
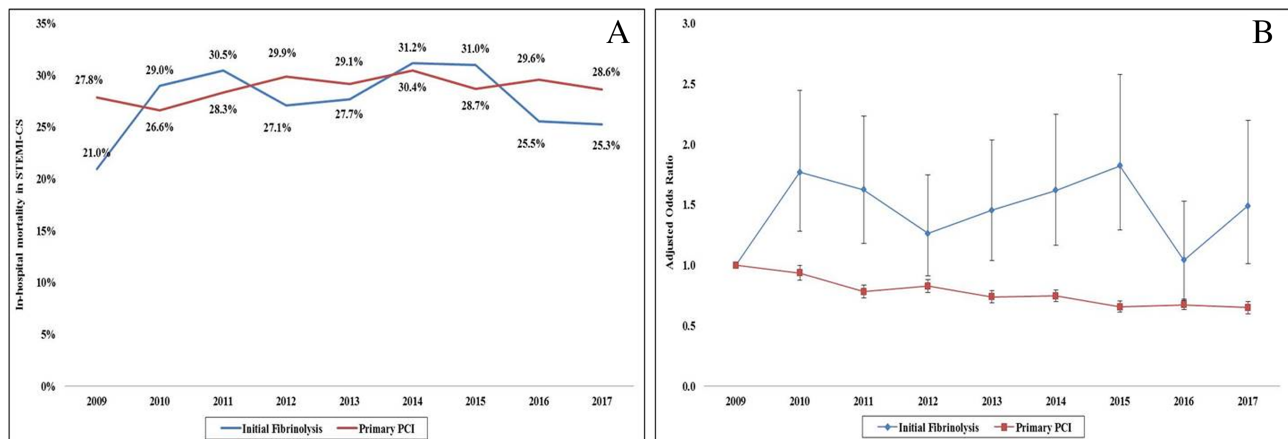
Table 3 Clinical outcomes of STEMI-CS admissions

	Unmatched groups			Propensity-matched groups		
Outcome	Initial fibrinolysis (N = 5297)	Primary PCI (N = 110 452)	P	Initial fibrinolysis (N = 526)	Primary PCI (N = 526)	P
In-hospital mortality	28.5	28.8	0.59	30.8	30.3	0.89
Length of stay (days)	7.7 ± 7.7	7.6 ± 8.6	0.44	5.5 ± 3.8	5.0 ± 3.5	0.02
Hospitalization costs (US dollars)	148 ± 138	161 ± 163	<0.001	82 ± 37	88 ± 33	0.39
Do-not-resuscitate status	9.9	10.1	0.66	9.1	8.0	0.57
Palliative care referral	7.4	7.6	0.53	7.0	5.5	0.36
Discharge disposition						
Home	58.5	57.3	<0.001	44.9	51.1	0.21
Transferred to other hospitals	9.5	9.4		7.4	5.5	
Skilled nursing facility	16.4	19.8		7.4	6.5	
Home with home health care	14.7	12.8		8.9	5.9	
Against medical advice	0.9	0.6		0.6	0.8	

PCI, percutaneous coronary intervention; STEMI-CS, ST-segment elevation myocardial infarction cardiogenic shock.
Represented as percentage or mean ± standard deviation.

Figure 4 Subgroup analyses for in-hospital mortality in admissions receiving initial fibrinolysis as compared with primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) cardiogenic shock. Multivariable adjusted odds ratios (95% confidence intervals)* for in-hospital mortality in those receiving initial fibrinolysis compared with primary revascularization admissions stratified by age, sex, race, presence of cardiac arrest, hospital location, STEMI location, do-not-resuscitate (DNR) status, and palliative care referral. *Adjusted for age, sex, race, primary payer, socio-economic status, hospital characteristics, co-morbidities, acute non-cardiac organ failure, pulmonary artery catheterization, invasive mechanical ventilation, acute haemodialysis, mechanical circulatory support, vascular complications, intracranial haemorrhage, haemorrhagic complications, mechanical complications, palliative care referral, and DNR status.
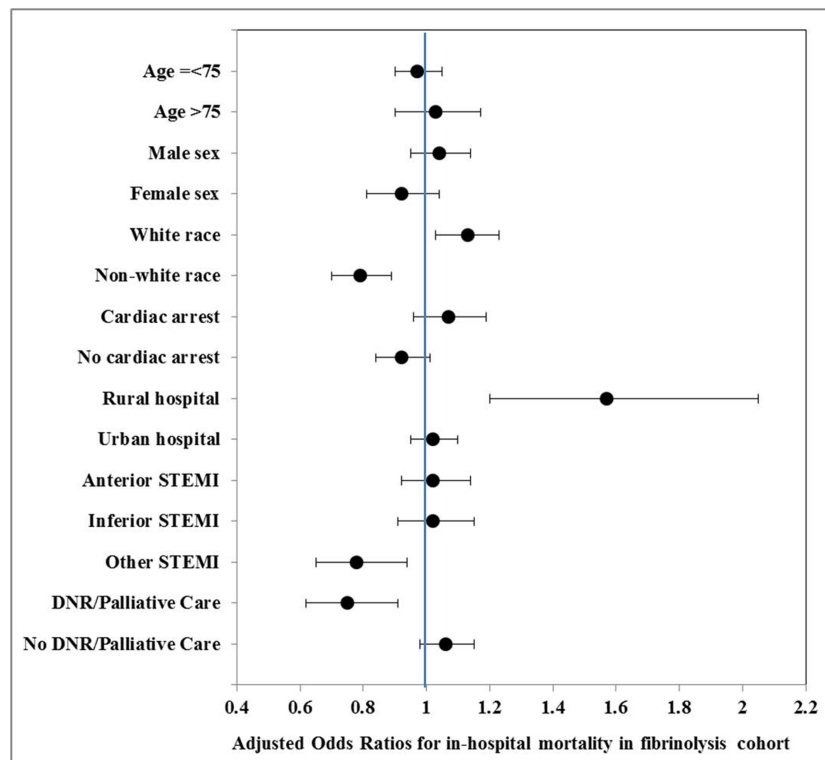
Limitations

This study has several limitations, some of which are inherent to the analysis of a large administrative database. The HCUP-NIS attempts to mitigate potential errors by using internal and external quality control measures. The lack of time to reperfusion and detailed angiography data, such as the target vessel for PCI, classification and the presence of multi-vessel disease with/without chronic total occlusions, and success of planned treatment strategy, were not available in this database. This study only included CS shock admissions and therefore cannot be generalized to all STEMI patients. This study does not record details regarding the total ischaemic time, dose of fibrinolytic administered, proportion of admissions that did not receive fibrinolytics due to absolute or relative contraindications, and patients receiving pre-hospital fibrinolytics that died *en route* to the hospital. Additionally, measures of CS severity such as mixed venous oxygen saturation, lactate, haemodynamics, and vasopressor doses were not available through this database. Although we performed multivariable adjustment and propensity matching, we may not have fully captured these confounders in this analysis. Because this was an inpatient database only, we are unable to comment if PCI, which was deferred in some patients, was subsequently performed as an outpatient procedure. The HCUP-NIS database lacks information on medical therapy, including antiplatelet and anticoagulant strategy, which has a strong influence on outcomes. Despite these limitations, this study addresses an important knowledge gap highlighting the contemporary temporal trends and outcomes of fibrinolysis use in STEMI-CS in the USA.

Conclusions

In this contemporary national study of over 115 000 STEMI-CS admissions, we note a decrease in fibrinolysis as the initial strategy for reperfusion. Over 90% of fibrinolytic admissions need subsequent revascularization with either PCI or CABG. The admissions receiving fibrinolysis had comparable in-hospital mortality. Our results need to be carefully interpreted within the limitations of an observational study. These data should be used to guide further dedicated studies evaluating healthcare policy on fibrinolysis use in STEMI-CS.

Conflict of interest

None declared.

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Author contributions

S.V., D.V., D.H.M., W.C., and P.E.M. contributed in the study design, literature review, data analysis, statistical analysis, data management, data analysis, and drafting of the manuscript. S.V., D.V., M.R.B., D.H.M., W.C., P.E.M., S.M.D., A.P., G.S.S., R.G., M.S., A.L., B.J.G., D.R.H., and G.W.B. provided access to data. M.R.B., S.M.D., A.P., G.S.S., R.G., M.S., A.L., B.J.G., D.R.H., and G.W.B. contributed in the manuscript revision, intellectual revisions, and mentorship. S.V., D.V., M.R.B., D.H.M., W.C., P.E.M., S.M.D., A.P., G.S.S., R.G., M.S., A.L., B.J.G., D.R.H., and G.W.B. contributed in the final approval of the manuscript.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Administrative codes.
Table S2. Predictors of in-hospital mortality in STEMI-CS.

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