Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Last, we wholeheartedly agree that the ongoing underrepresentation of minorities in clinical studies is a major concern that requires multistakeholder efforts to address, including a plan to ensure adequate enrollment of minorities during the early trial planning stages.

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Dr. Stone has received speaker honoraria from Cook and Terumo; is a consultant to Valfix, TherOx, Vascular Dynamics, Robocath, HeartFlow, Gore, Ablative Solutions, Miracor, Neovasc, V-Wave, Abiomed, Ancora, MAIA Pharmaceuticals, Vectorious, Reva, and Matrizyme; and holds equity or options in Ancora, Qool Therapeutics, Cagent, Applied Therapeutics, the Biostar family of funds, SpectraWave, Orchestra Biomed, Aria, Cardiac Success, the MedFocus family of funds, and Valfix. Dr. Golomb has reported that he has no relationships relevant to the contents of this paper to disclose.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Interventions* author instructions page.

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RESEARCH CORRESPONDENCE

Trends and Outcomes of Fibrinolytic Therapy for STEMI

Insights and Reflections in the COVID-19 Era

During the ongoing COVID-19 pandemic, national societies have suggested various levels of reliance on fibrinolytic therapy because of anticipated delays in primary percutaneous coronary intervention (PPCI), resource limitations, and hazards to health care workers (1). Studies examining fibrinolytic therapy for ST-segment elevation myocardial infarction (STEMI) in the United States predated the widespread clinical adoption of the highly fibrin-specific tenecteplase, and the widespread adoption of timely reperfusion and other performance measures for STEMI (2). In this report, we evaluated the trends of utilization and outcomes of fibrinolytic therapy for STEMI using a large nationwide database.

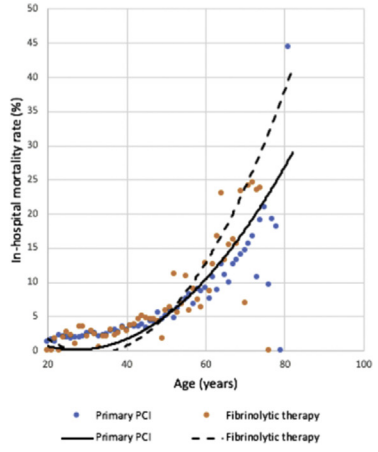
The National Inpatient Sample (NIS) database (2011 to 2017) was queried for hospitalizations with primary International Classification of Disease-9th Revision (ICD-9) or -10th Revision (ICD-10) diagnostic codes of acute STEMI. We identified patients receiving systemic fibrinolytic therapy using ICD-9 codes (V45.88 and 99.10) and ICD-10 codes (Z92.82, 3E04317, and 3E03317) and those receiving PPCI using ICD-9 and ICD-10 procedure codes for PCI, only if performed on day of admission. We accounted for hospital weights, bed size, and clustering. A multivariable regression analysis, adjusting for patient and hospital-related characteristics, was conducted to identify factors independently associated with in-hospital mortality among hospitalized patients receiving fibrinolytic therapy. The SPSS software (IBM SPSS Statistics for Windows, version 25.0, Armonk, New York) was used for statistical analyses. The study was exempt from institutional review board evaluation because the NIS data is deidentified and publicly available.

The final analysis included 738,206 acute STEMI hospitalizations: 699,150 (94.7%) underwent PPCI and 39,056 (5.3%) received fibrinolytic therapy. Among STEMI patients who received fibrinolytic therapy, 23,403 patients (59.9%) were transferred after receiving fibrinolytic therapy in another facility within 24 h of index admission. Of STEMI patients treated with fibrinolytic therapy, 28,108 patients (72.0%) received PCI during the same hospital admission. During the study period, there was a reduction in the number of patients receiving fibrinolytic therapy (6,886 in 2011 vs. 3,550 in 2017; $p_{trend} = 0.01$).

Patients in the fibrinolytic therapy group were younger and more likely to have chronic lung disease and smoking, but less likely to have chronic kidney disease, hypertension, diabetes, and prior cerebrovascular events. A secondary diagnosis of pneumonia was equally present among STEMI patients who received fibrinolytic therapy and PPCI (2.9% vs 2.9%). The fibrinolytic therapy group had an overall in-hospital mortality of 5.4%, with no change in the rates of in-hospital mortality over time ($p_{trend} = 0.28$). The PPCI group had an overall in-hospital mortality of 4.8%, with no change over time ($p_{trend} = 0.87$). In-hospital mortality after STEMI appeared comparable after fibrinolytic therapy and PPCI at younger age groups; however, there was a steeper rise in mortality in the fibrinolytic therapy group after 51 years of age (**Figure 1A**). There was a reduction in major bleeding rates ($p_{trend} < 0.001$) and blood transfusion

FIGURE 1 Trend in Mortality and Complications With Fibrinolytic Therapy and PPCI

A



B

Outcomes	Group	Overall %	2011 %	2012 %	2013 %	2014 %	2015 %	2016 %	2017 %	P_{trend}
In-hospital mortality	Fibrinolytic (n= 2,104)	5.4	5.5	4.3	5.2	6.0	6.1	5.3	5.8	0.28
	Primary PCI(n= 33,721)	4.8	4.5	4.6	4.7	4.8	4.8	5.2	5.0	0.87
Cardiogenic shock	Fibrinolytic (n= 3,872)	9.9	9.9	8.9	7.9	10.6	10.5	11.1	12.0	0.05
	Primary PCI (n=72,159)	10.3	9.8	9.4	9.8	10.4	10.7	11.0	11.1	0.61
Cardiac arrest	Fibrinolytic (n= 3,662)	9.4	8.2	7.5	8.8	11.3	10.6	10.3	10.3	0.29
	Primary PCI (n=71,815)	10.3	9.6	10.0	9.9	10.6	10.9	10.3	10.6	0.23
Acute hemorrhagic stroke	Fibrinolytic (n= 199)	0.5	0.7	0.4	0.6	0.4	0.4	0.6	0.6	0.14
	Primary PCI (n=8635)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.15
Major bleeding	Fibrinolytic (n= 30,13)	7.7	9.0	9.0	8.3	7.2	7.2	6.1	5.4	<0.01
	Primary PCI (n=44,732)	6.4	7.4	7.4	7.0	6.9	6.6	4.7	5.1	0.01
Blood transfusion	Fibrinolytic (n= 1698)	4.3	6.7	4.7	4.3	3.2	3.5	2.8	4.4	0.01
	Primary PCI (n=20,661)	3.0	3.4	2.9	2.7	2.5	2.9	3.2	3.0	0.07
Ventricular arrhythmias	Fibrinolytic (n= 4,007)	10.3	9.6	8.9	10.8	9.5	10.5	10.9	13.2	0.03
	Primary PCI (n=77,656)	11.1	10.2	10.2	10.6	11.4	11.8	11.3	12.2	0.01
Complete heart block	Fibrinolytic (n= 990)	2.5	2.4	2.6	2.8	2.0	2.8	2.4	2.7	0.77
	Primary PCI (n=18,336)	2.6	2.4	2.5	2.7	2.4	2.7	2.7	2.9	0.61
Pacemaker	Fibrinolytic (n=205)	0.5	0.4	0.6	0.4	0.6	0.4	0.6	0.7	0.12
	Primary PCI (n=3,872)	0.6	0.5	0.5	0.6	0.5	0.5	0.7	0.7	0.34

(A) Age-based trend in in-hospital mortality with fibrinolytic therapy and PPCI. **(B)** Trend in complications for fibrinolytic therapy and PPCI for acute STEMI.
PCI = percutaneous coronary intervention; PPCI = primary percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

(p_{trend} = 0.01) with fibrinolysis during the study period, but the rates of other complications including hemorrhagic stroke did not change (Figure 1B). Compared with PPCI, fibrinolytic therapy was associated with lower median (interquartile range) hospital charges US$67,340 (US$46,540 to US$101,480) vs. US$73,460 (US$52,761 to US$106,959) ($p < 0.001$), but longer hospital length of stay (4.05 ± 5.44 days vs. 3.66 ± 4.44 days; $p < 0.001$).

On multivariable analysis, factors associated with in-hospital mortality among patients receiving fibrinolytic therapy included: age >75 years (odds ratio [OR]: 5.95, 95% confidence interval [CI]: 4.68 to 7.57), women (OR: 1.38; 95% CI: 1.15 to 1.66), peripheral vascular disease (OR: 1.75; 95% CI: 1.30 to 2.36), chronic kidney disease (OR: 2.77; 95% CI: 2.17 to 3.53), chronic liver disease (OR: 2.33; 95% CI: 1.21 to 4.50), coagulopathy (OR: 3.48; 95% CI: 2.47 to 4.91), and a secondary diagnosis of acute pneumonia (OR: 2.20; 95% CI: 1.45 to 3.33).

In this nationwide analysis of ~738,000 hospitalizations with acute STEMI, we demonstrated that only a minority of patients received fibrinolytic therapy, with decreasing utilization over time. Compared with PPCI, the use of fibrinolytic therapy was associated with longer hospitalization but lower overall hospital charges. Among patients receiving fibrinolytic therapy, there was a significant decrease in rates of major bleeding and blood transfusions, but no change in the rates of hemorrhagic stroke.

Our results provide insight into the trends in the current era with respect to the use of fibrinolytic therapy as a reperfusion modality for STEMI. Among STEMI patients receiving fibrinolysis, the presence of pneumonia, which is a common manifestation of COVID-19, was independently associated with increased in-hospital mortality. We have also demonstrated that older age, known to be a poor prognosticator among patients with COVID-19, was an independent factor associated with increased in-hospital mortality among STEMI patients undergoing fibrinolytic therapy. These observations have important implications in the COVID-19 era.

This analysis is limited by the observational nature of the dataset. The NIS only provides data on hospitalizations, rather than patient-level data, with no available long-term data. Data on medications and the proportion of rescue PCI were irretrievable from this dataset. Given the limited number of patients with a secondary diagnosis of pneumonia, further adjudication of viral versus bacterial pneumonia was not feasible.

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RESEARCH CORRESPONDENCE

Ultrathin-Strut Versus Thin-Strut Drug-Eluting Stents for Primary PCI

A Subgroup Analysis of the BIOSTEMI Randomized Trial

Biodegradable polymer sirolimus-eluting stents (BP-SES) are superior to durable polymer everolimus-eluting stents (DP-EES) with respect to target lesion failure (TLF) at 1 year in patients with ST-segment elevation myocardial infarction (STEMI) (1). Beyond the biodegradable polymer, BP-SES differ from DP-EES in terms of metallic stent platform strut thickness for stent diameters ≤3.0 mm (60 μm), whereas strut thickness in stent sizes >3.0 mm (80 μm) is similar to DP-EES (81 μm). Ultrathin-strut drug-eluting stents (DES) have been shown to reduce TLF compared with thicker-strut DES (2). A potential advantage of BP-SES over DP-EES may therefore unfold in patients with STEMI treated with small stent sizes. We performed a post hoc subgroup analysis of the BIOSTEMI (A Comparison of an Ultrathin Strut Biodegradable Polymer Sirolimus-Eluting Stent With a Durable Polymer Everolimus-Eluting Stent for Patients With Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention) randomized trial to assess whether differences in stent strut thickness explain differential outcomes between BP-SES and DP-EES in patients with STEMI.

BIOSTEMI (NCT02579031) was an investigator-initiated, multicenter, prospective, randomized superiority trial comparing BP-SES with DP-EES in patients with STEMI (1). Patients with STEMI were randomly assigned in a 1:1 ratio to treatment with BP-SES or DP-EES and were further divided according to stent diameter into small (≥1 stent diameter ≤3.0 mm) or large (all stent diameters >3.0 mm) stent size subgroups. The primary endpoint was TLF, a composite of cardiac death, target vessel myocardial reinfarction, or clinically indicated target lesion revascularization, within 12 months. The study protocol complied with the Declaration of Helsinki and was approved by the institutional ethics committees at each participating site. All patients provided written informed consent for participation. As with the main analysis (1), we included individual patient data from patients with STEMI included in the BIOSCIENCE (Sirolimus-Eluting Stents With Biodegradable Polymer Versus an Everolimus-eluting Stents) trial (NCT01443104) (3). P values were obtained from chi-square tests, Fisher exact tests, generalized linear models, or mixed-effect models (for lesion-level analysis), as appropriate. Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) and p values for main effects and for the interaction between patient subgroup and stent type. We used the time to first event for each outcome and report numbers of patients and Kaplan-Meier estimates of cumulative incidence.

A total of 1,707 patients with STEMI (2,172 lesions) enrolled in the BIOSCIENCE (n = 407) and BIOSTEMI (n = 1,300) trials were randomly assigned to treatment with BP-SES (n = 860, 1,099 lesions) or DP-EES (n = 847, 1,073 lesions). There were no significant differences in terms of baseline characteristics between the treatment arms (1). At 1-year follow-up, TLF occurred in 28 patients (cumulative incidence