10.1161/CIRCOUTCOMES.120.006885

Why Fibrinolytic Therapy for STEMI in the COVID-19 Pandemic is Not Your New Best Friend

Ajay J. Kirtane, MD, SM and Sripal Bangalore MD, MHA

Columbia University Medical Center/NewYork-Presbyterian Hospital and the Cardiovascular Research Foundation, and NYU-Langone Medical Center, New York, New York

Address for Correspondence:
Ajay J. Kirtane, MD, SM
161 Fort Washington Ave, 6th Floor
New York, NY 10032
Tel: 212-305-7060
Fax: 212-342-3660
Email: akirtane@columbia.edu

Editor's Note from Brahmajee K. Nallamothu, MD, MPH: In this issue we publish 2 differing cardiovascular perspectives on how to manage ST-elevation myocardial infarction (STEMI) during the coronavirus disease 2019 (COVID-19) pandemic. COVID-19 has disrupted many processes of care related to emergency cardiac conditions. These perspectives offer 2 opinions understanding that capacity of treating hospitals will continue to evolve and management should change based on it. Placing these side-by-side will allow readers to understand the tradeoffs inherent in such decisions.

See Related Article by Bainey et al

The COVID-19 pandemic has strained global health care systems in ways that simply could not have been imagined just several months ago. Writing from the heart of New York City – the unfortunate new epicenter of this pandemic – we have been confronted with this new reality head-on. As directors of two major academic cardiac catheterization laboratories in the city, we both have had to operationalize logistical planning of physician and staff redeployments as well as modification of our respective hospital units including conversion of large portions of the catheterization laboratory into COVID-19 intensive care units in order to deal with the surge of COVID-19 patients within the hospital.

In the midst of all of these changes has always been the concern of how we could best deal with genuine cardiac emergencies such as acute ST-elevation myocardial infarction (STEMI). Decades of trials have established primary percutaneous coronary intervention (PPCI) as the preferred approach to STEMI.[1] Compared to the alternative of fibrinolytic therapy (FT), reperfusion with PPCI is more reliable and durable, and incurs a lower rate of adverse outcomes, resulting in a net clinical benefit to patients as proven through clinical trials demonstrating lower mortality, reinfarction and bleeding.[2] Yet in the midst of the unique operational challenges posed

by the COVID-19 pandemic, there has been a resurgent discussion of FT, with some algorithms even proposing it as a preferred approach.

We feel that this approach is misguided for several reasons (Figure). First, FT is an inferior reperfusion alternative to PPCI in patients with STEMI, achieving lower rates of TIMI-3 flow compared with PPCI.[3] Moreover, FT is even less likely to be effective in the COVID-19 era due to systemic delays in time to presentation which can lead to older (and more organized) clot.[4] Second, because of the high rate of reinfarction, modern implementations of a FT-based approach involve secondary cardiac catheterization, either rescue (in the case of failed reperfusion) or routine (in order to definitively treat the underlying lesion after successful fibrinolysis).[5] Thus, in this construct, the theoretical advantage of FT in reducing staff exposure and/or consumption of personal protective equipment (PPE) is largely negated when the patient undergoes eventual catheterization following FT. Third, the syndrome of COVID-19 myopericarditis is not an uncommon cause of ST-elevation on the electrocardiogram.[6] Administration of potent FT to a patient with myopericarditis (as opposed to for a thrombotic coronary occlusion) is not only likely to be ineffective, but incurs substantial bleeding risk while treating the incorrect pathophysiology. This potential clinical mistreatment is further exacerbated by the fact that ST-segment elevation will typically persist in this setting, necessitating emergent (rescue) cardiac catheterization, unless the operator decides to then medically manage what was initially considered to be a STEMI. Finally, the role of the cardiac catheterization laboratory in STEMI is not solely limited to PPCI. Diagnostic catheterization with coronary angiography accompanied by the judicious use of hemodynamic assessments can be instrumental in not only establishing diagnoses but in prognostication and further stabilization of patients through appropriate titration of medications and/or appropriate hemodynamic support.

The two most compelling reasons to advocate for a strategy of FT for STEMI in the COVID-19 era relate to reducing staff exposure/resources as well as in overcoming delays to reperfusion. It is our opinion that the solution to the former problem is easily overcome by appropriate procurement and use of full PPE for all STEMI cases. Further, delays to reperfusion even in the COVID-19 era are more pronounced between symptom onset to diagnosis (which already disfavors FT) than from diagnosis to reperfusion through PPCI. Decades of clinical trials have clearly shown inferiority of FT over PPCI especially when treatment delays are greater. Excepting scenarios of impeded or delayed transfer from hospitals without on-site catheterization facilities, it is unlikely that this relationship would change in an infectious disease pandemic. Whether FT is useful to target systemic micro-thrombi associated with COVID-19 remains to be proven. Until that time, PPCI remains the best treatment option for suspected STEMI, taking full precautions to minimize risks of exposure for the cardiac catheterization staff.

Disclosures: Dr Kirtane reports Institutional funding to Columbia University and/or Cardiovascular Research Foundation from Medtronic, Boston Scientific, Abbott Vascular, Abiomed, CSI, Philips, ReCor Medical. Personal: CME program honoraria and travel/meal reimbursements only. Dr. Bangalore reports research grants from Abbott Vascular, NHLBI and being on the advisory board for Abbott Vascular, Pfizer, Amgen and Biotronik.

References

1. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Jr., Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW, American College of Cardiology Foundation/American Heart Association Task Force on Practice G. 2013 accf/aha guideline for the management of st-elevation myocardial infarction: A report of the

american college of cardiology foundation/american heart association task force on practice guidelines. *Circulation*. 2013;127:e362-425
2. Huynh T, Perron S, O'Loughlin J, Joseph L, Labrecque M, Tu JV, Theroux P. Comparison of primary percutaneous coronary intervention and fibrinolytic therapy in st-segment-elevation myocardial infarction: Bayesian hierarchical meta-analyses of randomized controlled trials and observational studies. *Circulation*. 2009;119:3101-3109
3. investigators G. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *The New England journal of medicine*. 1993;329:673-682
4. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: Reappraisal of the golden hour. *Lancet*. 1996;348:771-775
5. Armstrong PW, Fu Y, Chang WC, Topol EJ, Granger CB, Betriu A, Van de Werf F, Lee KL, Califf RM. Acute coronary syndromes in the gusto-iib trial: Prognostic insights and impact of recurrent ischemia. The gusto-iib investigators. *Circulation*. 1998;98:1860-1868
6. Bangalore S, Sharma A, Slotwiner A, Yatskar L, Harari R, Shah B, Ibrahim H, Friedman GH, Thompson CR, Alviar C, Chadow H, Fishman G, Reynolds HR, Keller N, Hochman JS. St-segment elevation in patients with covid-19 — a case series. *The New England journal of medicine*. 2020;10.1056/NEJMc2009020

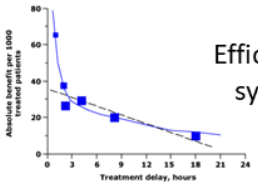
Figure Legend:

Figure. Considerations for how limitations of fibrinolytic therapy use in STEMI patients may apply in COVID-19 patients with ST-elevation on their electrocardiogram.

10.1161/CIRCOUTCOMES.120.006885

Limitations of Fibrinolytic Therapy vs. PPCI in STEMI

Non-COVID-19 patients



Efficacy decreases with longer time from symptom onset (Best within 60 mins)

TIMI 3 flow	50-60%
Recurrent ischemia	20-30%
Major Hemorrhage	2-3%
Non-obstructive CAD	5%

Applicability to COVID-19 patients

Substantial delays in presentation to the hospital and in recognition of STEMI

Up to 50%