Angiographic outcomes in STEMI patients receiving fibrinolysis with guideline directed optimal antithrombotic therapy

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1. Introduction

STEMI remains a major public health problem despite the advances in diagnosis and management.Timely reperfusion of the infarct-related coronary artery using fibrinolysis or percutaneous coronary intervention (PCI) is central to optimal STEMI treatment, minimizing myocardial damage, preserving left ventricular function, and decreasing morbidity and mortality.1 However, limited resources, affordability issues, and inadequate transportation facilities to PCI-capable hospitals prevent the PCI from becoming default reperfusion strategy, thus, making fibrinolysis the prevalent reperfusion strategy. Multitude of clinical trials have been conducted so far which demonstrated that earlier fibrinolytic administration, improves myocardial salvage, preserves left ventricular mechanical function and subsequently leads to significant mortality reduction, thus, favoring key role of pharmacological reperfusion in acute treatment of STEMI.2-4 Key component of the pharmacological “cocktail” is fibrinolytic therapy, but adjunctive antithrombotic agents are of utmost importance for maximizing and maintaining the benefit of dissolving the occlusive coronary artery thrombus as demonstrated by various prior studies.5-7 However, in previous studies, antiplatelet agents or anticoagulants were either not used together consistently or if at all these agents were used, then they were in suboptimal dosing. This study attempts to unfold the relationship between successful fibrinolysis and angiographic parameters on the background of routine loading with dual antiplatelet therapy (DAPT) and optimal anticoagulation with heparin.

2. Method

The objective of this observational study was to assess angiographic success of thrombolysis in terms of angiographic TIMI 3 flow and TMP 3 grade in context of routine loading with DAPT and heparin in patients (>18 years age) presenting with STEMI from January 2018 to December 2019. Patients presenting with NSTEMI, or with STEMI but having contraindications to thrombolysis or refusing consent for reperfusion therapies were excluded from the study. DAPT and anticoagulant therapy were administered to every patient prior to thrombolysis and then, for duration of index hospitalization.10 Only patients who ultimately underwent thrombolysis were enrolled for the study with exclusion of patients who underwent primary PCI. Choice of thrombolytic to be used was left at physician’s discretion after informed discussion with patient. Relief of chest pain after thrombolysis was assessed by visual analog scale and repeat ECG was done at 90 min after the administration of thrombolytic agent.
to look for settling of ECG changes (resolution of ST segment elevation by >50% in the index lead showing greatest degree of elevation on presentation) and development of reperfusion arrhythmias. Success of thrombolysis was assessed via measurement of angiographic parameters such as TIMI (Thrombolysis in Myocardial Infarction trial) flow rates and TMP-3 grades as shown in Videos 1–4. Statistical data were analyzed using SPSS software version 26. Categorical variables were compared by Chi-square test while continuous variables were compared using Student t-test and a ‘p’ value of less than 0.05 was significant.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.ijh.2020.11.011

### 3. Results

100 patients were recruited in the study, with 90 (90%) males. Baseline characteristics of patients in relation to thrombolytic agent used, are shown in Table 1. Average age of study population was 54.89 ± 11.19 years. TIMI 3 flow was present in 37% (n = 37) patients while 33% (n = 35) patients achieved TIMI 3 grade. Among patients thrombolysed with streptokinase, TIMI-3 flow was established in 53% (n = 19) patients and among patients thrombolysed with reteplase, TIMI 3 flow was present in relatively higher number of patients i.e. 41.5% (n = 17). Combined TIMI 2/3 flow rates were 93.2% and 85.4% with streptokinase and reteplase respectively. Similar trends were present in relation to the TMP grade, although these differences were statistically insignificant. Out of 41 patients thrombolysed with Reteplase, mortality was reported in 2.4% (n = 1) patients in comparison to Streptokinase with mortality rates of 3.4% (n = 2). In our study, patients with TIMI 3 flow were younger and had lesser duration of symptoms before presentation to the hospital than the patients with TIMI flow less than 3. Other characteristics and predictors of TIMI flow rates are detailed in Table 2.

### 4. Discussion

In this study, TIMI-3 flow rates and TMP-3 grades were reported in higher proportion of patients thrombolysed with reteplase as compared to streptokinase. However, these differences were statistically insignificant, and lack of significance could reflect insufficient study size to detect such a difference. Overall TIMI-3 flow rates as well as combined TIMI 2/3 flow rates were significantly higher than prior studies which were lacking in optimal antithrombotic therapies as evident from the data shown in Table 3.11–15 This synergistic effect of antithrombotic therapies with thrombolysis improves outcomes in STEMI in terms of coronary artery patency. However, one should keep in mind, the potential imbalances in infarct-artery location as suggested by the study results shown in Table 3.11–15

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**Table 1**

Baseline characteristics of patients in relation to the thrombolytic agent used.

| CHARACTERISTICS          | Overall       | Streptokinase (n = 59) | Reteplase (n = 41) | P-Value |
|--------------------------|---------------|-----------------------|-------------------|---------|
| Mean age                 | 54.89 ± 11.19 | 54.76 ± 10.89         | 55.07 ± 11.76     | 0.892   |
| Angina duration*         |               |                       |                   |         |
| Upto 3 h                 | 38% (n = 38)  | 30.5% (n = 18)        | 48.8% (n = 20)    | 0.064   |
| <6 h                     | 75% (n = 75)  | 71.2% (n = 42)        | 80.5% (n = 33)    | 0.361   |
| 6–12 h                   | 23% (n = 23)  | 25.4% (n = 15)        | 19.5% (n = 8)     |         |
| >12 h                    | 2% (n = 2)    | 3.4% (n = 2)          | 0% (n = 0)        |         |
| Mean angina duration (h) | 5.16 ± 3.99   | 5.71 ± 4.51           | 4.37 ± 2.99       | 0.098   |
| Door-to-needle time (min)| 20 ± 16.22    | 21.61 ± 16.54         | 18.17 ± 15.72     | 0.299   |
| Relief of chest pain     | 74% (n = 74)  | 72.85% (n = 43)       | 75.6% (n = 31)    | 0.760   |
| ECG settling             | 70% (n = 70)  | 66.2% (n = 39)        | 75.6% (n = 31)    | 0.308   |
| Reperfusion arrhythmias  | 14% (n = 14)  | 8.5% (n = 5)          | 21.9% (n = 9)     | 0.056   |
| Killip class             |               |                       |                   |         |
| KC-I                     | 83% (n = 83)  | 81.4% (n = 48)        | 85.4% (n = 35)    | 0.163   |
| KC-II                    | 6% (n = 6)    | 8.5% (n = 5)          | 2.4% (n = 1)      |         |
| KC-III                   | 8% (n = 8)    | 5.1% (n = 3)          | 12.2% (n = 5)     |         |
| KC-IV (Cardiogenic shock)| 3% (n = 3)    | 5.1% (n = 3)          | 0% (n = 0)        |         |
| Guideline-based medications|            |                       |                   |         |
| ACEIs                    | 85% (n = 85)  | 84.7% (n = 50)        | 85.4% (n = 35)    | 0.932   |
| β-Blocker                | 89% (n = 89)  | 89.8% (n = 53)        | 87.8% (n = 36)    | 0.750   |
| Complications            |               |                       |                   |         |
| Access site hematoma     | 1% (n = 1)    | 0% (n = 0)            | 2.4% (n = 1)      | 0.498   |
| Bleeding                 | 2% (n = 2)    | 3.4% (n = 2)          | 0% (n = 0)        |         |
| Heart failure            | 3% (n = 3)    | 3.4% (n = 2)          | 2.4% (n = 1)      |         |
| Others (Shivering)       | 1% (n = 1)    | 1.7% (n = 1)          | 0% (n = 0)        |         |
| Cag timing after thrombolysis|          |                       |                   |         |
| 3–24 h                   | 53% (n = 53)  | 52.5% (n = 31)        | 53.6% (n = 22)    | 0.136   |
| >24–48 h                 | 27% (n = 27)  | 20.3% (n = 12)        | 36.6% (n = 15)    |         |
| >48–72 h                 | 6% (n = 6)    | 8.5% (n = 5)          | 2.4% (n = 1)      |         |
| >72 h                    | 14% (n = 14)  | 18.6% (n = 11)        | 7.3% (n = 3)      |         |
| TIMI-3 Flow              | 37% (n = 37)  | 33.8% (n = 20)        | 41.5% (n = 17)    | 0.441   |
| TMP-3 Grade              | 35% (n = 35)  | 33.8% (n = 20)        | 36.6% (n = 15)    | 0.782   |
| LVEF                     |               |                       |                   |         |
| <40%                     | 17% (n = 17)  | 23.8% (n = 15)        | 5.4% (n = 2)      | 0.048   |
| 40–<50%                  | 32% (n = 32)  | 31.7% (n = 20)        | 32.4% (n = 12)    |         |
| 50% or more              | 51% (n = 51)  | 44.4% (n = 28)        | 62.2% (n = 23)    |         |

Abbreviations: KC- Killip class; TIMI- Thrombolysis in Myocardial Infarction; TMP- TIMI Myocardial Perfusion; CAG- Coronary angiography; ACEIs- Angiotensin converting enzyme inhibitors; LVEF- Left ventricular ejection fraction.

* Angina duration- Represents time interval between onset of symptoms to presentation to casualty.
antithrombotic therapy for STEMI patients in contemporary primary PCI era when resource constraints exist.

5. Conclusion

This study reiterates the utility of thrombolysis in resource limited settings where mechanical reperfusion for STEMI cannot be performed in a timely manner. The outcomes are better as compared with historical controls when routine treatment with heparin and dual antiplatelet agents is given in conjunction with fibrinolysis. Thus, our study supports the pharmaco-invasive strategy for STEMI with fibrinolysis in conjunction with routine loading with dual antiplatelet therapy and anticoagulant and subsequent invasive assessment and PCI if needed, in areas where significant healthcare resource and infrastructure constraints exist.

Declaration of competing interest

None declared.

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