TIMI (Thrombolysis in Myocardial Infraction) flow grade in ST Elevation Myocardial Infarction after Primary Percutaneous Intervention

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ABSTRACT

Background: Timely reperfusion, preferably by primary percutaneous intervention (PCI) has been the guiding-principle for the treatment of patients with acute ST-elevation myocardial infarction (STEMI). TIMI flow grade of the culprit lesion after the procedure have shown to have significant implication in clinical outcome.

Objective: We aimed to study the relation of TIMI flow grade with the in-hospital outcome and complication among patients of STEMI.

Methods: All consecutive acute STEMI patients undergoing primary PCI during the study period (January 2020 to June 2020) were analyzed for correlation between TIMI flow grade and clinical outcome during the hospital stay. Prior approval was taken from institutional review board. The study design was retrospective observational study.

Result: 51(55%) patients had achieved the TIMI 3 flow after the primary PCI. Number of patients achieving TIMI flow of 2,1 and 0 after the procedure were 34(37%),6(6.5%) and 2(2%). Incidence of traditional risk factors like dyslipidemia, diabetes, hypertension was higher in TIMI flow ≤ 2 . TIMI flow ≤ 2 was also associated with more adverse events namely cardiogenic shock, arrythmias, in-hospital mortality and overall major adverse cardiovascular events.

Conclusion: Patients with dyslipidemia had poor TIMI flow grade during primary PCI. Similarly, patients having hypertension, diabetes mellitus and late presentation showed tendency for TIMI flow ≤ 2 . Also, the poor TIMI flow grade after primary PCI had unfavorable the clinical outcomes like increased complications and mortality.

Keywords: Primary percutaneous intervention (PCI), ST elevation MI (STEMI), TIMI flow grade

INTRODUCTION

Reperfusion therapy has been the cornerstone for the treatment of patients with acute ST-elevation myocardial infarction (STEMI). Primary percutaneous coronary intervention (PCI) is currently the method of choice and the best reperfusion strategy for patients presenting with STEMI. It has persistently shown to reduce cardiac mortality and re-infarction over the last decades.[1,2] Timely reperfusion of the infarct-related coronary artery using fibrinolysis or PCI is central to optimal STEMI treatment. [3-5]

The benefits of reperfusion therapy have been attributed to the prompt reestablishment of normal blood flow in the infarct-related artery, defined as thrombolysis in myocardial infarction (TIMI) 3 flow. TIMI flow grades have significant prognostic implication among patients undergoing reperfusion therapy for STEMI.[6-9] The TIMI Coronary flow grading is an effective and well-studied grading system of coronary reperfusion on angiogram. Achieving earlier TIMI grade 3 flow has been correlated with improved survival in both reperfusions with thrombolysis or primary percutaneous coronary intervention (PCI) and can also stratify patients at low to high risk for mortality and other complications post-STEMI. TIMI flow grading has proven a useful tool in patients with acute MI and is used routinely in clinical practice.[10,11] Because of its significant relevance to the overall outcomes, multiple investigations have focused on describing risk factors and strategies to minimize TIMI flow grades 0 to 2 following reperfusion.

The primary objective of the study is to evaluate the clinical outcome and major cardiovascular complications at index hospitalization in the patients of acute STEMI undergoing primary PCI with or without re-established TIMI 3 flow in infarct related artery. We also aimed to investigate correlation of TIMI flow grade with various variables like complexities of coronary lesion, diabetes, age and left ventricular ejection fraction. We hope that our data would help to identify and predict high risk STEMI patients and appropriate measures can be planned to optimize the reperfusion therapy. We can translate this knowledge for the better management of STEMI patients in the context resources poor situation like Nepal.

MATERIALS AND METHODS

The current study was hospital based, retrospective observational study. Data from consecutive patients admitted between 1st January 2020 and 30 June 2020 treated with primary PCI for acute STEMI in Shahid Gangalal National Heart Centre (SGNHC) were included in the study. Prior approval was taken from the institutional review board of SGNHC. The acute STEMI patients with no coronary intervention or unavailable data were excluded from the study. Also, STEMI patients with attempted PCI (inability to pass coronary wire across culprit lesion) were not included in the study. Acute STEMI was defined as per fourth universal definition of myocardial infarction.[12]

All interventions were performed according to current standard guidelines. Patients received 300 mg aspirin orally, 300 to 600mg clopidogrel and a weight adapted dose of intravenous heparin during the procedure as per hospital protocol. Other medications, including betablockers, ACE inhibitors, nitrates, statins were administered at the discretion of the treating physician.

The antegrade radiocontrast flow of the infarct-related artery was determined on the final coronary angiography of the patient by the use of TIMI flow criteria. The TIMI flow grades were defined as follows:[13,14]

Grade 0 (no perfusion): There is no antegrade flow beyond the point of occlusion.

Grade 1 (penetration without perfusion): The contrast material passes beyond the area of obstruction but "hang up" and fail to opacify the entire coronary bed distal to the obstruction for the duration of the cineangiographic filming sequence.

Grade 2 (partial perfusion): The contrast material passes across the obstruction and opacifies the coronary bed distal to the obstruction but the rate of clearance from the distal bed are perceptibly slower than its entry into or clearance from comparable areas not perfused by the previously occluded vessel.

Grade 3 (complete perfusion): Antegrade flow into the bed distal to the obstruction occurs as promptly as antegrade flow into the bed proximal to the obstruction, and clearance of contrast material from the involved bed is as rapid as clearance from an uninvolved bed in the same vessel or the opposite artery.

Thrombus burden(TB) was also calculated according to previous studies.[15] TB was graded (G) as G0 = no thrombus, G1 = possible thrombus, G2 = small [greatest dimension ≤ 1/2 vessel diameter (VD)], G3 = moderate (> 1/2 but < 2VD), G4 = large

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(≥ 2VD), G5 = unable to assess TB due to vessel occlusion. Patients with G5 were reclassified to a thrombus category after flow achievement either with a guidewire or a small (1.5 mm) balloon.

The incidence of major adverse cardiac events (MACE) was compared in relation with TIMI flow. MACE was defined in our study as in hospital mortality, re-infarction and infarct-related artery revascularization, stroke and development of cardiac failure requiring inotropic support.[16] Individual adverse events studied were in-hospital outcomes, mechanical complications(like acute mitral regurgitation, ventricular septal rupture, cardiac rupture), electrical complications (like sustained ventricular tachycardia/fibrillation, atrial fibrillation, brady-arrythmia requiring temporary pacemakers) and reinfarction/reintervention.

Statistical analysis

Data analysis was performed using Statical package for Social Sciences SPSS (Version 16.0, SPSS Inc, Chicago, IL). Continuous variables were expressed as mean $\pm$ SD whereas categorical data were expressed in frequency and percentages. Chi square test or Fischer exact test was used to analyze the categorical data whichever applicable. Differences in continuous variables will be analyzed using the Student's t test. P-values < 0.05 was considered statistically significant.

RESULTS

Total of 93 patients of acute STEMI who underwent primary PCI were analyzed during the study period. Out of 93 patients, 51(55%) patients had achieved the TIMI 3 flow after the primary PCI. Number of

Table 1: Baseline characteristics of patients undergoing primary PCI

Variables	TIMI flow = 3	TIMI flow ≤ 2	p-value
Delayed arrival (>12 hrs)	7(16%)	5(9.8)	0.39
Hypertension	18(35%)	22(52)	0.06
Diabetes	15(29%)	13(31)	0.76
Dyslipidemia	4(8%)	9(21)	0.04
Known ASCVD*	4(8%)	3(7)	0.94
Current tobacco smoker	15(29%)	6(14)	0.10
Family history of CAD**	3(6%)	4(10)	0.94

*ASCVD: Atherosclerotic Cardiovascular Disease, **CAD: coronary artery disease

Table 2: Clinical status of patients at presentation

Killip Class	TIMI flow = 3	TIMI flow ≤ 2	p-value
Class 1	40(78%)	25(60%)	0.1
Class 2	12(23%)	9((21%)	0.513
Class 3	0(0%)	5(14%)	NA
Cardiogenic shock requiring hemodynamic support	0(0%)	2((5%)	NA
DAPT* received at first medical contact outside	46(90%)	38(90%)	

*DAPT: dual antiplatelets

patients achieving TIMI flow of 2,1 and 0 after the procedure were 34(37%), 6(6.5%) and 2(2%). Mean age of patients that achieved TIMI flow 3 and TIMI flow ≤ 2 were 58 ± 11.5years and 57 ± 13 years respectively.

In TIMI flow 3 group, 84% of the patients were male whereas in TIMI flow ≤2, 66% of the patients were male (p value 0.105).

Baseline characteristics of the patients are presented in table 1. There was statistically higher incidence of dyslipidemia in patients with TIMI flow ≤2. Compared to the patients achieving TIMI 3 flow, the patients with TIMI ≤ 2 were more likely to be diabetic, hypertensive and delayed presentation though not statistically significant. Surprisingly,

Table 3: Angiographic data of patients in relation to TIMI flow grade

Variables	TIMI flow=3	TIMI flow ≤ 2
Left anterior descending	28(54)	26(64)
Right coronary	19(37)	12((29)
Left circumflex	5(10)	3(7)
Left main	0(0)	1(2)
No of coronary arteries with significant lesion		
SVD	28(59)	20(48)
DVD	18(35)	6(15)
TVD	6(12)	15(37)
Thrombus Burden		
Low burden (grade 0, 1, 2)	44(86)	35(69)
High burden (grade 3, 4)	7(14)	7((17)

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Table 4: In-hospital clinical outcome of the patients

Variables	TIMI flow =3	TIMI flow ≤ 2	P-value
Cardiogenic shock/need of ionotropic support	4(8%)	11(26%)	0.017
Mechanical complication	5(10%)	6(14%)	0.5
Electrical complication	3(6%)	8(19%)	0.05
Reinfarction / Reintervention	1(2%)	4(10%)	0.1
Mortality	0(0%)	7(17%)	0.002
Any MACE	11(26%)	20(48%)	0.008

percentage of smokers in TIMI 3 flow were more but it was also not statistically significant. We also found patients with TIMI flow ≤2 was more likely to have higher killip class. Two patients presented in cardiogenic shock in this group

The angiographic parameters are also different between two groups (table 3). Triple vessel disease was more common in patients in TIMI flow ≤2(37% vs 12%) whereas patients with TIMI 3 were more likely to have single vessel disease (59% vs 48%) or double vessel disease (35% vs 15%).

The patients with TIMI ≤2 had more adverse in-hospital outcomes as mentioned in table 4. The incidence of major adverse cardiac events (MACE) – as defined in our study previously was significantly higher in patients with TIMI flow ≤2 (p=0.008). Similarly, when we analyzed individual adverse outcomes, the study found that incidence of cardiogenic shock, electrical complications and mortality were statistically higher in patients with TIMI flow ≤2.

DISCUSSION

As primary PCI is becoming more accessible for acute STEMI patients, the assessment of procedural success including like TIMI flow grade and other objective assessments are increasingly being recognized. No reflow and TIMI ≤ 2 flow is a condition with possible multi-factorial mechanisms, like microvascular damage or spasm, capillary plugging, distal embolization, residual stenosis, dissection, increased thrombus burden .[17]

The previous studies have identified various factors like TIMI 0 flow at initial angiography, anterior myocardial infarction, increased blood sugar level as predictors of TIMI ≤2.[18] In our study also, we find various risk factors were associated with poor TIMI flow after the primary PCI. Incidence of dyslipidemia was significantly higher and there was trend towards higher incidence of hypertension, diabetes and delayed presentation with post procedure TIMI ≤2. Kammler et al[19] found four independent predictors of TIMI ≤2 namely prehospital thrombolytic therapy, cardiogenic shock, three vessel disease, and diabetes mellitus and most powerful predictors being cardiogenic shock and three vessel disease. Prehospital thrombolytic therapy and diabetes mellitus were also associated with a higher probability of a TIMI ≤2.

Similarly, post procedure TIMI flow also corelates with clinical outcomes. Metha et al[20] found patients with TIMI ≤2 were more likely to have experienced an adverse event during the procedure. The incidence of sustained hypotension, requirement for endotracheal intubation or cardio-pulmonary resuscitation, and death was more common in this group of patients during primary PCI. The increased complications in the catheterization laboratory were further reflected in the higher rates of virtually all adverse events seen during hospital stay in patients with TIMI 2 flow, resulting in longer length of stay in these patients. Our study also found that that incidence of MACE was significantly higher in TIMI flow ≤2. There was also association of post procedural TIMI flow and mortality, arrythmias and cardiogenic shock.

Thus, our findings underscore the importance of preventing the development of low TIMI flow score and to utilize optimal strategy to improve outcomes and decrease resources utilization in patients. However further studies larger scale are warranted to definitely identify the strength of adverse factors and low post procedure TIMI flow grade. In this way, we can stratify the patients in different risk group, anticipate the complications and outcome. Finally, we can plan beforehand to improve the final outcome of the PCI and increase survival of the patients.

The main limitation of our study is that it was a retrospective observational study. There may be unknown confounding factors that may have effect the results. The sample size was also relatively small. So, the study might not have adequate power to differentiate the outcome of different variables in

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relation to TIMI flow.

CONCLUSION

Our study showed dyslipidemia was associated poor TIMI flow grade during primary PCI. Similarly, various baseline risk factors like hypertension, diabetes mellitus and late presentation showed tendency for TIMI flow ≤ 2 though not statistically significant. The study also found TIMI flow ≤ 2 during the procedure were more likely to have increased complications and mortality. Hence, we recommend appropriate measures to be taken for the good TIMI flow after the primary percutaneous intervention.

REFERENCES

1. Grines CL, Browne KF, Marco J, Rothbaum D, Stone GW, O'Keefe J, Overlie P, Donohue B, Chelliah N, Timmis GC, Vlietstra RE. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. New England Journal of Medicine. 1993;328(10):673-9. https://doi.org/10.1056/NEJM199303113281001 [Pubmed] [Google Scholar]

2. Boersma E, Mercado N, Poldermans D, Gardien M, Vos J, Simoons ML. Acute myocardial infarction. The Lancet. 2003;361(9360):847-58. https://doi.org/10.1016/S0140-6736(03)12712-2 [Pubmed] [Google Scholar]

3. Boden WE, Eagle K, Granger CB. Reperfusion strategies in acute ST-segment elevation myocardial infarction: a comprehensive review of contemporary management options. Journal of the American College of Cardiology. 2007;50(10):917-29. https://doi.org/10.1016/j.jacc.2007.04.084, [Pubmed] [Google Scholar]

4. Pohlen M, Bunzemeier H, HusemannW, Roeder N, Breithart G, Reinecke H (2008) Risk predictors for adverse outcomes after percutaneous coronary interventions and their related costs. Clin Res Cardiol 97(7):441–448. https://doi.org/10.1007/s00392-008-0647-8 [Pubmed] [Google Scholar]

5. Ribichini F, Ferrero V, Wijns W. Reperfusion treatment of ST-elevation acute myocardial infarction. Progress in cardiovascular diseases. 2004;47(2):131-57 https://doi.org/10.1016/j.pcad.2004.07.007 [Pubmed] [Google Scholar]

6. Mehta RH, Harjai KJ, Cox D, Stone GW, Brodie B, Boura J, O'Neill W, Grines CL, Primary Angioplasty in Myocardial Infarction (PAMI) Investigators. Clinical and angiographic correlates and outcomes of suboptimal coronary flow inpatients with acute myocardial infarction undergoing primary percutaneous coronary intervention. Journal of the American College of Cardiology. 2003;42(10):1739-46. https://doi.org/10.1016/j.jacc.2003.07.012 [Pubmed] [Google Scholar]

7. Mehta RH, Harjai KJ, Stone GW, Boura J, O'Neill W, Grines CL. Prognostic significance of transient no-reflow during primary percutaneous coronary intervention for ST elevation acute myocardial infarction. Am J Cardiol 2003;92:1445–7. https://doi.org/10.1016/j.amjcard.2003.08.056

8. Kenner MD, Zajac EJ, Kondos GT, Dave R, Winkelmann JW, Joftus J, Laucevicius A, Kybarskis A, Berukstis E, Urbonas A, Feinstein SB. Ability of the no-reflow phenomenon during an acute myocardial infarction to predict left ventricular dysfunction at one-month follow-up. The American journal of cardiology. 1995;76(12):861-8. https://doi.org/10.1016/S0002-9149(99)80250-1 [Pubmed] [Google Scholar]

9. Ito H, Maruyama A, Iwakura K, et al. Clinical implications of "no-reflow" phenomenon: a predictor of complications and left ventricular remodeling in perfused anterior wall infarction. Circulation 1996; 93:223– 8. https://doi.org/10.1161/01.CIR.93.2.223 [Pubmed] [Google Scholar]

10. Sun B, Liu J, Yin H, Yang S, Liu Z, Chen T, Li J, Guo C, Jiang Z. Delayed vs. immediate stenting in STEMI with a high thrombus burden. Herz. 2019 ;44(8):726-34. https://doi.org/10.1007/s00059-018-4699-x [Pubmed] [Google Scholar]

11. Bulluck H, Hammond-Haley M, Weinmann S, Martinez-Macias R, Hausenloy DJ. Myocardial Infarct Size by CMR in Clinical Cardioprotection Studies: Insights From Randomized Controlled Trials. JACC Cardiovasc Imaging. 2017;10(3):230-240 https://doi.org/10.1016/j.jcmg.2017.01.008 [Pubmed] [Google Scholar]

12. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD, Mickley H, Crea F, Van de Werf F, Bucciarelli-Ducci C. Fourth universal definition of myocardial infarction. European heart journal. 2019;40(3):237-69. https://doi.org/10.1016/j.jacc.2018.08.1038 [Pubmed] [Google Scholar]

13. The TIMI Study Group (1985) The thrombolysis in myocardial infarction(TIMI) trial. NEJM 312(Suppl):932–936. https://doi.org/10.1056/NEJM198504043121437 [Pubmed] [Google Scholar]

14. Sarkar A, Grigg WS, Lee JJ. TIMI grade flow. StatPearls [Internet]. 2020 Aug 16. https://www.ncbi.nlm.nih.gov/books/NBK482412/ [Pubmed] [Google Scholar]

15. Sianos G, Papafaklis MI, Serruys PW. Angiographic thrombus burden classification in patients with ST-segment elevation myocardial infarction treated with percutaneous coronary intervention. Journal of invasive cardiology. 2010;22(10):6B-14B. [Pubmed] [Google Scholar]

16. Poudel I, Tejpal C, Rashid H, Jahan N. Major Adverse Cardiovascular Events: An Inevitable Outcome of ST-elevation myocardial infarction? A Literature Review. Cureus. 2019;11(7):e5280. https://doi.org/10.7759/

https://doi.org/10.46405/ejms.v3i1.299

Tamrakar et al. TIMI flow grade in STEMI ...

cureus.5280 [Pubmed] [Google Scholar]

17. Ito H, Maruyama A, Iwakura K, et al. Clinical implications of 'no-reflow'phenomenon: a predictor of complications and left ventricular remodeling in perfused anterior wall infarction. Circulation 1996; 93:223–8. https://doi.org/10.1161/01.CIR.93.2.223 [Pubmed] [Google Scholar]

18. Elakabawi K, Huang X, Shah SA, Ullah H, Mintz GS, Yuan Z, Guo N. Predictors of suboptimal coronary blood flow after primary angioplasty and its implications on short-term outcomes in patients with acute anterior STEMI. BMC Cardiovascular Disorders. 2020; 20(1):1-2.https://doi.org/10.1186/s12872-020-01673 [Pubmed] [Google Scholar]

19. Kammler J, Kypta A, Hofmann R, Kerschner K, Grund M, Sihorsch K, Steinwender C, Lambert T, Helml W, Leisch F. TIMI 3 flow after primary angioplasty is an important predictor for outcome in patients with acute myocardial infarction. Clin Res Cardiol. 2009;98(3):165-70. https://doi.org/10.1007/s00392-008-0735-9 [Pubmed] [Google Scholar]

20. Mehta RH, Harjai KJ, Cox D, Stone GW, Brodie B, Boura J, O'Neill W, Grines CL; Primary Angioplasty in Myocardial Infarction (PAMI) Investigators. Clinical and angiographic correlates and outcomes of suboptimal coronary flow inpatients with acute myocardial infarction undergoing primary percutaneous coronary intervention. J Am Coll Cardiol. 2003; 42(10):1739-46. https://doi.org/10.1016/j.jacc.2003.07.012 [Pubmed] [Google Scholar]

21. Gitt AK, Bauer T, Zahn R, Zeymer U, Hamm C. Non-achievement of TIMI-3-flow results in significant increase in hospital mortality of primary PCI for STEMI and PCI for NSTE-ACS-findings of the Euro Heart survey PCI-registry. European Heart Journal. 2013;34(suppl_1):109. https://doi.org/10.1093/eurheartj/eht307.109 [Pubmed] [Google Scholar]

22. Caixeta A, Lansky AJ, Mehran R, Brener SJ, Claessen B, Genereux P, et al. Predictors of suboptimal TIMI flow after primary angioplasty for acute myocardial infarction: results from the HORIZONS-AMI trial. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2013;9(2):220-7. https://doi.org/10.4244/EIJV9I2A37 [Pubmed] [Google Scholar]

23. Vichova T, Maly M, Ulman J, Motovska Z. Mortality in patients with TIMI 3 flow after PCI in relation to time delay to reperfusion. Biomedical Papers. 2016;160(1):118-24. https://doi.org/10.5507/bp.2015.015 [Pubmed] [Google Scholar]