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Pre-Percutaneous Coronary Intervention TIMI Flow Grade in STEMI Patients Treated with Pre-Hospital Ticagrelor Loading

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Abstract

Aim

We hypothesised that pre-hospital ticagrelor loading would result in a higher proportion of STEMI patients presenting with pre percutaneous coronary intervention TIMI flow grade (ppTFG) 3 than had previously been reported in the clopidogrel era.

Methods

Retrospective observational analysis of all STEMI patients attending our centre from 01/01/2016 to 31/12/2019. Patients presenting with STEMI were required to have received pre-hospital loading with 180 mg ticagrelor. The coronary angiography images were assessed for each patient to determine the ppTFG in the infarct related artery.

Results

590 patients met the inclusion criteria. 125 patients (21.2%) presented with ppTFG 3 on pre-PCI angiography with the remaining 465 patients (78.8%) presenting with ppTFG ≤ 2. In-hospital mortality was comparable between the two groups (4% vs 5.6%, p=0.48).

Conclusion

In STEMI patients loaded with ticagrelor in the field, over one-fifth present with ppTFG 3 on angiography pre-PCI. This data is comparable to data from the clopidogrel era.

Introduction

For patients presenting with ST elevation myocardial infarction (STEMI), primary percutaneous coronary intervention (PPCI) is the recommended treatment[1]. While $P2Y_{12}$ inhibitor therapy is recommended for all patients presenting with STEMI, there is limited evidence with respect to the timing of $P2Y_{12}$ inhibitor initiation. In Ireland, ticagrelor is now commonly used as a P2Y12 inhibitor for pre-hospital loading of STEMI patients.

Ticagrelor has a fast onset of action, with a peak effect at about 1.5 hours and has been shown to demonstrate more potent anti-thrombotic effects compared to clopidogrel[2,3]. In light of this increased anti-thrombotic potency, we hypothesised that the use of pre-hospital ticagrelor loading would result in a higher proportion of STEMI patients presenting with pre percutaneous coronary intervention TIMI (Thrombolysis in Myocardial Infarction) flow grade (ppTFG) 3 than has previously been reported in the literature from the clopidogrel era. The TFG is a widely used method for the assessment of coronary artery flow in acute coronary syndromes and ppTFG 3 has been reported to be an independent predictor of mortality in patients with ACS[4].

We conducted the current analysis, with the primary objective of defining the proportion of unselected STEMI patients presenting with ppTFG 3 on angiography after pre-hospital loading with ticagrelor.

Methods

This retrospective observational analysis was vetted and approved by the University Hospital Limerick (UHL) research and ethics committee. Data was extracted from our comprehensive electronic database of all STEMI presentations to our centre. We screened all patients presenting with STEMI from 01/01/2016 to 31/12/2019.

To be included in this analysis, patients presenting with STEMI were required to have received pre-hospital loading with 180 mg ticagrelor. The coronary angiography images were assessed for each patient to determine the ppTFG in the infarct related artery. The TIMI (Thrombolysis in Myocardial Infarction) flow grade was classified as grade 0 (no flow), grade 1 (penetration without perfusion), grade 2 (partial perfusion) or grade 3 (complete perfusion). For the purposes of this analysis, patients were classified as presenting with ppTFG 3 or ppTFG ≤ 2. Cardiovascular risk factors, ECG to wire time and in-hospital mortality was also scrutinised.

Results

Over the study period, 590 patients met the inclusion criteria and were included in our analysis. 125 patients (21.2%) presented with ppTFG 3 on pre-PCI angiography with the remaining 465 patients (78.8%) presenting with ppTFG ≤ 2.

The characteristics and in-hospital mortality for the two groups are summarised in **Table 1**. Patients presenting with ppTFG 3 had a longer positive ECG to wire time on average (101±34mins vs 92±44mins, p=0.04). However, the effect size was small (Hedges' g=0.21) and logistic regression analysis did not show a statistically significant relationship between increase in ECG to wire time and TIMI 3 flow at pre-PCI angiography (odds ratio: 1.043, 95% CI: 0.99-1.01, p=0.06). In-hospital mortality was also comparable between the two groups (4% vs 5.6%, p=0.48).

Table 1. Baseline Characteristics and Mortality.

	ppTFG 3	**pTFG ≤2**	**p value**
N	125	465	-
Diabetes	12 (9.6%)	40 (8.6%)	0.73
Hypertension	28 (22.4%	89 (19.1%)	0.42
Dyslipidemia	24 (19.2%)	105 (22.6%)	0.41
Active Smoker	44 (35.2%)	153 (32.9%)	0.63
Previous PCI	14 (11.2%)	40 (8.6%)	0.37
Positive ECG to wire time (mins)	101.8±3.1	92.0±2.1	0.04
Mortality	5 (4.0%)	26 (5.6%)	0.48

Discussion

In Irish STEMI patients loaded with ticagrelor in the field, over one-fifth of patients presented with ppTFG 3 on coronary angiography. Patients with ppTFG 3 had a longer positive ECG to wire time on average (101±34mins vs 92±44mins, p=0.04). One potential hypothesis that could explain this finding is that an increased wire to ECG time provides more time for spontaneous reperfusion of the infarct related artery to occur. However, given the observational nature of this analysis, a causal relationship between ECG and wire time and ppTFG 3 cannot be determined and these data should be considered hypothesis generating. Mortality was comparable in patients with ppTFG 3 and ppTFG ≤ 2.

There is considerable variability in the reported proportion of STEMI patients who present with ppTFG 3 on coronary angiography. This may reflect the underlying heterogeneity of these studies, with previously published data including both data derived from clinical trials and real-world data on unselected STEMI presentations[4-6]. Data derived from a real-world STEMI registry[4] reported that 77.5% of STEMI patients presented with ppTFG 0/1, 14.5% with ppTFG 2 and only 8% with ppTFG 3.

In the ARMYDA-6 MI trial, 600 mg and 300 mg loading doses of clopidogrel were compared for patients presenting with STEMI[7]. The authors reported that 21% of patients in the 600 mg arm and 12% of patients in the 300 mg arm presented with ppTFG 2/3.

It is well reported that using ticagrelor for ACS treatment is cost-effective in reducing morbidity and mortality associated with STEMI[8-9]. There is concern however that twice daily dosing may lead to reduced compliance, however in the PLATO trial discontinuation was largely driven by non-serious adverse events [10]. Our study's limitations are the relatively small population size, it was observational and the patients from the literature cited were loaded in the centre performing PPCI, not in the field.

The observed proportion of STEMI patients presenting with ppTFG 3 in our study (~20%) is lower than that described in modern randomised controlled trials but compares favourably to previously published real world registry data from the clopidogrel loading era. These data do not suggest that pre-hospital loading with ticagrelor results in a higher proportion of STEMI patients presenting with ppTFG 3 on coronary angiography than has previously been reported in the clopidogrel era.

Declaration of Conflicts of Interest:
The authors report no relationships that could be construed as a conflict of interest.

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References:

1. B. Ibanez, S. James, S. Agewall, M.J. Antunes, C. Bucciarelli-Ducci, H. Bueno et al, ESC Scientific Document Group, 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC), *European Heart Journal*, Volume 39, Issue 2, 07 January 2018, Pages 119–177, https://doi.org/10.1093/eurheartj/ehx393
2. Zafar MU, Vorchheimer DA, Tewar MP, et al. Ticagrelor reduces thrombus formation more than clopidogrel, even when co-administered with bivalirudin. *Thromb Haemost*. 2014;112(5):1069-1070. doi:10.1160/TH14-03-0269

3. Zafar MU, Baber U, Smith DA, et al. Antithrombotic potency of ticagrelor versus clopidogrel in type-2 diabetic patients with cardiovascular disease. *Thromb Haemost*. 2017;117(10):1981-1988. doi:10.1160/TH17-04-0277
4. De Luca G, Ernst N, Zijlstra F, van 't Hof AW, Hoorntje JC, Dambrink JH, Gosslink AT, de Boer MJ, Suryapranata H. Preprocedural TIMI flow and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol. 2004 Apr 21;43(8):1363-7. doi: 10.1016/j.jacc.2003.11.042. PMID: 15093868.
5. M. C Nguyen, D.S. Pinto, C. Hochberg, A. Almahameed, Y. Pride, J.E Abraham et al, Abstract 3163: Association of Pre-PCI TIMI flow grade (TFG) with Subsequent Mortality in Patients Presenting with ST-Elevation Myocardial Infarction (STEMI) 22 Mar 2018 Circulation. 2007;116:II_710
6. M. Golomb, R. Wolny, Y. Liu, P. Smits, C. von Birgelen, B. Redfors, et al, TCT-499 Prognostic Implications of Pre-procedural TIMI Flow in Patients with STEMI Undergoing PCI with Drug-Eluting Stent Implantation Journal of the American College of Cardiology Volume 72, Issue 13 Supplement, September 2018 DOI: 10.1016/j.jacc.2018.08.1675
7. G. Patti, G. Bárczi, D. Orlic, F. Mangiacapra, G. Colonna, V. Pasceri et al, Outcome Comparison of 600- and 300-mg Loading Doses of Clopidogrel in Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: Results From the ARMYDA-6 MI (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty-Myocardial Infarction) Randomized Study, Journal of the American College of Cardiology, Volume 58, Issue 15, 2011, Pages 1592-1599, ISSN 0735-1097
8. Theidel U, Asseburg C, Giannitsis E, Katus H. Cost-effectiveness of ticagrelor versus clopidogrel for the prevention of atherothrombotic events in adult patients with acute coronary syndrome in Germany. Clinical Research in Cardiology. 2013 Jun;102(6):447-58.
9. Liew D, Lourenço RD, Adena M, Chim L, Aylward P. Cost-effectiveness of 12-month treatment with ticagrelor compared with clopidogrel in the management of acute coronary syndromes. Clinical therapeutics. 2013 Aug 1;35(8):1110-7.
10. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. New England Journal of Medicine. 2009 Sep 10;361(11):1045-57.