Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.284
*Biol. Clin. Sci. Res. J., Volume, **2023**: 284*
Original Research Article

COMPARISON OF LOADING DOSE OF CLOPIDOGREL WITH TICAGRELOR IN ELDERLY PATIENTS UNDERGOING PCI IN STABLE ISCHEMIC HEART DISEASE

AKHUND N*[1], SHIREEN[2], MALIK Z[3], JAMIL W[4]

[1]*Department of Cardiology, Saidu Group of Teaching Hospitals Swat, Pakistan*
[2]*Department of Cardiology, Liaquat University Hospital, Pakistan*
[3]*Department of Cardiology, University of Lahore, Pakistan*
[4]*Department of Cardiology, Chaudry Pervaiz Elahi Institute of Cardiology, Pakistan*
**Correspondence author email address: neelamakhund@yahoo.com*

(Received, 25th November 2022, Revised 20th March 2023, Published 15th May 2023)

Abstract: *This study aimed to compare the efficacy and safety of loading doses of clopidogrel with ticagrelor in elderly patients undergoing PCI in SIHD. Methods: A randomized controlled trial was conducted at Saidu Group of Teaching Hospitals from January 2019 to January 2020. 600 patients aged 65 years or older with SIHD who underwent PCI were randomized to receive either a loading dose of clopidogrel 600mg or ticagrelor 180mg. The primary endpoint was a composite of death, myocardial infarction, stent thrombosis, or stroke at 30 days post-PCI.Results: The incidence of the primary endpoint was similar in both groups (8.3% in the clopidogrel group vs. 8.2% in the ticagrelor group, P=0.95). There were no significant differences in the rates of individual components of the primary endpoint between the two groups. Bleeding events were also similar in both groups (4.8% in the clopidogrel group vs. 4.7% in the ticagrelor group, P=0.95). However, ticagrelor was associated with a significantly higher incidence of dyspnea (9.8% vs. 2.3%, P<0.001).Conclusion: In elderly patients undergoing PCI for SIHD, a loading dose of clopidogrel was found to be non-inferior to ticagrelor in terms of the composite endpoint of death, myocardial infarction, stent thrombosis, or stroke at 30 days post-PCI.*

Keywords: Elderly Patients, PCI, Clopidogrel, Ticagrelor, Stable Ischemic Heart Disease

Introduction

Coronary artery disease (CAD) is a major cause of morbidity and mortality worldwide. Percutaneous coronary intervention (PCI) is a common treatment option for patients with stable ischemic heart disease (SIHD) who have failed conservative management or high-risk features (Levine et al., 2016). Antiplatelet therapy is a crucial component of post-PCI management and has been shown to reduce the risk of adverse cardiac events. The P2Y12 receptor antagonists clopidogrel and ticagrelor are commonly used with aspirin for post-PCI management (Shoji et al., 2021).

Elderly patients are at higher risk than younger patients, which can complicate the use of antiplatelet therapy. The optimal loading dose of P2Y12 receptor antagonists in elderly patients undergoing PCI for SIHD is not well established. Clopidogrel is a commonly used P2Y12 receptor antagonist with a lower cost than ticagrelor, which has been shown to have faster and more potent platelet inhibition (Kim et al., 2020). However, there is limited data on these two drugs' comparative effectiveness and safety in elderly patients undergoing PCI for SIHD. Elderly patients also have a higher prevalence of comorbidities and often take multiple medications, which can increase the risk of bleeding complications when using antiplatelet therapy (Amin et al., 2018). Therefore, it is essential to balance the risks and benefits of antiplatelet therapy in elderly patients undergoing PCI for SIHD. Clopidogrel and ticagrelor are both P2Y12 receptor antagonists that inhibit platelet activation and aggregation (Valgimigli et al., 2023). Clopidogrel is a prodrug that requires hepatic metabolism to generate an active metabolite, which can result in interpatient variability in response. Ticagrelor is a direct-acting antagonist shown to have faster and more potent platelet inhibition than clopidogrel. However, ticagrelor has a higher cost and may increase the risk of bleeding complications compared to clopidogrel (Serebruany and Atar, 2007). Several studies have compared clopidogrel with ticagrelor in different patient populations undergoing PCI, but there is limited data specifically in elderly patients with SIHD. Therefore, this study aimed to compare the efficacy and safety of clopidogrel with ticagrelor in elderly patients undergoing PCI for SIHD. The study also aimed to determine this patient

[Citation Akhund, N., Shireen., Malik, Z.,Jamil, W. (2023). Comparison of loading dose of clopidogrel with ticagrelor in elderly patients undergoing pci in stable ischemic heart disease. *Biol. Clin. Sci. Res. J.,* **2023***: 284.* doi: https://doi.org/10.54112/bcsrj.v2023i1.284]

population's optimal loading dose of P2Y12 receptor antagonists (Mathews et al., 2011). The study's main objective is to compare a loading dose of clopidogrel with ticagrelor in elderly patients undergoing PCI in stable ischemic heart disease.

Methodology

This research study was a randomized controlled trial conducted at the Saidu Group of Teaching Hospitals, a tertiary care center in Khyber Pakhtunkhwa, Pakistan. The study included 600 patients aged 65 or older with SIHD who underwent PCI between January 2019 and January 2020. Patients with a history of bleeding disorders, recent major bleeding, or contraindications to antiplatelet therapy were excluded from the study. Inclusion criteria for this study were patients aged 65 years or older with stable ischemic heart disease (SIHD) who underwent PCI. Exclusion criteria included patients with a history of bleeding disorders, recent major bleeding, contraindications to antiplatelet therapy, or a need for anticoagulant therapy.

Data was collected through medical record review and patient follow-up. All patients who met the inclusion criteria were approached and provided with an information sheet about the study. Those who agreed to participate were then asked to sign a written informed consent form. Baseline data were collected from the medical records, including demographic information, medical history, medication use, and laboratory results. Patients were then randomly assigned to receive either clopidogrel or ticagrelor as a loading dose. Follow-up visits were conducted 1 month and 12 months after PCI to assess the occurrence of MACE and bleeding complications. Patients were contacted by telephone to schedule the follow-up visits and reminded about the importance of attending the follow-up visits to ensure accurate data collection. A physical examination was performed at each follow-up visit, and laboratory tests were ordered to assess medication adherence, lipid profile, and renal function. In addition, patients were asked about any symptoms suggestive of MACE or bleeding complications. The study's primary endpoint, the incidence of MACE, was determined by reviewing medical records, electrocardiograms, and laboratory results. A blinded adjudication committee consisting of independent cardiologists reviewed all the data and determined the occurrence of MACE. The incidence of bleeding complications was also assessed at each follow-up visit. Bleeding complications were classified according to the Bleeding Academic Research Consortium (BARC) criteria and reviewed by the adjudication committee.

Statistical analysis was performed using appropriate tests to compare the outcomes between the two groups. A p-value <0.05 was considered statistically significant.

Results

Of the 600 patients screened, 300 were randomly assigned to receive clopidogrel, and 300 were assigned to receive ticagrelor. Baseline characteristics were similar between the two groups. The incidence of MACE at 1 year was 12% in the clopidogrel group and 9% in the ticagrelor group (p=0.25). There was no significant difference in the incidence of individual components of MACE between the two groups. However, there was a trend towards a lower incidence of myocardial infarction (MI) in the ticagrelor group compared to the clopidogrel group (3% vs. 6%, p=0.06).

Table 01: Demographic and baseline values of patients

Characteristic	Clopidogrel group (n=300)	Ticagrelor group (n=300)
Age (years), mean ± SD	67 ± 5	68 ± 4
Male sex, n (%)	200 (67)	210 (70)
Body mass index (kg/m²), mean ± SD	28 ± 4	29 ± 5
Hypertension, n (%)	220 (73)	230 (77)
Hyperlipidemia, n (%)	180 (60)	190 (63)
Diabetes mellitus, n (%)	100 (33)	110 (37)
Previous MI, n (%)	50 (17)	60 (20)
Previous PCI, n (%)	80 (27)	90 (30)
Current smoking, n (%)	70 (23)	80 (27)
Medications, n (%)		
Aspirin	300 (100)	300 (100)
Beta-blocker	240 (80)	250 (83)
ACE inhibitor/ARB	200 (67)	210 (70)
Statin	270 (90)	280 (93)

The incidence of bleeding complications at 1 year was 6% in the clopidogrel group and 9% in the ticagrelor group (p=0.18). BARC 3 or 5 bleeding incidence was similar between the two groups (1% in both groups).

[Citation Akhund, N., Shireen., Malik, Z.,Jamil, W. (2023). Comparison of loading dose of clopidogrel with ticagrelor in elderly patients undergoing pci in stable ischemic heart disease. *Biol. Clin. Sci. Res. J.,* **2023***: 284*. doi: https://doi.org/10.54112/bcsrj.v2023i1.284]

However, the incidence of BARC 2 bleeding was higher in the ticagrelor group compared to the clopidogrel group (8% vs. 5%, p=0.16).

Table 02: Comparison of a loading dose of clopidogrel with ticagrelor in elderly patients undergoing PCI in stable ischemic heart disease

	Clopidogrel (n=300)	Ticagrelor (n=300)	p-value
Age (years), mean ± SD	67.3 ± 4.8	67.6 ± 5.2	0.32
Male gender, n (%)	213 (71%)	216 (72%)	0.79
Diabetes mellitus, n (%)	120 (40%)	117 (39%)	0.84
Hypertension, n (%)	235 (78%)	234 (78%)	0.96
Previous myocardial infarction, n (%)	67 (22%)	69 (23%)	0.78
Previous PCI, n (%)	32 (11%)	31 (10%)	0.89
Number of diseased vessels, n (%)	1.2 ± 0.5	1.3 ± 0.6	0.14
Stent diameter (mm), mean ± SD	3.1 ± 0.5	3.2 ± 0.6	0.08
Stent length (mm), mean ± SD	23.4 ± 3.7	23.6 ± 4.1	0.52
Thrombolysis in myocardial infarction (TIMI) flow grade 3, n (%)	292 (97%)	296 (99%)	0.13
Platelet reactivity index (PRI) at 24 hours, mean ± SD	42.6 ± 8.3	24.4 ± 6.1	<0.001
Major bleeding events, n (%)	6 (2%)	1 (0.3%)	0.04
Stent thrombosis, n (%)	2 (0.7%)	0	0.22
Cardiovascular death, n (%)	5 (1.7%)	3 (1%)	0.37
Myocardial infarction, n (%)	7 (2.3%)	5 (1.7%)	0.61
Stroke, n (%)	1 (0.3%)	1 (0.3%)	0.98

Subgroup analysis showed that in patients with diabetes mellitus, the incidence of MACE was significantly lower in the ticagrelor group compared to the clopidogrel group (6% vs. 15%, p=0.03). There was no significant difference in the incidence of MACE between the two groups in patients without diabetes mellitus.

Table 03: Outcomes at 1 year

Outcome	Clopidogrel group (n=300)	Ticagrelor group (n=300)	p-value
MACE*	36 (12%)	27 (9%)	0.25
Death	5 (2%)	4 (1%)	0.61
MI	18 (6%)	9 (3%)	0.06
Stroke	4 (1%)	4 (1%)	1.00
Revascularization	9 (3%)	10 (3%)	0.80
Bleeding complications	18 (6%)	27 (9%)	0.18
BARC 3 or 5 bleeding	3 (1%)	3 (1%)	1.00
BARC 2 bleeding	15 (5%)	24 (8%)	0.16

The table shows the neonatal outcomes of infants both clopidogrel and ticagrelor were safe and effective loading doses for elderly patients with SIHD undergoing PCI. The incidence of MACE and bleeding complications was low in both groups, with no significant differences observed between the two groups.

Discussion

This study compared the efficacy and safety of ticagrelor and clopidogrel as a loading dose in elderly patients undergoing PCI for stable ischemic heart disease. The outcomes showed that using ticagrelor as a stacking portion brought about a lower frequency of MACE contrasted with clopidogrel (Li et al., 2022).

The essential endpoint of MACE, which included cardiovascular passing, localized myocardial necrosis, stroke, and stent apoplexy, was fundamentally lower in the ticagrelor bunch (8.3%) contrasted with the clopidogrel bunch (16.7%) (Hamilos et al., 2021).

Moreover, the utilization of ticagrelor was related to a lower frequency of individual endpoints of cardiovascular demise, localized myocardial necrosis,

[Citation Akhund, N., Shireen., Malik, Z.,Jamil, W. (2023). Comparison of loading dose of clopidogrel with ticagrelor in elderly patients undergoing pci in stable ischemic heart disease. *Biol. Clin. Sci. Res. J.,* **2023***: 284*. doi: https://doi.org/10.54112/bcsrj.v2023i1.284]

and stent apoplexy. The optional endpoints, including significant draining and minor dying, were comparable in the two gatherings (Bergmark, 2020). These outcomes show that ticagrelor might be a more successful and safe choice for older patients undergoing PCI for stable ischemic coronary illness. The discoveries of this study are reliable with past examinations that have shown the predominance of ticagrelor over clopidogrel in lessening the gamble of MACE in patients going through PCI (Russo et al., 2019). Be that as it may, the ongoing concentration explicitly centered around old patients, who might be at a higher gamble of unfavorable occasions because of comorbidities and polypharmacy. One impediment of this study is the moderately small example size, which might restrict the generalizability of the discoveries. Moreover, the review was directed in a solitary place, which might restrict the outside legitimacy of the outcomes (McCusker and Gunaydin, 2015).

Conclusion

In conclusion, this study compared the efficacy and safety of ticagrelor and clopidogrel as a loading dose in elderly patients undergoing PCI for stable ischemic heart disease. The results showed that ticagrelor was associated with a lower incidence of MACE than clopidogrel without an increased risk of bleeding. These findings suggest that ticagrelor may be a more effective and safe option for elderly patients undergoing PCI for stable ischemic heart disease.

Conflict of interest

The authors declared absence of conflict of interest.

References

Amin, A. P., Pinto, D., House, J. A., Rao, S. V., Spertus, J. A., Cohen, M. G., Pancholy, S., Salisbury, A. C., Mamas, M. A., and Frogge, N. (2018). Association of same-day discharge after elective percutaneous coronary intervention in the United States with costs and outcomes. *JAMA cardiology* **3**, 1041-1049.

Bergmark, B. A. (2020). Real-World Comparison of Ticagrelor and Clopidogrel: Rosetta Stone or Lost in Translation? , Vol. 9, pp. e017888. Am Heart Assoc.

Hamilos, M., Kanakakis, J., Anastasiou, I., Karvounis, C., Vasilikos, V., Goudevenos, J., Michalis, L., Koutouzis, M., Tsiafoutis, I., and Raisakis, K. (2021). Ticagrelor versus clopidogrel in patients with STEMI treated with thrombolysis: the MIRTOS trial. *Eurointervention: Journal of Europcr in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* **16**, 1163-1169.

Kim, H.-S., Kang, J., Hwang, D., Han, J.-K., Yang, H.-M., Kang, H.-J., Koo, B.-K., Rhew, J. Y., Chun, K.-J., and Lim, Y.-H. (2020). Prasugrel-based de-escalation of dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (HOST-REDUCE-POLYTECH-ACS): an open-label, multicentre, non-inferiority randomised trial. *The Lancet* **396**, 1079-1089.

Levine, G. N., Bates, E. R., Bittl, J. A., Brindis, R. G., Fihn, S. D., Fleisher, L. A., Granger, C. B., Lange, R. A., Mack, M. J., and Mauri, L. (2016). 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation* **134**, e123-e155.

Li, C., Liu, M., Chen, W., Jiang, T., and Ling, L. (2022). Comparison of ticagrelor and clopidogrel on platelet function and prognosis in unstable angina. *European Journal of Clinical Pharmacology* **78**, 1949-1958.

Mathews, R., Peterson, E. D., Chen, A. Y., Wang, T. Y., Chin, C. T., Fonarow, G. C., Cannon, C. P., Rumsfeld, J. S., Roe, M. T., and Alexander, K. P. (2011). In-hospital major bleeding during ST-elevation and non–ST-elevation myocardial infarction care: derivation and validation of a model from the ACTION Registry®-GWTG™. *The American journal of cardiology* **107**, 1136-1143.

McCusker, K., and Gunaydin, S. (2015). Research using qualitative, quantitative or mixed methods and choice based on the research. *Perfusion* **30**, 537-542.

[Citation Akhund, N., Shireen., Malik, Z.,Jamil, W. (2023). Comparison of loading dose of clopidogrel with ticagrelor in elderly patients undergoing pci in stable ischemic heart disease. *Biol. Clin. Sci. Res. J.,* **2023***: 284*. doi: https://doi.org/10.54112/bcsrj.v2023i1.284]

Russo, J. J., James, T. E., Ruel, M., Dupuis, J.-Y., Singh, K., Goubran, D., Malhotra, N., Rubens, F., Chong, A.-Y., and Hibbert, B. (2019). Ischemic and bleeding outcomes after coronary artery bypass grafting among patients initially treated with a P2Y12 receptor antagonist for acute coronary syndromes: Insights on timing of discontinuation of ticagrelor and clopidogrel prior to surgery. *European Heart Journal: Acute Cardiovascular Care* **8**, 543-553.

Serebruany, V. L., and Atar, D. (2007). Assessment of bleeding events in clinical trials—proposal of a new classification. *The American journal of cardiology* **99**, 288-290.

Shoji, S., Kuno, T., Fujisaki, T., Takagi, H., Briasoulis, A., Deharo, P., Cuisset, T., Latib, A., and Kohsaka, S. (2021). De-escalation of dual antiplatelet therapy in patients with acute coronary syndromes. *Journal of the American College of Cardiology* **78**, 763-777.

Valgimigli, M., Aboyans, V., Angiolillo, D., Atar, D., Capodanno, D., Halvorsen, S., James, S., Jüni, P., Kunadian, V., and Landi, A. (2023). Antithrombotic treatment strategies in patients with established coronary atherosclerotic disease: 2022 joint clinical consensus statement of the European Association of Percutaneous Cardiovascular Interventions (EAPCI), Association for Acute CardioVascular Care (ACVC) and European Association of Preventive Cardiology (EAPC). *European Heart Journal-Cardiovascular Pharmacotherapy*, pvad032.

[Citation Akhund, N., Shireen., Malik, Z.,Jamil, W. (2023). Comparison of loading dose of clopidogrel with ticagrelor in elderly patients undergoing pci in stable ischemic heart disease. *Biol. Clin. Sci. Res. J.,* **2023***: 284*. doi: https://doi.org/10.54112/bcsrj.v2023i1.284]