PAKISTAN JOURNAL OF Cardiovascular Intervention

OPEN ACCESS

CASE REPORT

Ticagrelor-Induced Junctional Bradycardia Following Primary Percutaneous Coronary Intervention: A Clinically Significant and Reversible Adverse Effect

Sadaf Shabbir Kiani[1], Sana Munir[2], Laiba Ansari[2]

[1]Divisional Headquarters Teaching Hospital, Mirpur, AJK-Pakistan.

[2]Mohtarma Benazir Bhutto Shaheed Medcial College, Mirpur, AJK-Pakistan.

Citation:
Kiani SS, Munir S, Ansari L. Ticagrelor-Induced Junctional Bradycardia Following Primary Percutaneous Coronary Intervention: A Clinically Significant and Reversible Adverse Effect. PJCVI. 2025; 5(2): 74-79

Corresponding Author Email:
sadafkiani88@gmail.com

DOI: 10.58889/PJCVI.5.2.74.79

Funding:
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of Interests:
The authors declare no conflict of interest related to this publication.

Received 07/05/2025
Accepted 11/07/2025
First Published 01/12/2025

Abstract

Background: Ticagrelor, a potent and reversible P2Y12 receptor antagonist, is a cornerstone of dual antiplatelet therapy (DAPT) in patients with acute coronary syndromes (ACS). While generally well tolerated, ticagrelor has been associated with conduction abnormalities, often considered transient and clinically insignificant. However, emerging evidence suggests that clinically meaningful bradyarrhythmias may occur, particularly in high-risk populations.

Case Presentation: We report the case of a 75-year-old hypertensive male presenting with acute anterior ST-elevation myocardial infarction (STEMI), who underwent successful primary percutaneous coronary intervention (PCI) to the left anterior descending artery. Standard post-PCI therapy, including ticagrelor, was initiated. Within 30 hours, the patient developed syncope, hypotension, and electrocardiographically confirmed junctional bradycardia.

Management and Results: Initial management included withholding beta-blocker therapy; however, the bradyarrhythmia persisted beyond expected pharmacological effects. Ticagrelor was subsequently discontinued and replaced with clopidogrel. Following this intervention, normal sinus rhythm was restored within 36 hours, and the patient remained hemodynamically stable. No recurrence of bradyarrhythmia was observed during three months of follow-up.

Conclusion: This case highlights ticagrelor as a potential reversible cause of clinically significant junctional bradycardia in elderly patients following PCI. Recognition of this adverse effect is crucial to avoid unnecessary invasive interventions and to enable timely modification of antiplatelet therapy. Clinicians should maintain vigilance for bradyarrhythmias associated with ticagrelor, particularly in susceptible individuals.

Keywords

Ticagrelor, Junctional Bradycardia, Acute Coronary Syndrome, Percutaneous Coronary Intervention, Bradyarrhythmia

Introduction

Junctional bradycardia is a cardiac rhythm disorder characterized by a reduced heart rate (typically 40–60 beats per minute) originating from the atrioventricular (AV) node, usually as a compensatory response to impaired sinoatrial (SA) node function or atrial conduction abnormalities[1]. It may arise secondary to intrinsic cardiac pathology or as an adverse effect of pharmacological agents that suppress nodal activity[2].

Ticagrelor, a reversible P2Y12 receptor antagonist, is widely used as part of dual antiplatelet therapy (DAPT) in patients with acute coronary syndromes (ACS) undergoing percutaneous coronary intervention (PCI). While its superiority over clopidogrel has been demonstrated in the PLATO trial[3], emerging evidence suggests an association with bradyarrhythmias, likely mediated through adenosine-related mechanisms.

Although initially considered clinically insignificant, recent reports indicate that ticagrelor-induced conduction disturbances may have meaningful clinical consequences. This case highlights a clinically significant episode of junctional bradycardia temporally associated with ticagrelor initiation following primary PCI.

Patient Information

A 75-year-old male with a known history of hypertension (not on regular antihypertensive therapy) presented with acute onset chest pain lasting two hours. There was no history of diabetes mellitus, smoking, chronic kidney disease, or prior cardiovascular events. At presentation, the patient was hemodynamically stable with a blood pressure of 160/100 mmHg and heart rate of 85 beats per minute, classified as Killip class I.

Clinical Findings

Electrocardiography revealed extensive anterolateral ST-segment elevation involving leads V2–V6, I, and aVL, with reciprocal changes in inferior leads, consistent with acute anterior ST-elevation myocardial infarction (STEMI).

Following successful primary PCI to the left anterior descending artery, post-procedural ECG demonstrated satisfactory ST-segment resolution. Transthoracic echocardiography revealed preserved left ventricular systolic function with an estimated ejection fraction of approximately 45% and no baseline conduction abnormalities.

Approximately 30 hours post-intervention, the patient developed syncope associated with hypotension (80/50 mmHg) and junctional bradycardia. ECG findings demonstrated a narrow complex rhythm with retrograde P waves and a slow, regular ventricular rate, consistent with SA node suppression and AV junctional escape rhythm.

Timeline

The patient presented with acute STEMI and underwent immediate primary PCI with initiation of standard DAPT including ticagrelor. Within 30 hours of ticagrelor administration, symptomatic bradycardia developed. Initial management involved withholding beta-blocker (bisoprolol) and ACE inhibitor (ramipril), along with temporary hemodynamic support using noradrenaline.

Despite these measures, bradycardia persisted beyond 48 hours. Subsequently, ticagrelor was discontinued and replaced with clopidogrel, after which sinus rhythm was restored within 36 hours. The patient remained stable during hospitalization and follow-up over three months.

Diagnostic Assessment

The diagnosis of ticagrelor-induced junctional bradycardia was established based on clinical presentation, ECG findings, and temporal association with drug administration.

Differential diagnoses including ischemia-related conduction disturbances, electrolyte imbalance, and beta-blocker toxicity were systematically excluded. Electrolyte levels remained within normal limits. Although bisoprolol could contribute to bradycardia, its half-life of approximately 12 hours suggests that drug effects would diminish after 48 hours (four half-lives). However, the persistence of

bradycardia beyond this period made beta-blocker toxicity unlikely.

The temporal relationship between ticagrelor initiation and symptom onset, along with rapid resolution following drug discontinuation, strongly supported a causal association.

Therapeutic Intervention

The patient was initially managed with standard ACS therapy including aspirin 300 mg, ticagrelor 180 mg loading dose, rosuvastatin 40 mg, and intravenous unfractionated heparin prior to PCI. Maintenance therapy included aspirin, ticagrelor (90 mg twice daily), rosuvastatin, ramipril, and bisoprolol.

Following the onset of bradycardia, bisoprolol and ramipril were withheld, and temporary vasopressor support was initiated. As the bradyarrhythmia persisted, ticagrelor was discontinued and replaced with clopidogrel (loading dose followed by maintenance therapy), in accordance with clinical guidelines[7].

Follow-up and Outcomes

Within 36 hours of ticagrelor discontinuation, normal sinus rhythm was restored, and the patient achieved hemodynamic stability. He remained asymptomatic and was discharged in stable condition.

During follow-up over three months, repeated electrocardiographic evaluations demonstrated persistent normal sinus rhythm with no recurrence of bradyarrhythmia or associated symptoms, confirming complete clinical resolution.

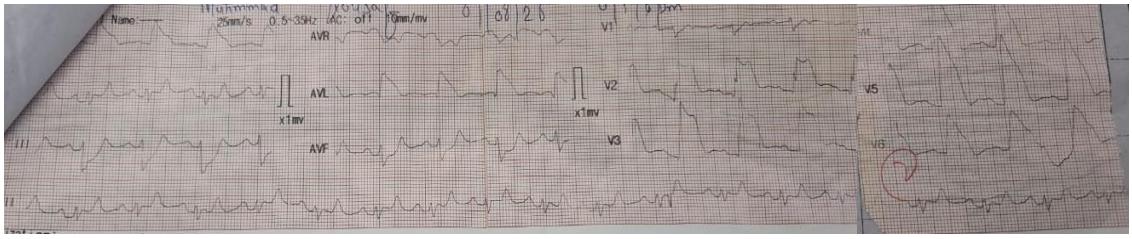

Figure 1: ECG showing tomb stone ST-elevation in V2-V6 and I, aVL suggesting acute anterolateral Myocardial infarction

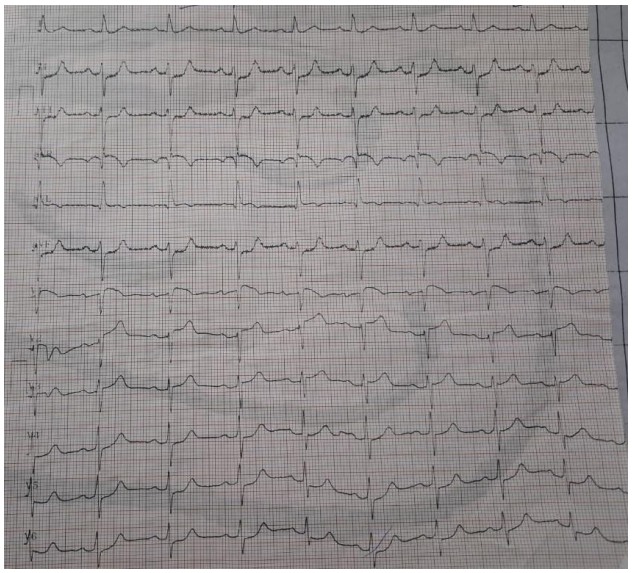

Figure 2: Post-PCI ECG showing normal sinus rhythm with successful reperfusion.

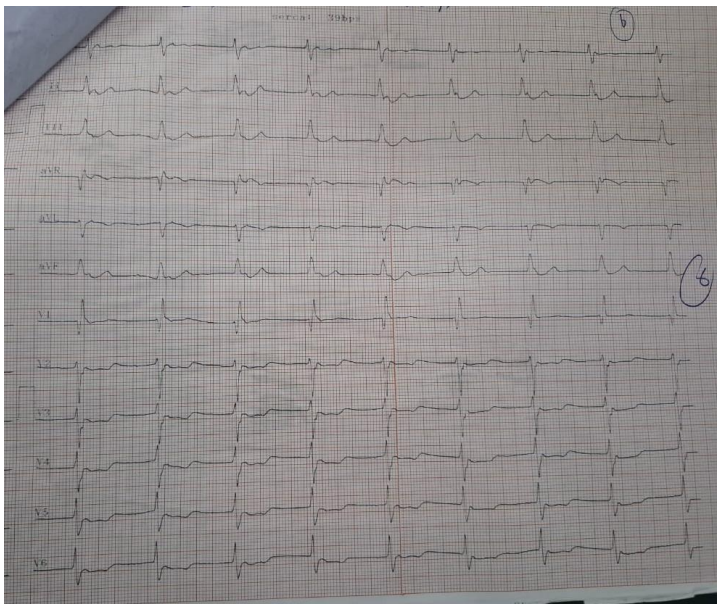

Figure 3: ECG showing Junctional Bradycardia

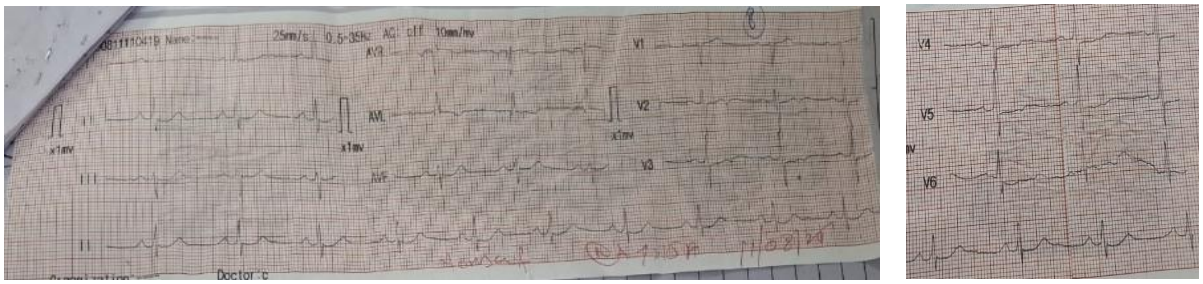

Figure 4: ECG showing sinus rhythm restoration

Discussion

Ticagrelor is an orally active, reversible P2Y12 receptor antagonist with rapid onset of action, approximately 36% bioavailability, and peak plasma concentration achieved within 1.5 hours, leading to near-maximal platelet inhibition within 2 hours[4]. In addition to its antiplatelet properties, ticagrelor exerts off-target pharmacodynamic effects, particularly through modulation of adenosine metabolism, which has important electrophysiological implications.

Mechanistically, ticagrelor inhibits equilibrative nucleoside transporter-1 (ENT-1), thereby reducing cellular uptake of adenosine and increasing its extracellular concentration. Elevated adenosine levels stimulate A1 and A2B receptors in cardiac tissue, leading to activation of inward rectifier potassium channels and inhibition of L-type calcium channels[5,6]. This results in reduced sinus node automaticity, delayed atrioventricular (AV) conduction, and an increased propensity for bradyarrhythmias. These effects provide a plausible pathophysiological explanation for the development of junctional bradycardia observed in this patient.

Compared with other P2Y12 inhibitors such as clopidogrel and prasugrel, ticagrelor uniquely influences adenosine-mediated pathways, which may account for its higher association with conduction disturbances[7,8]. While clopidogrel lacks significant effects on cardiac conduction,

ticagrelor's adenosine-related activity introduces a distinct electrophysiological profile that may predispose susceptible individuals to bradyarrhythmias.

The PLATO trial, which established the clinical superiority of ticagrelor over clopidogrel, reported a higher incidence of ventricular pauses among patients receiving ticagrelor; however, these were largely considered transient and clinically insignificant[9]. Subsequent analyses and real-world evidence, including case series and systematic reviews, have challenged this assumption by demonstrating clinically relevant bradyarrhythmias, particularly in elderly patients and those with underlying conduction vulnerabilities[5].

In the present case, several key observations strengthen the causal association between ticagrelor and junctional bradycardia. First, the temporal relationship between drug initiation and onset of symptoms (within 30 hours) aligns with the known pharmacokinetic profile of ticagrelor[4]. Second, alternative etiologies were systematically excluded. Electrolyte disturbances were ruled out, and ischemia-related conduction abnormalities were unlikely given successful reperfusion and absence of persistent ischemic changes. Although beta-blocker therapy (bisoprolol) could contribute to bradycardia, its half-life of approximately 12 hours[10] suggests that its effects should have resolved after 48 hours (four half-lives). The persistence of bradycardia beyond this period argues against beta-blocker toxicity as the primary cause.

Furthermore, the prompt resolution of bradyarrhythmia within 36 hours following ticagrelor discontinuation provides strong evidence of reversibility and supports a direct drug-related effect. Ticagrelor has a half-life of approximately 8 hours[11], and its pharmacodynamic effects are expected to diminish within a similar timeframe after cessation. The observed clinical improvement is therefore consistent with its pharmacokinetic and pharmacodynamic properties.

This case also highlights the importance of patient-specific risk factors in modulating susceptibility to ticagrelor-induced conduction disturbances. Advanced age, even in the absence of overt structural heart disease or baseline conduction abnormalities, may increase vulnerability due to age-related decline in autonomic regulation and nodal reserve. Although our patient did not exhibit comorbidities such as hepatic or biliary dysfunction that could alter drug metabolism, the occurrence of clinically significant bradycardia underscores that such adverse effects may arise even in relatively uncomplicated clinical settings.

From a clinical perspective, this case emphasizes the importance of vigilance for bradyarrhythmias following initiation of ticagrelor, particularly in the early post-ACS period. Recognition of this association is critical, as timely discontinuation of ticagrelor and substitution with an alternative agent such as clopidogrel can lead to rapid resolution of symptoms and avoidance of unnecessary interventions, including temporary or permanent pacing.

This case contributes to the growing body of evidence suggesting that ticagrelor-induced bradyarrhythmias may be underrecognized and clinically significant, particularly in elderly and high-risk populations[9]. Further studies are warranted to better define the incidence, risk factors, and mechanisms underlying these conduction disturbances, as well as to guide risk stratification and personalized antiplatelet therapy in ACS patients.

Conclusion

This case demonstrates that ticagrelor can act as a reversible cause of clinically significant junctional bradycardia in post-PCI patients. Early identification and prompt substitution with an alternative P2Y12 inhibitor such as clopidogrel can prevent unnecessary invasive interventions, including pacemaker implantation. Clinicians should maintain a high index of suspicion for drug-induced bradyarrhythmias, particularly in elderly patients.

Learning Points

- Ticagrelor may induce clinically significant bradyarrhythmias through adenosine-mediated electrophysiological effects.
- Junctional bradycardia in post-PCI patients should prompt evaluation for drug-induced causes, especially when temporally related to ticagrelor initiation.
- Exclusion of alternative causes such as electrolyte imbalance, ischemia, and beta-blocker toxicity is essential for accurate diagnosis.
- Discontinuation of ticagrelor and substitution with clopidogrel is an effective and guideline-supported management strategy.
- Early recognition of this adverse effect can prevent unnecessary invasive procedures and improve patient outcomes.

References

1) Hafeez Y, Wollard K, Grossman SA. Junctional Rhythm. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright 2025, StatPearls Publishing LLC.; 2025.
2) Kim GS, Uhm JS, Kim TH, Lee H, Park J, Park JK, et al. Junctional bradycardia is a potential risk factor of stroke. BMC Neurol. 2016;16:113.
3) Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes. New England Journal of Medicine. 2009;361(11):1045-57.
4) Juneja S, Gupta K, Kaushal S. Ticagrelor: An emerging oral antiplatelet agent. J Pharmacol Pharmacother. 2013;4(1):78-80.
5) Gorzynska-Schulz A, Stencelewski D, Daniłowicz-Szymanowicz L, Lica-Gorzynska M, Firkowska A, Wabich E. Unveiling the Hidden Risk: Ticagrelor-Induced Bradyarrhythmias and Conduction Complications in ACS Patients-Case Series. J Cardiovasc Dev Dis. 2025;13(1).
6) Cesarini D, Muraca I, Berteotti M, Gori AM, Sorrentino A, Bertelli A, et al. Pathophysiological and Molecular Basis of the Side Effects of Ticagrelor: Lessons from a Case Report. International Journal of Molecular Sciences. 2023;24(13):10844.
7) Rao SV, O'Donoghue ML, Ruel M, Rab T, Tamis-Holland JE, Alexander JH, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2025;151(13):e771-e862.
8) Bravo PE, Di Carli MF. Does clopidogrel affect the efficacy of myocardial perfusion imaging? J Nucl Cardiol. 2016;23(4):780-2.
9) Scirica BM, Cannon CP, Emanuelsson H, Michelson EL, Harrington RA, Husted S, et al. The incidence of bradyarrhythmias and clinical bradyarrhythmic events in patients with acute coronary syndromes treated with ticagrelor or clopidogrel in the PLATO (Platelet Inhibition and Patient Outcomes) trial: results of the continuous electrocardiographic assessment substudy. J Am Coll Cardiol. 2011;57(19):1908-16.
10) Leopold G, Pabst J, Ungethüm W, Bühring KU. Basic pharmacokinetics of bisoprolol, a new highly beta 1-selective adrenoceptor antagonist. J Clin Pharmacol. 1986;26(8):616-21.
11) Dobesh PP, Oestreich JH. Ticagrelor: pharmacokinetics, pharmacodynamics, clinical efficacy, and safety. Pharmacotherapy. 2014;34(10):1077-90.