International Journal of Research in Medical Sciences
Maity A et al. Int J Res Med Sci. 2025 Nov;13(11):4671-4675
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20253583

Original Research Article

Clinical characteristics and outcomes of rivaroxaban 2.5 mg in chronic coronary syndrome: insights from the RICCS India study

Agnibha Maity[1], Kingshuk Kar[2], Sutakshee D.[3], Purneshwar Kumar Pandey[4], Srishti Sonwani[5], Nigil Cletus[6], Sumeshraj[7], Suneesh Kalliath[1], Amit Gupta[8]*

[1]Department of General Medicine, Seth Sukhlal Karnani Memorial Hospital, Howrah, West Bengal, India
[2]Department of Cardiology, SUM Hospital, Kolkata, West Bengal, India
[3]Department of Cardiology, Max Hospital Saket, New Delhi, India
[4]Department of Cardiology, Fortis Hospital, New Delhi, India
[5]Department of Cardiology, Indira Gandhi Cooperative Hospital, Ernakulam, Kerala, India
[6]Department of Cardiology, Sree Gokulam Medical College, Trivandrum, Kerala, India
[7]Department of Cardiology, District Cooperative Hospital, Calicut, Kerala, India
[8]Scientific Services, USV PVT Limited, Mumbai, Maharashtra, India

Received: 04 April 2025
Revised: 05 August 2025
Accepted: 24 September 2025

***Correspondence:**
Dr. Amit Gupta,
E-mail: amit.gupta@usv.in

ABSTRACT

Background: The US Food and Drug Administration approved rivaroxaban 2.5 mg twice daily for the prevention of recurrent adverse cardiovascular events in patients with stable coronary heart disease and peripheral artery disease. This study aimed to understand the clinical characteristics and outcomes of Indian patients with chronic coronary syndrome (CCS) treated with rivaroxaban 2.5 mg, either as monotherapy or in combination therapy.
Methods: This retrospective, non-randomized, non-comparative, multi-center study was conducted across approximately 175 sites in India. Patients of either gender, aged >18 years, diagnosed with CCS, and who received rivaroxaban 2.5 mg were included. Patient data, including demographic details, medical history, and the treatment pattern of rivaroxaban 2.5 mg, were collected from the medical records and analyzed.
Results: A total of 1299 patients were included, with a median age of 62.00 years. Most patients were men (67.82%). The median systolic and diastolic blood pressures of the patients were 138.00 mmHg and 90.00 mmHg, respectively. Patients had a medical history of diabetes mellitus (41.72%), hypertension (38.95%), and cardiovascular disease (36.25%). Nearly 70% of patients received rivaroxaban 2.5 mg twice daily with low-dose aspirin (75 mg). The treatment duration was >3 months for 21.94% of patients, 1-3 months for 41.57%, and ≤1 month for 11.24%. Major bleeding events were reported in 24 patients (1.85%), while major adverse cardiovascular events occurred in 35 patients (2.69%).
Conclusions: This study provides real-world insights into clinical characteristics, treatment pattern, and outcomes of rivaroxaban 2.5 mg in patients with CCS in India.

Keywords: Anticoagulant, MACE, Major bleeding events, Rivaroxaban

INTRODUCTION

The 2019 European Society of Cardiology (ESC) guidelines introduced the term chronic coronary syndromes (CCS) to describe the clinical manifestations of coronary artery disease (CAD) during stable periods, particularly those occurring before or after an acute coronary syndrome (ACS). Further, the 2024 ESC guidelines emphasized that "CCS are a range of clinical presentations or syndromes that arise due to structural

and/or functional alterations related to chronic diseases of the coronary arteries and/or microcirculation".[1]

Although patients with established cardiovascular disease (CVD) receive guideline-based therapy and optimal treatment, they may still experience further cardiovascular events (CVE).[2] The risk of recurrence can be attributed to elevated thrombin levels following the index event, which leads to CVD progression through inflammation, endothelial dysfunction, and thrombosis.[3]

While antiplatelet therapy, especially aspirin, remains a cornerstone in the management of CCS to prevent atherothrombotic events, the role of anticoagulant therapies in reducing events in atheromatous disease has been largely neglected until recently.[4] For many years, vitamin K antagonists (VKAs), such as warfarin and acenocoumarol, were the sole oral anticoagulants used. However, newer agents, known as non-vitamin K antagonist oral anticoagulants (NOACs), have recently emerged. These newer anticoagulants offer more predictable anticoagulant effects compared to VKAs and have proven effective in preventing and treating venous thromboembolism (VTE), as well as in reducing the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF). Their ability to provide effective antithrombotic therapy with a lower risk of bleeding compared to VKAs makes them a promising alternative for patients with CCS.[5]

Rivaroxaban is an oral anticoagulant that does not exhibit VKA activity. It works by directly and selectively inhibiting free factor Xa, as well as factor Xa bound to prothrombinase or associated with thrombi.[2] Rivaroxaban was the first NOAC to gain European approval for preventing atherothrombotic events in patients with ACS.[5] Following the results of the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial,[6] the US Food and Drug Administration (FDA) recently approved rivaroxaban 2.5 mg twice daily for the prevention of recurrent adverse cardiovascular events in patients with stable coronary heart disease and peripheral artery disease (PAD).

There is a lack of adequate nationwide real-world data on the use of rivaroxaban 2.5 mg in patients with CCS in the Indian population. To address this gap, the study investigated the real-world treatment patterns of rivaroxaban 2.5 mg in patients with CCS. The study aimed to understand the clinical characteristics and outcomes of patients with CCS who were treated with rivaroxaban 2.5 mg, either as monotherapy or in combination therapy.

METHODS

Study design and ethical consideration

This retrospective, non-randomized, non-comparative, multi-center study (RICCS: Rivaroxaban in Chronic Coronary Syndrome) was conducted across approximately 175 sites in India between August 2021 and April 2022. The study sites included Indian healthcare centers with medical records of patients with CCS who had received treatment with rivaroxaban 2.5 mg. The study was conducted in compliance with the principles of the Declaration of Helsinki, and the study protocol was approved by the Independent Ethics Committees. Additionally, approvals were obtained from the treating physicians or medical practitioners prior to data collection from patient medical records.

Inclusion and exclusion criteria

Patients of either gender, aged >18 years, diagnosed with CCS, and who received rivaroxaban 2.5 mg were included in the study. The inclusion criteria also required a diagnosis of CAD and at least one high-risk factor for ischemic events. Patients at high-risk were defined as those with one of the following: CAD + PAD, a history of documented thrombotic cerebrovascular accident (CVA), recurrent myocardial infarction (MI), CAD + diabetes mellitus (all types), CAD + chronic kidney disease (CKD) with an estimated glomerular filtration rate (eGFR) of 30-59 mL/min/1.73 m² (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula), CAD + heart failure (ejection fraction ≥30% - 50%) and New York Heart Association (NYHA) class I or II.

Patients with incomplete data files or with any condition not suitable for inclusion, as indicated by the investigator's discretion were excluded from the study.

Sample size

The estimated sample size was approximately 5,000 patients with CCS.

Data collection

The medical records of patients with CCS who were treated with rivaroxaban 2.5 mg were identified. Comprehensive patient information, including demographic details, medical history, and the treatment pattern of rivaroxaban 2.5 mg, was collected from the medical records. The collected data were then entered into the case report forms and analyzed.

Study endpoints

The study endpoints were to determine the number of patients who reported major adverse cardiovascular events (MACE), including cardiac death, MI, and all-cause mortality; and the number of patients with hemorrhagic events (minor or major bleeding).

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software, version 23.0. Descriptive analysis was used to present the study outcomes.

Continuous variables were described as mean and standard deviation (SD) or median and range (depending on the normality of data), whereas categorical variables were described as numbers and percentages.

RESULTS

The demographic and clinical characteristics of the patients are presented in Table 1. A total of 1299 patients were included in the study. The median (range) age of the patients was 62.00 (19.00-96.00) years. Men constituted 67.82% of the study population. The median (range) body mass index (BMI) of the patients was 27.24 (14.20-68.06) kg/m^2. The median systolic and diastolic blood pressures of the patients were 138.00 mmHg and 90.00 mmHg, respectively. Regarding medical history, 41.72% of patients had diabetes mellitus, followed by hypertension (38.95%), and CVD (36.25%).

Table 1: Demographic and clinical characteristics of the patients.

Parameters	Number of patients (n=1299)
Age [years], median (range)	62.00 (19.00-96.00)
Gender	
Men	881 (67.82)
Women	418 (32.18)
Weight [kg], median (range)	75.00 (44.00-110.00)
Height [cm], median (range)	165.00 (69.00-190.00)
BMI [kg/m^2], median (range)	27.24 (14.20-68.06)
Respiratory rate, median (range); (n=726)	16.00 (11.00-30.00)
Pulse rate, median (range); (n=784)	78.00 (60.00-180.00)
SBP (mmHg), median (range); (n=745)	138.00 (100.00-189.00)
DBP (mmHg), median (range); (n=1025)	90.00 (50.00-149.00)
Alcohol consumption	350 (26.94)
Allergy	18 (1.39)
Medical history	
Diabetes mellitus	542 (41.72)
Hypertension	506 (38.95)
CVD	471 (36.25)
Any other*	8 (0.61)

Data presented as n (%), unless otherwise specified. *Any other: PAD (n=7), PVD (n=1). CVD, cardiovascular disease; PAD, peripheral arterial disease; PVD, peripheral vascular disease

The treatment pattern and outcomes of rivaroxaban 2.5 mg is shown in Table 2. Nearly 70% of patients received rivaroxaban 2.5 mg twice daily with low-dose aspirin (75 mg). The duration of treatment was >3 months for 21.94% of patients, 1-3 months for 41.57%, and ≤1 month for 11.24%. Major bleeding events were reported in 24 patients (1.85%). Major adverse cardiovascular events occurred in 35 patients (2.69%), while adverse events were reported in 23 patients (1.77%).

Table 2: Treatment pattern and outcomes of rivaroxaban 2.5 mg.

Parameters	Number of patients (n=1299)
Patient on rivaroxaban 2.5 mg twice daily with low-dose aspirin 75 mg	887 (68.28)
Duration of drug (n=1150)	
≤1 month	146 (11.24)
1-3 months	540 (41.57)
>3 months	285 (21.94)
Occurrence of major bleeding event	24 (1.85)
MACE	35 (2.69)
Adverse event	23 (1.77)

Data presented as n (%). MACE, major adverse cardiovascular events

DISCUSSION

Patients with existing CVD are at risk for further cardiovascular (CV) events, even with optimal medical treatment. While platelet inhibition is crucial for preventing new events, the potential benefits of anticoagulant therapies in reducing events associated with atheromatous disease have only recently gained attention.[2]

Non-vitamin K antagonist oral anticoagulants are more convenient, safer, and equally effective as VKAs in treating NVAF.[7] This raises questions about their potential role in the secondary prevention of atherothrombotic events. Given their favorable safety profile and greater ease of use compared to VKAs, NOACs, as an anti-thrombotic therapy, may contribute to the management of CCS.[8,4]

In the context above, the only available human clinical data currently pertain to rivaroxaban, which is the most widely studied of the NOACs.[4,2] While several trials have been published on NOACs in patients post-ACS (ATLAS ACS 2-TIMI 51, RE-DEEM, APPRAISE-2), the COMPASS trial provides the only available data supporting anticoagulant therapy for the prevention of CV events in stable CVD.[2] Moreover, the 2024 ESC guidelines recommend adding very low-dose rivaroxaban (2.5 mg BD) to aspirin in high ischemic risk CCS patients without high-bleeding risk, based on the COMPASS trial.[9]

The COMPASS trial demonstrated that rivaroxaban plus aspirin was associated with fewer adverse cardiovascular events (4.1% vs. 5.4%; p<0.001), but a higher incidence of major bleeding events (3.1% vs. 1.9%; p<0.001) compared with aspirin alone.[6] There was no significant difference in intracranial or fatal bleeding between the two treatment

arms, and death rates were lower in the rivaroxaban plus aspirin group. Although the trial was prematurely terminated, potentially overestimating the treatment effect, the results suggest that rivaroxaban 2.5 mg twice daily could become a treatment option for patients with CCS at high ischemic risk.

The mean age of participants in the COMPASS trial was 68.3 years, with 22.5% of the population being female. In contrast, the median age of patients in the present study was 62 years, with 32.18% females. In the COMPASS trial, the mean systolic blood pressure was 136 mmHg and the mean diastolic blood pressure was 78 mmHg, whereas the present study showed median systolic and diastolic blood pressure values of 138 mmHg and 90 mmHg, respectively. Additionally, 37.7% of participants in the COMPASS trial had diabetes, compared to 41.72% in the current study.

In this study, nearly 70% of patients received rivaroxaban 2.5 mg twice daily in combination with low-dose aspirin (75 mg), while the remaining patients likely received rivaroxaban monotherapy. The overall occurrence of major bleeding events in the study was 1.85%. However, in the COMPASS trial, the rate of major bleeding was higher in both the rivaroxaban plus aspirin group and the rivaroxaban alone group, compared to aspirin alone (3.1% vs. 2.8% vs. 1.9%; $p<0.001$ for both rivaroxaban plus aspirin vs. aspirin alone and rivaroxaban alone vs. aspirin alone).

The present study reported MACE in 2.69% of patients and adverse events in 1.77%. It is well reported that in the COMPASS trial, low-dose oral anticoagulation and antiplatelet therapy, compared with single antiplatelet therapy, reduced the primary MACE outcome of CV death, MI, or stroke in patients with stable coronary artery disease (CCS) or PAD. However, a meta-analysis revealed that low-dose rivaroxaban with antiplatelet monotherapy did not reduce cardiovascular or all-cause mortality in patients with recent ACS or stable coronary heart disease, and that the reduction in MI and stroke occurred at the cost of an increased risk of major bleeding.[3]

A recent study revealed the current trends in the management of CCS and the utilization of NOACs among physicians in India.[10] In this study, 42.19% of physicians preferred rivaroxaban, with a prescription rate of 40%. However, around 51% of physicians reported bleeding risk as the primary barrier to prescribing rivaroxaban and aspirin for patients with CCS, and 33.33% of physicians reported that multiple risk factors influenced their decision to prescribe rivaroxaban in these patients. While this combination has been shown to reduce the risk of stroke or cardiovascular death compared to aspirin alone, concerns about an increased bleeding risk remain significant among physicians, affecting treatment decisions in clinical practice in India.

To summarize, adding an oral anticoagulant to antiplatelet monotherapy helps prevent recurrent MACE, but at the cost of a higher bleeding risk. Therefore, low-dose rivaroxaban should be carefully considered for patients whose ischemic risk is higher than their bleeding risk.

This study has several limitations. The small sample size limits the generalizability of the findings to the broader population of patients with CCS in India. Additionally, the study does not account for concurrent medications, which could influence the efficacy or safety of rivaroxaban 2.5 mg. The retrospective design, which relies on patient medical records, may introduce biases in treatment adherence and outcome reporting, potentially affecting the accuracy and robustness of the conclusions.

CONCLUSION

This study provides real-world insights into clinical characteristics, treatment pattern, and outcomes of rivaroxaban 2.5 mg in patients with CCS in India. In conclusion, rivaroxaban 2.5 mg combined with low-dose aspirin may be an effective treatment for reducing CV events in patients with CCS, although bleeding risks remain a significant concern.

ACKNOWLEDGMENTS

The medical writing support was provided by Rupika Pawar (Sqarona Medical Communications LLP, Pune).

Funding: This study was funded by USV Private Limited., India
Conflict of interest: Amit Gupta is an employee of USV Private Limited. All other authors have no conflict of interest to declare
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, et al. ESC Scientific Document Group. 2024 ESC Guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024;45(36):3415-537.
2. Gradolí J, Vidal V, Brady AJ, Facila L. Anticoagulation in patients with ischaemic heart disease and peripheral arterial disease: clinical implications of COMPASS Study. Eur Cardiol. 2018;13(2):115-8.
3. Khan SU, Khan MZ, Asad ZUA, Valavoor S, Khan MU, Khan MS, et al. Efficacy and safety of low dose rivaroxaban in patients with coronary heart disease: a systematic review and meta-analysis. J Thromb Thrombolysis. 2020;50(4):913-20.
4. Sorbets E, Steg PG. Direct-acting anticoagulants in chronic coronary syndromes. Eur Cardiol. 2020;15:1-7.

5. Mekaj YH, Mekaj AY, Duci SB, Miftari EI. New oral anticoagulants: their advantages and disadvantages compared with vitamin K antagonists in the prevention and treatment of patients with thromboembolic events. Ther Clin Risk Manag. 2015;11:967-77.
6. Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakovska O, et al. COMPASS Investigators. Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease. N Engl J Med. 2017;377(14):1319-30.
7. Gibson CM, Mehran R, Bode C, Halperin J, Verheugt FW, Wildgoose P, et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. N Engl J Med. 2016;375(25):2423-34.
8. Hirschl M, Kundi M. Safety and efficacy of direct acting oral anticoagulants and vitamin K antagonists in nonvalvular atrial fibrillation - a network meta-analysis of real-world data. Vasa. 2019;48(2):134-47.
9. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, et al. ESC Scientific Document Group. 2024 ESC Guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024;45(36):3415-537.
10. Guthe A, Vishwakarma P, Pradhan A, Ali M, Sharma A, Gupta A, et al. Clinical practices and treatment preferences in chronic coronary syndrome management among Indian physicians. World J Adv Res Revi. 2024;24(01):1913-192.

Cite this article as: Maity A, Kar K, Sutakshee D, Pandey PK, Sonwani S, Cletus N, et al. Clinical characteristics and outcomes of rivaroxaban 2.5 mg in chronic coronary syndrome: insights from the RICCS India study. Int J Res Med Sci 2025;13:4571-5.