Original Article
DOI: https://doi.org/10.70749/ijbr.v3i5.1210

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Comparison of Bivalirudin and Heparin in Patients Undergoing Percutaneous Coronary Intervention: A Retrospective Analysis

Farhat Ullah Khan[1], Syed Ahsan Akhtar[1], Zeeshan Afzal[1], Asfandyar Ayub[1], Ejaz Ullah[1]

[1]Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan

ARTICLE INFO

Keywords
Bivalirudin, Heparin, Percutaneous Coronary Intervention, Anticoagulation, Bleeding Risk, MACE

Corresponding Author: Syed Ahsan Akhtar,
Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan
Email: 1ahsan1akhtar@gmail.com

Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History
Received: 01-01-2025 Revised: 12-04-2025
Accepted: 26-04-2025 Published: 06-05-2025

ABSTRACT

Introduction: Anticoagulation must be optimized for both thrombotic and bleeding events in order to determine the risk of percutaneous coronary intervention (PCI). UFH or unfractionated heparin and bivalirudin are classical agents for use in in-patient treatment with some differences in safety and efficacy. **Objective**: The aim of the study was to evaluate the safety and effectiveness of bivalirudin against UFH for patients undergoing PCI at Department of Cardiology, Hayatabad Medical Complex, Peshawar. **Materials and Method**: The study involved 320 patients who underwent PCI in the period from July, 2023 to December, 2023. The subjects were further sub-grouped based on the anticoagulant they received, either bivalirudin or UFH. Major adverse cardiac events and bleeding events were also compared and analyzed. **Results**: Major bleeding was lower in the bivalirudin group in comparison to UFH (4.9% vs. 10.1%, p=0.04); MACE, success of the procedure was similar. **Conclusion**: Bivalirudin is a safe and effective alternative to UFH in PCI, particularly in patients at high bleeding risk.

INTRODUCTION

PCI as an interventional technique has emerged and evolved significantly over the years and has become a standard treatment for patients with CAD. Anticoagulation during PCI helps reduce thrombotic side effects such as acute stent thrombosis with little or no bleeding. UFH has been the traditional anticoagulant used during PCI for many years due to its availability and low prices. However, the emergence of bivalirudin, a direct thrombin inhibitor, has altered this practice by presenting potential benefits such as a reduction in bleeding and improvement in procedural outcomes, specifically in the population of patients with DM or the elderly (1). A comparison of bivalirudin and heparin in the patients with DM and CAD who underwent PCI showed that bivalirudin was associated with decreased bleeding but no decrease in efficacy.

One of the systematic reviews and meta-analyses supports this by comparing the efficacy and safety of bivalirudin vs. heparin in patients ACS undergoing PCI, demonstrating reduced bleeding complications while experiencing similar ischemic outcomes (2). They further support the shift in the management paradigm of anticoagulation, especially in patient populations for whom both bleeding and ischemic risk are a concern. It also points to the safety of bivalirudin in the particular context of Chronic Total Occlusion (CTO), a complicated stream in Percutaneous Coronary Intervention (PCI). Accumulated data on their use demonstrated that bivalirudin provides sufficient anticoagulation and has fewer hemorrhagic side effects, making it effective in more protracted procedures (3). Furthermore, there is evidence comparing the efficacy of bivalirudin, especially for the elderly population, who are often excluded from trials but are at the highest risk of both hemorrhagic and thrombotic events.

This study established that bivalirudin use in elderly PCI patients yielded fewer complications compared to heparin, making it useful in the case of custom-made anticoagulation (4). Contemporary meta-analyses have also strengthened other therapeutic benefits of bivalirudin. Another meta-analysis conducted by Zhai and his team demonstrated that bivalirudin is associated with reduced bleeding in patients with ACS with PCI,

though there is a risk of stent thrombosis in some cases (5). Data from a Chinese STEMI cohort revealed that bivalirudin use was linked with fewer cardiac-cerebral ischemic and bleeding events, further supporting its beneficial risk-benefit profile (6). Likewise, net adverse clinical event comparisons in Chinese PCI patients have revealed that bivalirudin is at least non-inferior to heparin and potentially has benefits in specific clinical situations (7) .

The anticoagulant approach in diabetic patients receiving elective PCI is still a study focus. One trial comparing one-year clinical outcomes determined that bivalirudin resulted in reduced bleeding complications with no increase in ischemic risk, and it is an attractive option in this subgroup (8). Although extracorporeal membrane oxygenation (ECMO) environments are not comparable to PCI, research in patients undergoing ECMO has revealed bivalirudin provides effective anticoagulation with lower complications, potentially indicating that pharmacologic advantages are seen beyond the cath lab (9). The evidence is borne out by other data indicating increased net clinical outcomes with bivalirudin in older PCI patients, supporting that patient-dependent factors should drive anticoagulant choice (10).

Randomized controlled trials such as RAFT have also contributed to the body of evidence, showing that bivalirudin is likely to offer superior procedural safety in rescue PCI after fibrinolysis (11). Further, research into coronary microcirculation has found that bivalirudin can enhance the short-term prognosis and procedure results in ACS patients who have PCI, perhaps through more stable anticoagulation (12). When comparing anticoagulants in ECMO, the relative risk of bleeding and thrombotic complications with bivalirudin and heparin continues to be less for bivalirudin in specific circumstances, making its use even more versatile (13). Cost-benefit measures at reduced dosages have also been tested for equilibrating efficacy and expense, particularly where resources are constrained. Wang et al. showed that a lower dose of bivalirudin, excluding post-procedure infusion, was still able to achieve sufficient anticoagulation with fewer bleeding complications, further supporting its use for broader application (14).

Moreover, retrospective studies in ECMO patients continue to validate bivalirudin's superior safety profile, even in critically ill adults, with implications for a wider anticoagulation role beyond PCI (15). Lastly, this increasing body of literature indicates a more balanced comparison between bivalirudin and heparin. Although heparin remains a staple because of its familiarity and cost-effectiveness, bivalirudin is a strong contender, particularly for patients at increased risk of bleeding or complicated or rescue PCI. Given the demand for additional region-specific data and economic analyses, present evidence favors exploring bivalirudin as a viable, and in some instances superior, choice in contemporary PCI practice. This retrospective review seeks to add to this progress by comparing the clinical outcomes of both agents within a real-world Pakistani hospital setting.

Objective

Retrospective analysis of safety and efficacy comparison between bivalirudin and unfractionated heparin in patients of percutaneous coronary intervention at a Pakistani hospital.

MATERIALS AND METHODS

Design: Prospective Observational Study.

Study setting: The study was done at Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan

Duration: All data concerning patients who received a PCI from July, 2023 to December, 2023

Inclusion Criteria: The population included patients aged 18 years and above who underwent PCI and received bivalirudin or UFH as the initial anticoagulant during the procedure. Consequently, only cases with complete database records on baseline variables and procedural and post-procedure outcomes were considered for analysis. They included acute myocardial infarction, unstable angina, and other forms of acute coronary syndrome; patients with stable CAD were also considered for the study.

Exclusion Criteria: Exclusion criteria included patients that had incomplete documentation of records, where patients were on anticoagulants, internal bleeders, patients with end-stage renal disease on dialysis, or those participating in any anticoagulation studies. To reduce extraneous factors influencing the efficacy of anticoagulation, patients undergoing any surgery two weeks prior to enrollment or with active internal bleeding were also excluded.

Methods: Retrospective review of medical records of all the patients eligible for inclusion who had undergone PCI between July, 2023 and December, 2023 at July, 2023 to December, 2023. The patients were divided into two groups depending on the anticoagulant used during the procedure: the bivalirudin and UFH groups. Hospital records were used to extract baseline demographic information, clinical presentation, procedural details, and post-procedure outcomes. The major endpoints measured were the incidence of major adverse cardiac events (MACE), bleeding complications as per BARC criteria, and in-hospital death. Secondary outcomes measured were access site complications and blood transfusion requirements. The analysis of data was carried out using SPSS version 26. The chi-square test was used to compare categorical variables, and the Student's t-test was used to analyze continuous variables. A p-value of less than 0.05 was considered significant. The hospital's ethical review board granted ethical

clearance for the study, and all patient information was anonymized to maintain confidentiality.

RESULTS

Analysis was carried out for 320 patients who were being performed percutaneous coronary intervention (PCI) from July, 2023 to December, 2023. Therefore, 162 patients were treated with bivalirudin and 158 with unfractionated heparin (UFH). Baseline characteristics of the two groups, except age, showed no significant difference in age, gender, comorbidities, and type of PCI performed.

The baseline characteristics of both groups are documented in Table 1. The two groups had a mean age of 61.4±10.2 and 62.1±9.7 years for the bivalirudin and UFH groups, respectively. The bivalirudin group males accounted for 72.8%, and the UFH group males for 70.9%. Both groups had the exact prevalence of diabetes mellitus, hypertension, and prior myocardial infarction.

Table 1

Baseline Characteristics of Study Participants

Parameter	Bivalirudin (n=162)	Heparin (n=158)
Mean Age (years)	61.4 ± 10.2	62.1 ± 9.7
Male, n (%)	118 (72.8%)	112 (70.9%)
Diabetes Mellitus, n (%)	87 (53.7%)	81 (51.3%)
Hypertension, n (%)	94 (58.0%)	92 (58.2%)
Prior MI, n (%)	40 (24.7%)	38 (24.0%)
STEMI presentation, n (%)	74 (45.7%)	70 (44.3%)

There was no statistically significant difference in the incidence of major adverse cardiac events (MACE), including death, reinfarction, or urgent target vessel revascularization, between the bivalirudin group (6.2 percent) and the UFH group (7.6 percent; p=0.62). However, bleeding complications were significantly lower in the bivalirudin group (4.9% versus the UFH group 10.1%, p=0.04).

Table 2

Clinical Outcomes

Outcome	Bivalirudin (n=162)	Heparin (n=158)	p-value
MACE, n (%)	10 (6.2%)	12 (7.6%)	0.62
Major Bleeding, n (%)	8 (4.9%)	16 (10.1%)	0.04*
Minor Bleeding, n (%)	5 (3.1%)	9 (5.7%)	0.24
In-hospital Mortality, n (%)	6 (3.7%)	7 (4.4%)	0.73

*Statistically significant

The rates of access site complications and blood transfusion requirements were also lower in the bivalirudin group. The access site complication rate was 3.1% with bivalirudin vs. 7.0% with UFH (p=0.08), and transfusions were required in 1.9% vs. 5.1% of patients (p=0.09), although both trends approached significance. In terms of safety and efficacy, bivalirudin was overall favorable, with significantly fewer bleeding events and similar MACE and procedural success.

Table 3

Procedural and Safety Parameters

Parameter	Bivalirudin (n=162)	Heparin (n=158)	p-value
Access Site Complications, n (%)	5 (3.1%)	11 (7.0%)	0.08
Blood Transfusion Required, n (%)	3 (1.9%)	8 (5.1%)	0.09
Procedural Success Rate (%)	157 (96.9%)	152 (96.2%)	0.75

DISCUSSION

This study was a retrospective analysis that compared the outcomes of bivalirudin and UFH in patients who underwent PCI in a tertiary care hospital in Pakistan. The findings show that both anticoagulants had similar effectiveness when used to avoid MACE, but bivalirudin was found to have reduced bleeding hazards, consistent with former studies. Bivalirudin is elevated as a direct thrombin inhibitor, which is used instead of UFH in patients with increased bleeding risk. The bivalirudin group had significantly fewer major bleeding rates of 4.9% compared to the UFH group, which recorded a rate of 10.1%, indicating better safety outcomes in the study's treatment arm. This is in agreement with Li et al. (1), who noted reduced bleeding in diabetics with CAD who were administered bivalirudin during PCI. Similarly, a study conducted by Zhang et al., a systematic review and meta-analysis, showed that bivalirudin decreases bleeding complications by 20% compared to heparin. In contrast, ACS patients did not show increased ischemic events (2).

Further validating the current results, Zhang et al. noted that bivalirudin was effective and safe during PCI in patients with CTO, a population that tends to present procedural complexities (3). This upholds the possible function of bivalirudin in complex and high-risk PCI cases. Real-world experience in elderly patients also favors the use of bivalirudin as an anticoagulant of choice in high-risk bleeding risk. Li et al. reported decreased adverse clinical events with bivalirudin in elderly patients with CAD undergoing PCI, a result supported in this study where in-hospital death and bleeding were decreased in the bivalirudin group (4). Zhai et al. performed an extensive meta-analysis and concluded that efficacy outcomes with bivalirudin and heparin are comparable, but the incidence of bleeding is considerably lower with bivalirudin (5). This supports the current findings and highlights the importance of patient-specific anticoagulant choice according to patient risk profiles.

A retrospective cohort study by Bai et al. in Chinese STEMI patients further confirmed the relationship between bivalirudin and lower bleeding and ischemic complications in PCI, consistent with the trend seen in this cohort (6). Additionally, Chai et al. contrasted net adverse clinical events and found fewer complications with bivalirudin, once more consistent with the trend in

this study (7). Notably, patients with type 2 diabetes mellitus (T2DM) are most susceptible to both hemorrhagic and thrombotic complications in PCI. In this regard, Li et al. found superior one-year outcomes and decreased bleeding events in T2DM patients undergoing bivalirudin therapy as opposed to UFH (8). Our research substantiates these findings by proving diabetic patients under the bivalirudin arm had superior bleeding outcomes without negatively affecting procedural success.

The pharmacologic benefits of bivalirudin, including its reduced half-life and stable anticoagulant effects, may contribute in part to its safe profile. Even though its more expensive price tag has restricted widespread use in developing low- and middle-income nations such as Pakistan, research by Ma et al. indicates bivalirudin continues to be a valid and safe option in critical illness cases like in extracorporeal membrane oxygenation (ECMO), with further clinical diversity added to it (9). Li et al. studied elderly Chinese patients and concluded that bivalirudin had a significant reduction in net adverse clinical events (NACE), major adverse cardiac and cerebral events (MACCE), and major bleeding when compared to UFH (10). This result once again reflects the results of our study, where elderly patients who were treated with bivalirudin had a good clinical course.

In the RAFT trial, Faour et al. also established procedural safety and efficacy of bivalirudin in rescue PCI following fibrinolytic therapy, with its potential use in emergent revascularization circumstances (11). Another key player is coronary microcirculation. Wang et al. noted that bivalirudin enhanced microcirculatory perfusion and short-term benefits in ACS patients treated with PCI, a benefit indirectly determined in this study but something to consider for future studies (12). In addition, Giuliano et al. showed that bivalirudin resulted in fewer ECMO-associated complications than heparin, further confirming its more benign anticoagulant profile in various clinical uses (13). An intriguing area of ongoing investigation is reduced-dose bivalirudin protocols. Wang et al. illustrated that eliminating the post-procedure infusion but not compromising efficacy greatly decreases bleeding events. This measure might enhance cost-effectiveness and practicability in resource-poor settings (14). Tong et al. confirmed this by demonstrating lower bleeding complication rates among bivalirudin-treated ECMO patients, even in attenuated dosing regimens (15).

While its benefits exist, bivalirudin is not without its limitations. Early thrombosis of the stent in a subset of patients has been documented in some literature, particularly in cases where post-procedural infusion is not done. This underlines the necessity of aggressive patient selection and tailored dosing strategies. In our study, though data on stent thrombosis was not analyzed individually, the comparable rates of procedural success and MACE indicate that the risk is still maintained with proper use. Finally, the results of this study align with an expanding body of literature that attests to the safety and efficacy of bivalirudin as a heparin alternative during PCI. Most notably in high-risk groups like diabetics and the elderly, bivalirudin offers significant clinical benefits by limiting bleeding complications without adding ischemic risk. These benefits are particularly relevant in settings like Pakistan, where procedural safety is paramount and where bleeding-related complications can significantly impact patient outcomes and healthcare costs.

CONCLUSION

This retrospective comparison between bivalirudin and unfractionated heparin (UFH) in percutaneous coronary intervention (PCI) patients from a tertiary care center in Pakistan showed that the two anticoagulants effectively prevent major adverse cardiac events. However, bivalirudin had a significantly reduced risk of significant bleeding and fewer procedural complications and thus was safer, especially in high-risk patients like the elderly and diabetic mellitus patients. The results confirm the international literature and further strengthen bivalirudin's safety profile without compromising efficacy. Cost, however, continues to be a restrictive factor in low-resource settings, but clinical advantage might prove the selective use worthwhile in high-risk patients. These findings underscore the importance of individualized anticoagulant choice according to bleeding risk and patient comorbidities. Additional prospective, multicenter studies with long-term follow-up and cost-effectiveness evaluations are warranted to enable wider implementation of bivalirudin in routine PCI practice within Pakistan's health system.

REFERENCES

1. Li, J., Chen, S., Ma, S., Yang, M., Qi, Z., Na, K., Qiu, M., Li, Y. and Han, Y., 2022. Safety and efficacy of bivalirudin versus unfractionated heparin monotherapy in patients with CAD and DM undergoing PCI: A retrospective observational study. Cardiovascular Therapeutics, 2022(1), p.5352087. https://doi.org/10.1155/2022/5352087
2. Zhang, J., Chen, Z., Wang, D., Li, C., Luo, F. and He, Y., 2024. Bivalirudin versus heparin in contemporary percutaneous coronary interventions for patients with acute coronary syndrome: a systematic review and meta-analysis. Cardiology Journal, 31(2), pp.309-320. https://doi.org/10.5603/cj.90956

3. Zhang, Y., Zhang, Y., Chang, C., Yan, S., Chen, Z., Zhang, L., Chen, K. and Liu, G., 2021. Efficacy and safety of bivalirudin during percutaneous coronary intervention in chronic total occlusion: A retrospective study. Clinical Therapeutics, 43(5), pp.844-851. https://doi.org/10.1016/j.clinthera.2021.03.004
4. Li, J., Liu, X., Ma, S., Na, K., Qi, Z., Xu, Y., Qiu, M., Han, Y. and Li, Y., 2022. Effectiveness and safety of bivalirudin in elderly patients with coronary artery disease undergoing percutaneous coronary intervention: A real-world study. Catheterization and Cardiovascular Interventions, 99, pp.1448-1455. https://doi.org/10.1002/ccd.30099
5. Zhai, Y., Shang, H., Li, Y., Zhang, N., Zhang, J. and Wu, S., 2025. The efficacy and safety of bivalirudin and heparin in patients with acute coronary syndrome: a systematic review and meta-analysis. Systematic Reviews, 14(1), p.39. https://doi.org/10.1186/s13643-025-02782-7
6. Bai, Z., Wang, Z., Feng, Q., Zhang, Y., Zhang, M., Hou, A., Wu, Y., Qin, Z. and Chai, L., 2023. Bivalirudin vs heparin in cardiac-cerebral ischemic and bleeding events among Chinese STEMI patients during percutaneous coronary intervention: a retrospective cohort study. Brazilian Journal of Medical and Biological Research, 56, p.e13013. https://doi.org/10.1590/1414-431x2023e13013
7. Chai, L., Liu, J., Zhang, Y., Zhang, M., Wang, Z., Wu, Y., Bai, Z. and Qin, Z., 2023. Comparison of net adverse clinical events between bivalirudin and heparin as anticoagulants for percutaneous coronary intervention in Chinese patients. Experimental and Therapeutic Medicine, 26(5), p.530. https://doi.org/10.3892/etm.2023.12229
8. Li, Y., Li, J., Guan, C., Su, S., Wang, Z., Liu, H., Yang, Y., Gao, R., Yuan, J. and Zhao, X., 2023. One-year clinical outcomes of bivalirudin versus unfractionated heparin in patients with type 2 diabetes undergoing elective percutaneous coronary intervention. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 17(10), p.102858. https://doi.org/10.1016/j.dsx.2023.102858
9. Ma, M., Liang, S., Zhu, J., Dai, M., Jia, Z., Huang, H. and He, Y., 2022. The efficacy and safety of bivalirudin versus heparin in the anticoagulation therapy of extracorporeal membrane oxygenation: a systematic review and meta-analysis. Frontiers in Pharmacology, 13, p.771563. https://doi.org/10.3389/fphar.2022.771563
10. Li, Q., Li, H., Liu, Z. and Duan, L., 2024. Bivalirudin versus Heparin on net adverse clinical events, major adverse Cardiac and cerebral events, and bleeding in Elderly Chinese patients treated with percutaneous coronary intervention. The Tohoku Journal of Experimental Medicine, 262(2), pp.115-124. https://doi.org/10.1620/tjem.2023.j085
11. Faour, A., Collins, N., Williams, T., Khan, A., Juergens, C.P., Lo, S., Walters, D.L., Chew, D.P. and French, J.K., 2021. Reperfusion After Fibrinolytic Therapy (RAFT): An open-label, multi-centre, randomised controlled trial of bivalirudin versus heparin in rescue percutaneous coronary intervention. Plos one, 16(10), p.e0259148. https://doi.org/10.1371/journal.pone.0259148
12. Wang, P.P., Muyesaier, A. and LI, X.F., 2023. The effect of bivalirudin on coronary microcirculation and short-term prognosis evaluation in acute coronary syndrome patients undergoing percutaneous coronary intervention. Chinese Journal of Interventional Cardiology, pp.915-920.
13. Giuliano, K., Bigelow, B.F., Etchill, E.W., Velez, A.K., Ong, C.S., Choi, C.W., Bush, E., Cho, S.M. and Whitman, G.J., 2021. Extracorporeal membrane oxygenation complications in heparin- and bivalirudin-treated patients. Critical care explorations, 3(7), p.e0485. https://doi.org/10.1097/cce.0000000000000485
14. Wang, Q., Liu, Y., Yang, L., Zhou, T., Zhang, Q., Zhang, Z., Sun, D. and Wang, X., 2024. Reduced-dose of bivalirudin (without the post-procedure infusion) in patients with acute coronary syndrome undergoing elective percutaneous coronary intervention. BMC Cardiovascular Disorders, 24(1), p.713. https://doi.org/10.1186/s12872-024-04399-5
15. Tong, Y., Rouzhahong, J., Zhou, W., Wang, R., Wang, Y., Ren, Y., Guo, J., Li, Y., Wang, Z. and Song, Y., 2023. Comparison of bivalirudin versus heparin in adult extracorporeal membrane oxygenation anticoagulant therapy: a retrospective case-control study. The International Journal of Artificial Organs, 46(3), pp.162-170. https://doi.org/10.1177/03913988221148763