Original Article

Reduced dose of Bivalirudin in patients undergoing percutaneous coronary intervention in Bangladeshi population: A single center study

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Abstract

Introduction: Bivalirudin as an anticoagulant that reduces bleeding as compared to heparin after percutaneous coronary intervention (PCI) At present, the recommended dose of Bivalirudin is mainly based on European and American guidelines. It is widely accepted that the East Asian population has a lower risk of ischemia and a higher risk of bleeding than non-East Asian populations. In clinical practice, the dose of Bivalirudin may not be fully applicable to the Bangladeshi population. Therefore, this study aimed to explore the efficacy and safety of a reduced dose (Two thirds of the recommended bolus dose followed by half of recommended maintenance dose) of Bivalirudin in patients undergoing PCI.

Methods: This was a single-center observational study which was conducted in the department of Cardiology National Heart Foundation hospital & Research Institute from May 2016 to March 2023. Patients who met the inclusion and exclusion criteria were included. All the patients were given Bivalirudin (reduced dose) & observed for in hospital outcomes (major bleeding or hematoma needed blood transfusion, minor bleeding, stent thrombosis, cardiogenic shock & all-cause mortality).

Results: In total 1143 patients were included. Mean age of study population was 58.26±11.38 & majority of patients were male (54.9%). Majority of patients were chronic coronary syndrome (CCS) (58.2%) while the rest of the patients were acute coronary syndrome (ACS). 52.9% patients underwent Multivessel PCI, among them Rotabalation were done in 4.8% cases & left main (LM) PCI were done in 19.2 % patients. The Mean activated clotting time (ACT) after 5 min was 298.3 ± 68.511sec. Regarding the in-hospital outcomes, 1.7 % patients developed major bleeding or hematoma needed blood transfusion, 1.2 % patient developed minor bleeding, 1.7% patient had cardiogenic shock, all-cause mortality were 2.0% & only 0.8% patient had in hospital stent thrombosis.

Conclusion: In Bangladeshi population, patients undergoing PCI, reduced dose Bivalirudin can be used for anticoagulation without increasing the risk of thrombosis and bleeding.

Key words: Bivalirudin, Percutaneous Coronary Intervention; Bleeding risk; Activated Clotting Time

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Introduction

Percutaneous coronary intervention (PCI) requires anticoagulation to prevent thrombotic complications. Rational and standardized application of anticoagulants is crucial for ensuring the efficacy and safety of interventional procedures [1]. Bivalirudin, a reversible direct thrombin inhibitor, is favored in many settings due to rapid onset, brief half-life, and reduced bleeding risk compared to heparin-based strategies. Major trials such as HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction), ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) and REPLACE-2 (Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events) have shown that Bivalirudin reduces bleeding without compromising ischemic protection in Western populations [2-4]. At present, the recommended dose of Bivalirudin is mainly based on European and American guidelines. It is widely accepted that the East Asian population has a lower risk of ischemia and a higher risk of bleeding than non-East Asian populations [5]. The cytochrome P450 2C19 (CYP2C19) gene has a high percentage of loss-of-function phenotypes in East Asian populations [6]. This finding suggests that East Asian patients have higher levels of platelet reactivity during clopidogrel therapy than platelet reactivity associated with Caucasians. High platelet reactivity (HPR)

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sug-gests a high risk of ischemia and low platelet reactivity (LPR) indicates a high risk of bleeding. Clinical evidence suggests that both HPR and LPR cutoff values are higher in East Asian patients than in Caucasians [7,8]. At the same level of platelet reactivity, East Asian populations are less prone to thromboembolic events but are prone to bleeding [9]. Asian cohorts frequently exhibit lower thrombotic risk and heightened bleeding susceptibility, leading to interest in reduced dosing strategies. Chinese single-center studies using 80% standard bolus without post-PCI infusion demonstrated non-inferior ischemic outcomes and similar bleeding rates as full-dose regimens. Meanwhile, multicenter Chinese data confirm favorable safety profiles in high-risk patients [5].

Our study investigates whether a reduced Bivalirudin regimen (two-thirds of recommended bolus dose, half dose of maintenance infusion) is safe and effective in a Bangladeshi cohort undergoing PCI.

Materials and methods

This single-center observational study was done in National Heart Foundation Hospital & Research Institute from May 2016 to March 2023. Purposive sampling was done. All patients undergoing PCI who were given Bivalirudin during the study period were included in this study. Bivalirudin was used because of each patient's risks of bleeding. The patients receive 3–4 h intravenous infusions of Bivalirudin after PCI. The exclusion criteria included the following: use of oral anticoagulants, such as rivaroxaban, before the procedure; patients with use of antiplatelet drugs other than aspirin and P2Y12 receptor antagonists, such as eptifibatide, contraindications to PCI or without PCI after coronary angiography and patients unwilling to give consent. Bivalirudin was adminis-tered in reduced dose: bolus dose (two thirds of the recommended dose of 0.75 mg/kg) followed by maintenance dose (half of recommended maintenance dose of 1.75 mg/kg /h).

Data Collection

Baseline demographic and clinical data were recorded, including age, gender, history of hypertension, diabetes, dyslipidemia, previous myocardial infarction (MI), and left ventricular ejection fraction (LVEF)and diagnosis: chronic coronary syndrome (CCS), acute coronary syndrome (ACS). Procedural variables (e.g., lesion complexity, use of Rotabalation, LMCA involvement) and laboratory values (serum hemoglobin, creatinine, LVEF) were also collected. The anticoagulant effect of Bivalirudin was monitored using the activated clotting time (ACT).

Outcome

The primary outcome was bleeding: major bleeding or hematoma needed blood transfusion, minor bleeding; cardiogenic shock, stent thrombosis, and all cause mortality. Adverse events were defined per standard criteria.

Statistical analysis

Categorical variables were compared using the $\chi 2$ or Fisher's exact test, and continuous data were compared using the Student's t-test. All statistical analyses were conducted using SPSS version 16.0.

Results

A total of 1143 patients who underwent PCI from May 2016 to March 2023 in the department of cardiology National Heart Foundation hospital & Research Institute and in whom Bivalirudin was used during the procedure were included. Mean age of the study population was 58.26±11.38 years. Majority of the patients were male (54.9%) & rest are female (45.1%). Among the lab parameters mean Hb% was 12.62±1.60 gm/dl, serum creatinine was 1.302±.4596; mean LVEF (%) was 47.42±9.33 (Table: 1).

Table 1: Baseline characteristics of study population (n=1143)

Variable	Mean±SD/Percentage
Age	58.26±11.38 years
Sex	
Male	54.9%
Female	45.1%
Hb% (gm/dl)	12.62±1.60
S. Creatinine(mg/dl)	1.302±.4596
LVEF (%)	47.42±9.330
Diagnosis:	
CCS	58.2%
ACS	41.8%

Majority of patients who underwent PCI were CCS (58.2%) while rest of the patients were ACS (41.8%). Among the ACS patients 16.4% patients were STEMI, 20.10% were NSTEMI & 5.2% patients were unstable angina (Figure: 1).

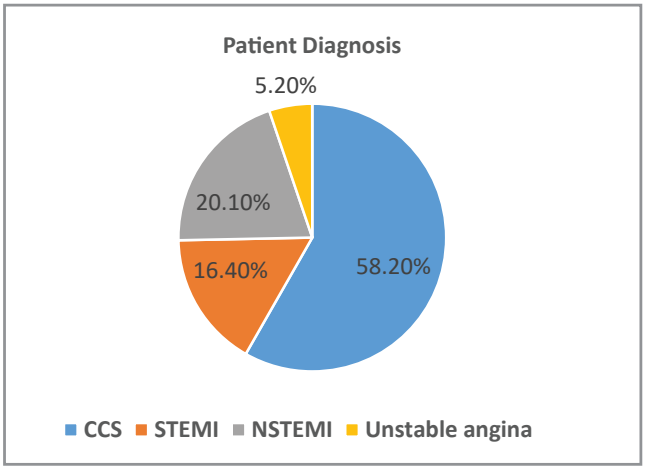


Figure 1: Pie Chart showing the diagnosis of patients underwent PCI

Regarding the risk factors of the study population, hypertension was the most prevalent (81.9%) followed by dyslipidemia 57.4% & diabetes mellitus (55.2%). 48.6% patients were obese & only 16% patient had family H/O coronary artery disease(CAD) (Figure : 2).

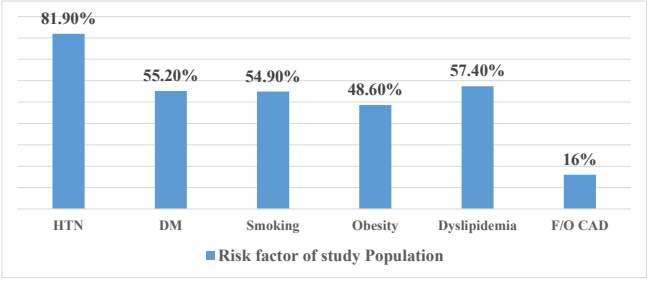


Figure 2: Risk factor distribution among the study population (n=1143)

Among the study population, 600(52.5%) patients underwent multivessel PCI & 543(47.5%) patients underwent single vessel PCI. Among these patients left main PCI were 219(19.2%) & 53(4.60%) patients underwent Rotabalation (Figure : 3).

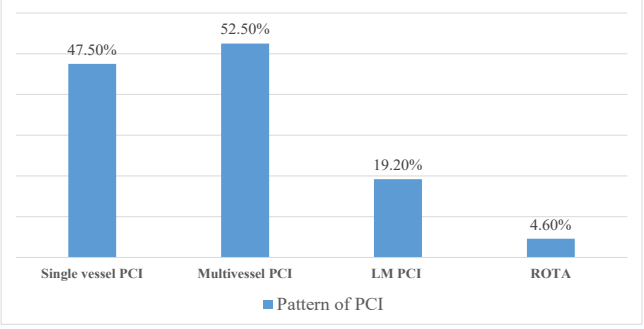


Figure 3: pattern of PCI among the study population (n=1143)

ACT value after 5 min: Mean ACT value of the study population was 298.38 ±68.51sec.

Regarding the in-hospital outcomes, 20(1.7 %) patients developed major bleeding or hematoma needed blood transfusion, 14 (1.2 %) patients developed minor bleeding, 20(1.7%) patients had cardiogenic shock, in hospital death were 2.0% (23 patients) & only 9 (0.8%) patients had in hospital stent thrombosis (Figure : 4).

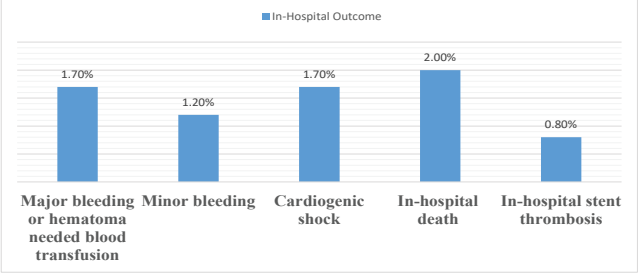


Figure 4: In-hospital outcomes among the study population (n=1143)

Discussion

In this single-center, observational study involving patients undergoing PCI, we found that reduced dose of the recommended dose of Bivalirudin can also achieve clinical effects.

In our study mean age of the study population was 58.26±11.38 years & majority of patients were male. Hypertension was the common risk factors among the study populations. In a study done by Li et al. among the Chinese populations, in whom Bivalirudin were used; found patients were older (mean age 73.4 ± 5.9 years and hypertension was the common risk factors and male predominant [10]. As in southeast Asian region, CAD prevalence is younger in comparison to European Population So early presentation of our cases.

Bivalirudin, a com¬monly used anticoagulant in clinical practice, does not activate platelets and does not bind to plasma proteins; it has linear pharmacokinetics with a short half-life of Bivalirudin has no inhibitors, and once bleeding occurs, there is no option aside from discontinuation of the drug. The Euro¬pean Society of Cardiology guidelines state that the ACT should be maintained at 200-250s if a glycopro¬tein inhibitor (GPI) is applied during PCI, and the ACT should be maintained at 250-350s if a GPI is not rou¬tinely applied [11,12]. In our patients mean ACT value of the study population was 298.38 ±68.51s. In a study done by Wang et al. [5] among the Chinese population found ACT value was 349±47.5s in whom they used 80% of recommended Bivalirudin dose.

Regarding the in-hospital outcomes, 1.7 % of patients developed major bleeding or hematoma needed blood transfusion, 1.2 % of patients developed minor bleeding, 1.6% patient had cardiogenic shock, all-cause mortality was 2.0% & only 0.8% of patients had in hospital stent thrombosis. In Chinese population, major bleeding with Bivalirudin was 2.2%, all-cause mortality was 4.5%, 1.6% patients had MI & 2.4% patient needed revascularization. They observed 30 days major adverse cardiovascular events (MACE), but we just monitored patients in hospital outcomes [10]. Though our bleeding rates are similar with the Chinese populations, Mortality rates are higher in Chinese populations. In another study done by Wang et al. among the Chinese population, found that all bleeding rate was lower (4.4%) in reduced dose Bivalirudin dose patients in compared to heparin [5]. In our population, 2.9% of patients developed bleeding out of them 1.7% had major bleeding & 1.2% had minor bleeding. Another meta-analysis for AMI patients with PCI shows that Bivalirudin decreases major bleeding compared to heparin (2.3% vs. 3.5%) [2]. Another meta-analysis for AMI patients with PCI shows that Bivalirudin decreases major bleeding compared to heparin (2.3% vs. 3. 5%) [13]. The results of the MATRIX (Minimizing Adverse Haemorrhagic

Events by TRansradial Access Site and Systemic Implementation of angioX) study showed that the 30-day incidence of acute stent thrombosis in the group that did not have continuous post procedural infusion was 1.0% which is similar with our study (0.8% stent thrombosis) [14].
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Therefore, the results of this study were applicable to patients undergoing PCI in terms of low in hospital bleeding events without increasing significant thrombotic events. Further studies are needed regarding the safety and efficacy of reduced-dose Bivalirudin in patients especially long term follow up (MACE, bleeding)

Cost and Clinical Practicality Dose reduction can reduce drug cost, important in resource-limited settings, while maintaining clinical benefits.

Limitation

This was a single-center study. Observational design without control group limits causality; and no long-term follow-up or randomized comparison to full-dose regimens were analyzed.

Conclusion

A reduced-dose Bivalirudin regimen (⅔ bolus, ½ maintenance infusion) among Bangladeshi patients undergoing PCI was associated with low in hospital bleeding, thrombotic events, and mortality. These results warrant multicenter randomized trials in South Asian populations to establish optimal, tailored dosing guidelines for use of Bivalirudin among the PCI patients.

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