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Validation of Long-term Benefits of Bivalirudin vs. Unfractionated Heparin in Routine Clinical Practice after Percutaneous Coronary Intervention

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Abstract

Randomized controlled trials have shown improved short-term bleeding outcomes for bivalirudin relative to unfractionated heparin (UFH) in patients undergoing percutaneous coronary intervention (PCI) for stable angina and acute coronary syndrome. This study analyzed the impact of bivalirudin based anticoagulation strategy versus UFH based anticoagulation strategy on long-term bleeding complications and major adverse cardiac events in patients undergoing PCI in routine clinical practice. Between September 2005 and April 2009, 3367 consecutive patients who underwent PCI for stable angina or Non ST-segment elevation acute coronary syndrome at Brigham and Women's Hospital were studied. Of these patients, 2228 (66%) patients received UFH and 1139 (34%) received bivalirudin. We compared the bleeding complication and major adverse cardiac event rates at discharge, 30-days and 1-year. In a propensity-score matched analysis, bivalirudin based anticoagulation strategy was associated with lower bleeding complications at 30 days (7.0% vs. 13.7%, p=0.001) and 1-year (12.7% vs.18.9%, p=0.013). The major adverse cardiac event rates was not significantly different between the groups at discharge, 30-days and 1-year (6.4% vs. 8.3%, p=0.103; 9.4% vs.10.9%, p=0.449; 12.1% vs.14.8%, p=0.235 respectively). There was no difference in all-cause mortality rates between the two groups (0.9% vs. 0.8%, p=0.808 at discharge; 1.9% vs. 3.6%, p=0.112 at 30-days; 3.6% vs. 5.5%, p=0.195 at 1 year). In conclusion, in a real-world cohort of patients undergoing PCI, Bivalirudin based anticoagulation strategy is associated with significant reduction in the risk of bleeding complications after 30-days and 1-year compared to UFH based anticoagulation strategy with no increase in the risk for major adverse cardiac events.

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Introduction

Optimal antithrombotic treatment in patients undergoing percutaneous coronary intervention (PCI) is crucial to balance the risk of post-PCI bleeding versus ischemic complications. Bivalirudin, a direct thrombin inhibitor has been extensively investigated as an intra-procedural antithrombotic therapy in patients with stable angina, Non ST-segment elevation acute coronary syndrome (NSTE ACS), and ST-segment elevation myocardial infarction (STEMI). [1–4] Bivalirudin, when used with or without glycoprotein IIb/IIIa inhibitors (GPI) during PCI has been found to be superior to Unfractionated heparin (UFH) with or without GPI in reducing 30-day bleeding complications without significant increase in the rate of ischemic events. [1–4] Moreover, studies have shown that Bivalirudin is non-inferior to UFH for the rates of 1-year mortality.[5–7] Other studies have shown the 1-year bleeding and mortality rates to be superior in bivalirudin treated patients undergoing PCI for acute ST-segment elevation myocardial infarction (STEMI) compared with UFH treated patients. [8] Whether this bleeding safety profile with bivalirudin over UFH in patients with stable angina and NSTE ACS is preserved at 1 year in routine clinical practice is not consistently reported. We sought to compare the risk of bleeding and major adverse cardiac events (MACE) at discharge, 30-days and 1-year, in a prospective cohort of patients who received UFH based or bivalirudin based anticoagulation strategy during PCI for stable angina or NSTE ACS in routine clinical practice.

Methods

We prospectively evaluated consecutive patients undergoing PCI between September 2005 and April 2009 at Brigham and Women's Hospital. All patients who received either UFH-based or bivalirudin-based anticoagulation at the time of PCI for stable angina, or NSTE ACS were included for analysis. Exclusion criteria included STEMI, chronic total occlusions, and patients who received both heparin and bivalirudin. If a patient had multiple PCI procedures during their admission, only the index procedure was included in the analysis. Patients were divided into 3 cohorts based on the length of follow-up: inpatients (in-patient follow-up group), patients who had 30-day follow-up (30-day group), and patients who had 1-year follow-up (1-year group). Informed written consent was obtained from all of the patients, and the study was approved by the local institutional review board.

A prospective catheterization laboratory database, based on the American College of Cardiology-National Cardiovascular Data Registry data collection tool, was used to record clinical and procedural data elements for each patient. [9,10] Thirty-day and 1-year outcomes were collected for PCI cases performed from September 2006 to March 2009 and September 2005 and April 2008, respectively. The 30-day and 1-year outcomes were obtained through telephone interviews where patients were surveyed regarding post procedural complications including bleeding, blood transfusions, repeat hospitalizations, access site complications, repeat cardiac catheterization or PCI, and myocardial infarction.

Percutaneous coronary interventions were performed according to standard protocol. [11–13] Unless contraindicated, all patients who underwent PCI received aspirin and clopidogrel according to the standard American College of Cardiology/American Heart Association recommendations. [11,12] Bivalirudin was recommended as the anticoagulant of choice for patients treated for stable coronary artery disease and low risk unstable angina. Patients presenting with high-risk unstable angina and non-ST elevation myocardial infarction were treated with bivalirudin at the discretion of the interventional cardiologist. Patients undergoing thrombectomy or rotational atherectomy, and those patients already on heparin with an activated clotting time greater than 180 seconds were recommended to be treated with UFH. Final anticoagulation treatment decisions were made at the discretion of the treating interventional cardiologist. Patients in the bivalirudin group received a bolus of 0.75 mg/kg of

bivalirudin before the guide wire crossed the lesion followed by an infusion of 1.75 mg/kg/hour for the duration of the procedure. Patients in the UFH group received a bolus of 60–80 units/kg plus an infusion of 12 units/kg/hour to achieve an activated clotting time of 250 to 300 seconds during PCI. When a GPI was considered, either eptifibatide or abciximab was used at standard recommended doses. Patients who received GPI along with UFH or Bivalirudin were also included in our study as such anticoagulation strategy was compared in the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) and Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE-2) trials. [1,2] When stenting occurred, it was at the discretion of the treating physician as to whether the patient received a bare-metal or drug-eluting stent. Standard post procedural therapy included aspirin (81mg to 325mg indefinitely), and clopidogrel (75mg per day for at least 1 month, in patients with bare-metal stents, and for at least 12 months in patients with drug-eluting stents, unless contraindicated).

Primary outcomes of the study included a composite bleeding endpoint at discharge, 30-days and 1-year. Secondary outcome was defined as a composite outcome of death, recurrent myocardial infarction and repeat revascularization (MACE). Composite bleeding endpoint for the inpatient cohort was defined as any access site bleeding (defined as external bleeding from the access site requiring a blood transfusion and/or prolongation of the hospital stay, and/or cause a drop in hemoglobin > 3.0 gm/dl; or a hematoma >10 cm for femoral access or >2 cm for radial access; or >5 cm for brachial access) or any bleeding from a gastrointestinal, genitourinary, retroperitoneal or unknown source that resulted in >3gms/dl drop in hemoglobin and/or requiring blood transfusion and/or prolongation of hospital stay. Composite bleeding endpoint for the 30-day and 1-year follow-up cohort was defined as any bleeding requiring hospitalization or blood transfusion or physician visit/intervention. Peri-procedural myocardial infarction was defined by the presence of at least 1 of the following criteria: 1. Evolutionary ST-segment elevation, development of new Q-waves in 2 or more contiguous ECG leads, or new left bundle branch. 2. Biochemical evidence of myocardial necrosis (Creatine Kinase-MB fraction > 3x the upper limit of normal).

Statistical analysis was performed using the Statistical Analysis System version 9.2 (SAS Institute Inc., Cary, NC) and SPSS for Windows version 17.0 (SPSS Inc., Chicago, IL). Data are expressed as mean ± S.D. for continuous variables and as percentages for categorical variables. Student's t test was used to compare continuous variables, and the Chi square test or Fisher's Exact Test was used to compare categorical variables. A p value <0.05 was considered to indicate statistical significance. To prevent selection bias, a propensity-score matching analysis using greedy matching protocol was performed for the propensity to use a given antithrombotic agent. [14,15] To calculate the propensity score, the following 31 variables were entered into a non-parsimonious logistic regression model [16]: Age, body mass index, female, smoking, diabetes, hypertension, hyperlipidemia, prior myocardial infarction, prior PCI, prior coronary artery bypass graft, history of congestive heart failure, history of cerebro-vascular disease, history of peripheral vascular disease, presence of cardiogenic shock, renal failure, salvage PCI, non ST-segment elevation myocardial infarction, unstable angina, high risk lesion, left main coronary artery PCI, presence of coronary thrombus, International normalized ratio, calcified coronary disease, use of drug-eluting stent, number of diseased vessels, rotablator use, maximum diameter of the vascular access sheath, access via femoral artery, access via radial artery, use of femoral venous access, use of vascular closure device. Subjects were matched using caliper width equal to 0.6 of the standard deviation of the logit of the propensity score. [17–19]

Results

The study patient flow for inclusion and follow-up, and the results of the propensity-score matching are shown in Figure 1. Of the 4825 patients who underwent PCI between 09/01/2005 to 04/30/2009, 1458 patients were excluded from this analysis based on the exclusion criteria noted above. Of the 3367 patients included in the final analysis, 2228 (66%) patients had received UFH based anticoagulation strategy and 1139 patients (34%) had received bivalirudin based anticoagulation strategy during PCI. GPI was used in 877 patients (39%) in the UFH group and in 44 patients (4%) in the Bivalirudin group. Inhospital outcomes were available for the entire cohort. One year follow-up interviews were begun in September 2006 for patients who underwent PCI the year prior. Therefore, 30-day outcomes were not available for the first year. Similarly, 1-year outcomes were not available for the cases performed in the last twelve months of the study period. As a result, 2224 patients were eligible for 30-day follow up and 2590 patients were eligible for 1-year follow up. The response rate for the 30-day and 1-year follow up was 67% (1488/2224) and 58% (1491/2590) respectively. A propensity-score matching algorithm successfully matched a total of 59% (1986/3367) of eligible inpatients, 63% (932/1488) of eligible patients with 30-day follow up, and 59% (878/1491) of eligible patients with 1-year follow up.

Baseline characteristics of the study cohort and the propensity-score matched in-patient cohort are shown in Table 1. After propensity-score matching, baseline characteristics were more evenly distributed, though there were still a higher proportion of UFH treated patients with GPI (30.4% vs. 4.1%, $p<0.001$) or rotational atherectomy (5.0% vs. 1.8%, $p<0.001$). The difference in the baseline characteristics of patients who did and did not respond to follow-up telephone inquiries is shown in Table 2.

The primary and secondary outcomes of this analysis for both the entire patient cohorts as well as the propensity-score matched groups are summarized in Table 3, and Figures 2 and 3. The composite bleeding end point during the in-hospital stay was found to be higher in the UFH group than in the bivalirudin group (4.8% vs. 1.8%, $p<0.001$ in the unadjusted patient cohort and 3.5% vs. 2.1%, $p=0.058$ in the propensity-score matched cohort). This difference in the composite bleeding end point was largely due to higher incidence of non-access site bleeding (bleeding from unknown location requiring a transfusion and/or prolong the hospital stay, and/or cause a drop in hemoglobin >3.0 gm/dl) noted in the UFH group than in the bivalirudin group. All other bleeding outcomes were not significantly different between the groups. At 30-days and 1-year, bleeding complications were significantly higher in the UFH group than in the bivalirudin group after propensity-score matching (13.7% vs. 7.1%, $p=0.001$ at 30-days and 18.9% vs. 12.8%, $p=0.013$ at 1-year). This difference in the composite bleeding end point at 30-days and 1-year was largely due to the bleeding that required physician visit or intervention.

The MACE rate was not significantly different between the groups at discharge, 30-days and 1-year (Table 3). All-cause mortality was not significantly different after propensity-score matching (3.6% vs. 1.9%, $p=0.112$ at 30-days and 5.5% vs. 3.6%, $p=0.195$ at 1-year). At discharge, peri-procedural myocardial infarction was significantly higher in the bivalirudin group (7.5% vs. 5.1%, $p=0.027$) but significantly more repeat PCI procedures were performed in the UFH group (1% vs. 0%, $p=0.002$).

Discussion

This study assessed the frequency of bleeding complications and MACE rates at discharge, 30-days and at 1year in patients without STEMI who received either an UFH-based or bivalirudin-based anticoagulation strategy during PCI in routine clinical practice. The results

revealed a significantly lower incidence of bleeding complications at 30-days and 1-year in the bivalirudin group with similar MACE outcomes when compared with UFH based anticoagulation strategy.

Our data is consistent with data from randomized clinical trials including the Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment (ISAR-REACT 3) trial, [3,7,20] that showed a significantly lower bleeding with bivalirudin when compared with UFH in patients with stable and unstable angina. The similar mortality outcomes in the two groups observed in this study are consistent with findings from the ACUITY [1,5] and the REPLACE-2 trials, [2,6] which evaluated patients who received UFH or bivalirudin in conjunction with GPI in similar clinical situations. Similar bleeding and mortality benefits were also observed in patients who had PCI for ST-segment elevation myocardial infarction in the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZON-AMI) trial. [4,8] The reduced rates of bleeding after PCI with bivalirudin in routine clinical practice is an important finding, as multiple studies have reported a strong association between bleeding complications and mortality following PCI. [21–24] In the REPLACE-2 trial, which included elective and lower-risk ACS patients undergoing PCI, [25] there were significantly higher mortality rates at 30 days, 6 months, and 1 year for patients who had bleeding complications compared with those who did not.

Although a non-significant trend towards higher peri-procedural MI rates with bivalirudin is noted in major trials [1,2,3], we noted a significantly higher rate of peri-procedural MI with bivalirudin at discharge. A lower proportion of GPI treated patients and the choice of stent use in the bivalirudin group in our study might have contributed to a higher peri-procedural MI in this group.

The 1-year findings of our study presented herein validate the durable efficacy of bivalirudin in routine clinical practice, which extends the observation from selected populations included in randomized controlled trials. Not only was there no excess of MACE rates with bivalirudin therapy, but also death rates trended lower in the bivalirudin group. This study showed a reduced bleeding complication rate observed at 30-days and at 1-year in the bivalirudin group, and there was no significant difference in the subsequent MACE rates both at 30-days and 1-year in the propensity-matched group. The lack of a significant difference in mortality between the bivalirudin and UFH treated patients in this study may have been due to a lack of power due to the sample size following the comprehensive propensity-score matching.

The acute and long-term findings of our study cannot be extrapolated to patient groups that were excluded from this study, principally those undergoing primary PCI for acute myocardial infarction or those with total occlusion. Despite exclusion of these patients, however, 30-day and 1-year MACE rates in our study were similar to those in other recent PCI trials. This study is limited by the inherent bias of an observational cohort study and non-randomized clinical data, as well as by a significant loss to follow up. There were also differences in the characteristics of the patients who followed up for 30-days but who did not participate in 1 year follow up. These results must also be interpreted in light of potential hidden bias of the propensity-score matching, as it may not account for all confounding variables.

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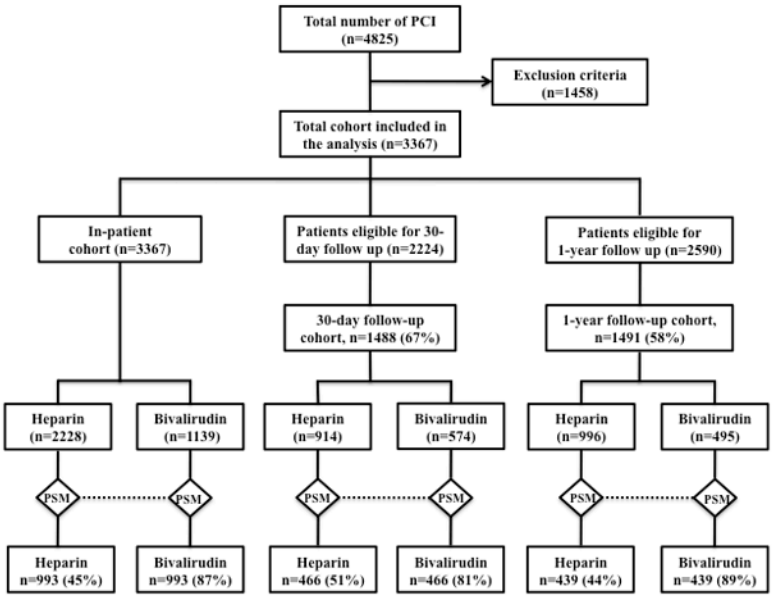

Figure 1.
Flow-Chart Showing The Enrolment And Follow-Up Of Patients In The Study. PCI = Percutaneous Coronary Intervention, PSM = Propensity-Score Matching

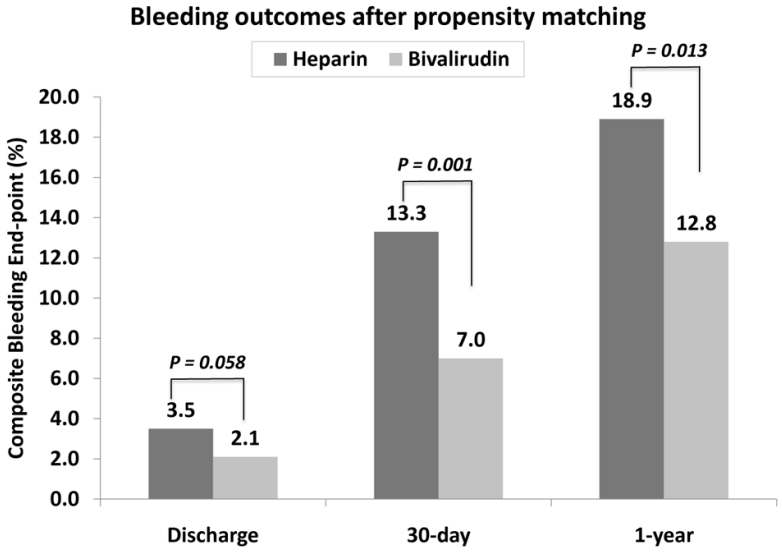

Figure 2.
Bleeding outcomes after propensity-score matching

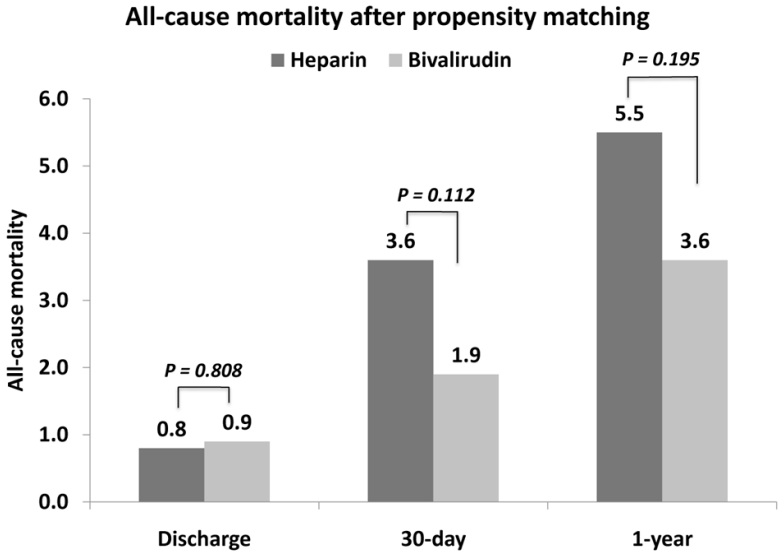

Figure 3.
All-cause mortality after propensity-score matching.

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Table 1

Baseline Characteristics Of All In-Patients In The Unfractionated Heparin And Bivalirudin Group

Variable	Before propensity-score matching			After propensity-score matching		
	Heparin (N=2228)	Bivalirudin (N=1139)	P Value	Heparin (N=993)	Bivalirudin (N=993)	P Value
Age (years), mean ± SD	68.2 ± 12	68.6 ± 11.7	0.304	68.6 ± 11.3	68.9 ± 11.7	0.506
Female	678 (30.4%)	339 (29.8%)	0.690	294 (29.6%)	303 (30.5%)	0.660
BMI (kg/m^2), mean ± SD	29.4 ± 6.2	29.2 ± 5.5	0.304	29.1 ± 5.35	29.2 ± 5.6	0.829
Diabetes mellitus	765 (34.3%)	407 (35.7%)	0.421	356 (35.9%)	348 (35%)	0.707
Hx of Renal Insufficiency	164 (7.4%)	70 (6.1%)	0.190	71 (7.2%)	63 (6.3%)	0.474
Renal Dialysis	68 (3.1%)	16 (1.4%)	0.004	26 (2.6%)	15 (1.5%)	0.083
CVD History	224 (10.1%)	118 (10.3%)	0.781	108 (10.9%)	101 (10.2%)	0.609
Prior PCI	694 (31.1%)	391 (34.3%)	0.062	339 (34.1%)	340 (34.2%)	0.962
Prior CABG	474 (21.3%)	215 (18.9%)	0.103	205 (20.6%)	200 (20.1%)	0.781
Prior MI	709 (31.8%)	359 (31.5%)	0.858	332 (33.4%)	317 (31.9%)	0.473
CSA History	601 (27%)	514 (45.1%)	<0.001	413 (41.6%)	420 (42.3%)	0.750
HF History	358 (16.1%)	155(13.6%)	0.06	143 (14.4%)	136 (13.7%)	0.651
Hypertension	1909 (85.7%)	1020(89.6%)	0.002	891 (89.7%)	882 (88.8%)	0.514
Hyperlipidemia	1978 (88.8%)	1060 (93%)	<0.001	917 (92.3%)	919 (92.5%)	0.865
Smoker	1505 (67.5%)	744 (65.3%)	0.194	663 (66.8%)	655 (66%)	0.704
PVD History	309 (13.9%)	143 (12.6%)	0.290	136 (13.7%)	127 (12.8%)	0.551
NSTEMI	736 (33%)	128(11.2%)	<0.001	136 (13.7%)	128 (12.9%)	0.597
Unstable angina	506 (22.7%)	201 (17.6%)	0.001	199 (20%)	198 (19.9%)	0.955
GPI Use	877 (39.4%)	44 (3.9%)	<0.001	302 (30.4%)	41 (4.1%)	<0.001
High Risk Lesion	630 (28.2%)	184 (16.2%)	<0.001	173 (17.4%)	180 (18.1%)	0.681
Left Main PCI	95 (4.3%)	26 (2.3%)	0.003	25 (2.5%)	26 (2.6%)	0.887
PCI with no stent	152 (6.8%)	76 (6.7%)	0.870	78 (7.9%)	71 (7.2%)	0.551
Drug-eluting stent	1729 (77.6%)	868 (76.2%)	0.361	752 (75.7%)	756 (76.1%)	0.834
Thrombus	184 (8.3%)	38 (3.3%)	<0.001	41 (4.13%)	35 (3.52%)	0.452
No. of narrowed coronary arteries	1.78±1.11	1.78±1.04	1.00	1.78±1.1	1.8±1.04	0.754
Calcified Lesion	204 (9.2%)	52 (4.6%)	<0.001	55 (5.5%)	51 (5.1%)	0.690
Rotablator Use	126 (5.7%)	18 (1.6%)	<0.001	50 (5.0%)	18 (1.8%)	<0.001

Variable	Before propensity-score matching			After propensity-score matching		
	Heparin (N=2228)	Bivalirudin (N=1139)	P Value	Heparin (N=993)	Bivalirudin (N=993)	P Value
Radial artery Access	152(6.8%)	19(1.7%)	<0.001	22 (2.22%)	19 (2%)	0.636
Venous Access	353 (15.8%)	154 (13.5%)	0.075	152 (15.3%)	144 (14.5%)	0.614
Vascular Closure Device	1752(78.7%)	958(84.1%)	<0.001	826 (83.2%)	838 (84.4%)	0.465

All values are expressed in n (%) unless stated otherwise. BMI= Body Mass Index, CABG = Coronary Artery Bypass Grafting, CSA = Chronic Stable Angina, CVD = Cardiovascular Disease, GPI=Glycoprotein IIb/IIIa Inhibitor, HF = Heart Failure, MI= Myocardial Infarction, NSTEMI = Non ST-segment elevation myocardial infarction, PCI= Percutaneous Coronary Intervention, PVD = Peripheral Vascular Disease.

Table 2

Table Showing Difference In The Baseline Characteristics Between The Patients Who Had Follow Up And Patients Who Did Not Have Follow Up (30-Day Follow Up And 1-Year Follow Up)

Variable	30-day follow up			1-year follow up		
	30-day follow-up (N=1488)	No 30-day follow-up (N=736)	P value	1-year follow-up (N=1491)	No 1-year follow-up (N=1099)	P value
Age (years), mean ± SD	68.2±11.6	67.4±12.7	0.139	69.4±11.1	67.9±12.7	0.001
Female	451 (30.3%)	230 (31.2%)	0.651	428 (28.7%)	349 (31.8%)	0.094
BMI (kg/m^2), mean ± SD	29.4±5.9	29.4±6.4	0.735	29.4±6	29.1±5.8	0.217
Diabetes mellitus	525 (35.3%)	272 (36.9%)	0.420	489 (32.8%)	398 (36.2%)	0.070
Hx of Renal Insufficiency	103 (6.9%)	65 (8.8%)	0.109	98 (6.6%)	72 (6.5%)	0.983
Renal Dialysis	33 (2.2%)	25 (3.4%)	0.101	30 (2%)	25 (2.3%)	0.647
CVD History	144 (9.7%)	83 (11.3%)	0.241	150 (10.1%)	131 (11.9%)	0.133
Prior PCI	498 (33.5%)	237 (32.2%)	0.550	476 (31.9%)	352 (32%)	0.955
Prior CABG	319 (21.4%)	152 (20.7%)	0.669	313 (21%)	219 (19.9%)	0.507
Prior MI	484 (32.5%)	255 (34.6%)	0.318	437 (29.3%)	365 (33.2%)	0.034
CSA History	523 (35.1%)	226 (30.7%)	0.037	525 (35.2%)	333 (30.3%)	0.009
HF History	222 (14.9%)	136 (18.5%)	0.032	206 (13.8%)	163 (14.8%)	0.465
Hypertension	1320 (88.7%)	646 (87.8%)	0.516	1290 (86.5%)	940 (85.5%)	0.473
Hyperlipidemia	1372 (92.2%)	665 (90.4%)	0.139	1337 (89.7%)	980 (89.2%)	0.683
Smoker	1010 (67.9%)	484 (65.8%)	0.317	1010 (67.7%)	719 (65.4%)	0.216
PVD History	212 (14.2%)	113 (15.4%)	0.487	182 (12.2%)	159 (14.5%)	0.093
NSTEMI	384 (25.8%)	219 (29.8%)	0.049	332 (22.3%)	303 (27.6%)	0.002
Unstable angina	278 (18.7%)	164 (22.3%)	0.045	302 (20.3%)	264 (24%)	0.022
GPI Use	319 (21.4%)	181 (24.6%)	0.094	424 (28.4%)	359 (32.7%)	0.021
High Risk Lesion	338 (22.7%)	172 (23.4%)	0.730	360 (24.1%)	286 (26%)	0.275
Left Main PCI	53 (3.6%)	19 (2.6%)	0.219	62 (4.2%)	33 (3%)	0.122
PCI with no stent	117 (7.9%)	47 (6.4%)	0.210	113 (7.6%)	71 (6.5%)	0.274
Drug-eluting stent	1051 (70.6%)	525 (71.3%)	0.733	1168 (78.3%)	848 (77.2%)	0.476
Thrombus	89 (6%)	51 (6.9%)	0.701	83 (5.6%)	74 (6.7%)	0.257
No. of narrowed coronary arteries	1.8±1.1	1.8±1.1	0.299	1.8±1.1	1.8±1.1	0.237
Calcified disease	104 (7%)	65 (8.8%)	0.123	125 (8.4%)	73 (6.6%)	0.099
Rotablator use	3 (0.2%)	0	0.223	9 (0.6%)	4 (0.4%)	0.394

Variable	30-day follow up			1-year follow up		
	30-day follow-up (N=1488)	No 30-day follow-up (N=736)	P value	1-year follow-up (N=1491)	No 1-year follow-up (N=1099)	P value
Radial artery Access	74 (4.9%)	38 (5.2%)	0.847	64 (4.3%)	38 (3.4%)	0.280
Venous Access	226 (15.2%)	103 (14%)	0.456	233 (15.6%)	169 (15.4%)	0.862
Vascular Closure Device	1210 (81.3%)	608 (82.6%)	0.458	1210 (81.2%)	913 (83%)	0.209

All values are expressed in n (%) unless stated otherwise. BMI= Body Mass Index, CABG = Coronary Artery Bypass Grafting, CSA = Chronic Stable Angina, CVD = Cardiovascular Disease, GPI=Glycoprotein IIb/IIIa Inhibitor, HF = Heart Failure, MI= Myocardial Infarction, NSTEMI = Non ST-segment elevation myocardial infarction, PCI= Percutaneous Coronary Intervention, PVD = Peripheral Vascular Disease.

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Table 3

Primary End-Points In Unfractionated Heparin And Bivalirudin Group (Before And After Propensity-Score Matching)

	Before propensity-score matching			**After propensity score matching**		
In-patient outcomes	**N=2228**	**N=1139**	**N=3367**	**N= 993**	**N= 993**	**N=1986**
	Heparin	**Bivalirudin**	**P value**	**Heparin**	**Bivalirudin**	**P-value**
Composite Bleeding End-point	106 (4.76%)	21 (1.84%)	<0.001	35 (3.52%)	21 (2.11%)	0.058
Gastrointestinal Bleeding	11 (0.49%)	2 (0.17%)	0.159	2 (0.2%)	2 (0.2%)	1.00
Retroperitoneal Bleeding	5 (0.22%)	1 (0.08%)	0.374	1(0.1%)	1 (0.1%)	1.00
Access site hematoma	9 (0.4%)	2 (0.17%)	0.272	2(0.2%)	2 (0.2%)	1.00
Genitourinary Bleeding	1 (0.04%)	0	0.475	0	0	-
Other Bleeding*	79 (3.54%)	16 (1.4%)	<0.001	30 (3.02%)	16 (1.61%)	0.037
Bleeding requiring Blood Tx.	35 (1.58%)	6 (0.53%)	0.009	6 (0.6%)	6 (0.6%)	1.00
Death/MI/Revascularization	157 (7%)	97 (8.5%)	0.127	64 (6.4%)	83 (8.3%)	0.103
Peri-procedural MI	121 (5.4%)	89 (7.8%)	0.007	51 (5.1%)	75 (7.5%)	0.027
Repeat PCI	22(0.9%)	1 (0.08%)	0.003	10 (1%)	0	0.002
Coronary artery bypass graft	2 (0.09%)	0	0.312	0	0	-
Death	25 (1.12%)	9 (0.8%)	0.362	8 (0.81%)	9 (0.91%)	0.808
30-Day outcomes	N=914	N=574	N= 1488	N= 466	N= 466	N=932
	Heparin	Bivalirudin	P value	Heparin	Bivalirudin	P value
Composite Bleeding End-point	121 (13.2%)	41 (7.14%)	<0.001	64 (13.73%)	33(7.08%)	0.001
Hospitalization due to bleeding	14 (1.53%)	7 (1.22%)	0.619	10 (2.14%)	4 (0.85%)	0.106
Bleeding requiring blood Tx.	9 (0.98%)	7 (1.22%)	0.669	5 (1.07%)	4 (0.85%)	0.738
Death/MI/Revascularization	98 (10.7%)	59 (10.3%)	0.786	44 (9.4%)	51 (10.9%)	0.449
Myocardial Infarction	41 (4.5%)	42 (7.3%)	0.021	22 (4.7%)	36 (7.7%)	0.058
Repeat PCI	21 (2.3%)	8 (1.4%)	0.220	7 (1.5%)	7 (1.5%)	1.000
Coronary artery bypass graft	2 (0.22%)	2 (0.35%)	0.638	2 (0.42%)	1 (0.21%)	0.563
Death	42 (4.6%)	9 (1.57%)	0.002	17 (3.64%)	9 (1.93%)	0.112
1-Year Outcomes	N=996	N=495	N=1491	N= 439	N= 439	N=878
	Heparin	Bivalirudin	P value	Heparin	Bivalirudin	P value

	Before propensity-score matching			After propensity score matching		
In-patient outcomes	**N=2228**	**N=1139**	**N=3367**	**N= 993**	**N= 993**	**N=1986**
	Heparin	**Bivalirudin**	**P value**	**Heparin**	**Bivalirudin**	**P-value**
Composite Bleeding End-point	186 (18.7%)	61 (12.32%)	0.002	83 (18.9%)	56 (12.75%)	0.013
Hospitalization due to bleeding	35(3.51%)	19(3.83%)	0.752	16 (3.64%)	17 (3.87%)	0.859
Bleeding requiring blood Tx.	19 (1.9%)	9 (1.81%)	0.905	6 (1.36%)	7 (1.59%)	0.780
Death/MI/Revascularization	137 (13.7%)	68 (13.7%)	0.993	53 (12.1%)	65 (14.8%)	0.235
Myocardial Infarction	51 (5.1%)	37 (7.5%)	0.069	21 (4.8%)	35 (8%)	0.053
Repeat PCI	27 (2.7%)	10 (2%)	0.419	8 (1.8%)	9 (2%)	0.807
Coronary artery bypass graft	7(0.7%)	5 (1.01%)	0.532	2 (0.45%)	5 (1.13%)	0.255
Death	59 (5.92%)	16 (3.23%)	0.025	24 (5.46%)	16 (3.64%)	0.195

All values are expressed in n (%). Blood Tx = Blood transfusion, MI = Myocardial Infarction, PCI = Percutaneous Coronary Intervention.

* Other Bleeding = Bleeding occurred at other or unknown locations (than mentioned above) during or after the cath lab visit until hospital discharge that required a transfusion and/or prolong the hospital stay, and/or cause a drop in hemoglobin >3.0 gm/dl.