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Impact of Bivalirudin on Patients with Acute Coronary Syndrome Undergoing Rotational Atherectomy in Real-Life Setting: A Retrospective Cohort Study

ABSTRACT

Background: No evidence exists on the impact of bivalirudin in patients with the acute coronary syndrome undergoing rotational atherectomy. This study aimed to evaluate the impact of bivalirudin on patients with acute coronary syndrome undergoing rotational atherectomy.

Methods: This was a retrospective cohort study conducted in our hospital between January 2017 and December 2019. The study included patients with acute coronary syndrome undergoing rotational atherectomy. Furthermore, 2 cohorts were included in this study (bivalirudin cohort and control cohort unfractionated heparin). The primary endpoint was in-hospital net adverse clinical events. The secondary endpoint was all-cause mortality at 23 months.

Results: The study included 157 patients with 33 (21.0%) in the bivalirudin cohort and 124 (79.0%) in the control cohort. Net adverse clinical events during hospitalization in the bivalirudin cohort were higher than that in the control cohort [9 (27.3%) vs. 14 (11.3%), $P = .021$]. However, there was no significant difference in all-cause mortality at 23 months between the 2 cohorts [25 (20.2%) vs. 10 (30.3%), $P = .214$]. After adjusting for potential confounders, the usage of bivalirudin was not associated with net adverse clinical event (odds ratio = 0.90; 95% CI: 0.18-4.45; $P = .890$), and the hazard ratio for all-cause mortality at 23 months was 1.01 (95% CI: 0.33-3.15; $P = .983$).

Conclusion: Bivalirudin appears to exhibit a similar impact as unfractionated heparin on patients with acute coronary syndrome undergoing rotational atherectomy in real-life setting.

Keywords: Heparin, bivalirudin, acute coronary syndrome, rotational atherectomy

INTRODUCTION

Rotational atherectomy (RA) has been well demonstrated as a mainstay of the percutaneous method for coronary calcification,[1,2] a serious challenge in patients undergoing percutaneous coronary intervention (PCI) that often leads to procedure failure through device delivery failure, stent under expansion, and restenosis after the procedure.[3,4] Since 30.4% of moderate-to-severe coronary calcifications occur in acute coronary syndrome (ACS),[3] RA in patients with ACS had been proved to be effective[5,6] but was associated with increased risk of ischemic and bleeding events during the perioperative period.[7-9] Thus, appropriate selection of the anticoagulant agent during RA is critically important for reducing ischemic and bleeding risk.

The most frequently used anticoagulant therapy is unfractionated heparin (UFH) and bivalirudin, and heparin was perfered as the standard anticoagulation theapy during PCI in previous trials.[9,10] Bivalirudin (20-amino-acid synthetic polypeptides) binds directly to blood coagulation, thus decreasing its enzymatic activity. Some published studies demonstrated that bivalirudin has emerged as an intriguing substitute to UFH, with the key benefit being the lower rates of major bleeding without increasing ischemic complications in patients with ACS.[11-15] But few data

ORIGINAL INVESTIGATION

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are available regarding the impact of bivalirudin on patients with ACS undergoing RA. Therefore, the present study aimed to determine the impact of bivalirudin on patients with ACS undergoing RA in a real-world setting.

METHODS

Study Design and Population

This was a retrospective cohort study. The patients included presented with ACS and were undergoing RA and PCI in our hospital between January 2017 and December 2019.

Inclusion criteria were as follows: (1) age 18-90 years old; (2) patients with clinically diagnosed coronary heart disease who underwent coronary angiography and who were found to have coronary artery stenosis (>70%) with severe calcification and received RA. Exclusion criteria were as follows: (1) patients who are in the menstrual period, pregnant, and lactating; (2) patients with long-term use of anticoagulant drugs (novel oral anticoagulants or oral anticoagulants) and patients who recently underwent thrombolytic therapy; (3) patients with abnormal coagulation function or hemorrhagic disease; (4) patients with severe anemia; (5) clinical diagnosis of stable angina pectoris and ischemic cardiomyopathy; (6) patients with tumor and life expectancy <1 year; (7) patients who were subjected to RA of venous bridge vessels; and (8) patients with incomplete clinical data.

Acute coronary syndrome was diagnosed according to the Fourth Universal Definition of Myocardial Infarction.[16] Rotational atherectomy was selected when there was severe calcification or as a bailout measure when device delivery failed. Given its retrospective observational study design, this study is exempt from ethics review. This study protocol was reviewed and approved by our hospital. Informed consent was waived due to the retrospective design.

Data Collection

We divided patients into 2 cohorts based on the anticoagulant therapy used: the UFH cohort and the bivalirudin cohort. Patients' demographic [age, gender, and body mass index (BMI)] and clinical characteristics [systolic blood pressure on admission, diastolic blood pressure on admission, heart rate on admission, prior PCI, hypertension, diabetes mellitus, clinical diagnosis, left ventricle ejection fraction, white blood cell count, hemoglobin (HGB) count, platelet count, glucose, creatine kinase-MB, cardiac troponin I, N-terminal pro-brain natriuretic peptide (NT-proBNP), creatinine, cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein, CYP2C19 genotype, medication during hospitalization, P2Y12 inhibitor, statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, β-blocker, diuretic, and nitrates] and procedural data were collected from the medical records. Periprocedural complications, in-hospital outcomes including ischemic events [all-cause death, perioperative myocardial infarction (MI), acute stent thrombus, target vessel revascularization (TVR), and heart failure], and bleeding events [Bleeding Academic Research Consortium (BARC) < 3, BARC ≥ 3] were also collected. All patients were followed up for an average of 23 months, and all-cause deaths within 23 months outside the hospital were recorded.

Outcomes

The primary outcome of this study was in-hospital rates of net adverse clinical events (NACEs), which included all-cause death, perioperative MI, TVR, heart failure, and major bleeding defined as BARC ≥ 3 bleeding.[17] Increases in cTnI (cardiac troponin I) values (>99th percentile URL) in patients with normal baseline values or an increase in cTn values (>20% of the baseline value) when it is above the 99th percentile URL are utilized to diagnose cardiac procedural MI.[16] Target vessel revascularization was defined as repeat revascularization of the target vessel.[16] Stent thrombosis was defined based on the Academic Research Consortium definition.[6] Procedural success was defined as angiographic success without periprocedural complications, residual stenosis <30% after stent implantation, and thrombolysis for myocardial infarction flow class III.[6] The secondary outcome was all-cause mortality at 23 months.

Statistical Analysis

Continuous variables are presented as means ± standard deviations (SDs) or median with interquartile ranges, as appropriate. Categorical variables are presented as numbers and percentages. Inter-cohort differences were compared using Student's *t*-test or the Mann–Whitney *U*-test where appropriate. Categorical variables were tested using the chi-square test or Fisher's exact test. A univariate and multivariable logistic regression model was used to identify the risk predictors of NACE, and both odds ratio (OR) and 95% CI were calculated. Net adverse clinical event was used as a dependent variable. Anticoagulant, age, gender, BMI, diagnosis, diuretic, target lesion location, target vessel, intra-aortic balloon pump (IABP), Global Registry of Acute Coronary Events (GRACE) ischemic score, Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines (CRUSADE) bleeding score, and procedural complications at baseline were added as independent variables in the multivariate analysis. Univariate and multivariable Cox-proportional hazards regression model was used to identify the risk predictors of all-cause mortality at 23 months, with risk estimates reported as hazard ratios (HRs) with a 95% CI. All variables with $P < .10$ in the univariate model and clinical factors that may influence outcome (such as age, gender, and BMI) were included in the multivariable

HIGHLIGHTS

- Twenty-one percent of patients with acute coronary syndrome undergoing rotational atherectomy received bivalirudin.
- Bivalirudin cohort had higher bleeding risks.
- In-hospital net adverse clinical events in the bivalirudin group were higher than that of heparin.
- All-cause mortality at 23 months was comparable between 2 cohorts.
- Perioperative anticoagulant did not affect in-hospital net adverse clinical event or all-cause death.

model. Proportional-hazards assumption was checked by the Schoenfeld residuals, and no violation was detected. Kaplan–Meier curves were plotted for the 2 cohorts, with the differences compared by the log-rank tests. A *P*-value <.05 was considered statistically significant. All data analyses were conducted using Statistical Package for Social Sciences software 24.0 (IBM, Armonk, NY, USA).

RESULTS

From 2017 to 2019, there were 256 patients treated with RA in our center. After the removal of 99 patients who met the exclusion criteria, 157 remaining patients were eligible for analysis, with 124 (79.0%) in the UFH cohort and 33 (21.0%) in the bivalirudin cohort. Patients in the bivalirudin cohort were older (75.1 ± 7.5 years vs. 71.1 ± 9.2 years, *P* = .024) and less likely to be males (36.4% vs. 60.5%, *P* = .013). They had significantly lower HGB [114 (103-126) × 10^9/L vs. 123 (112-130) × 10^9/L, *P* = .014] and a higher level of NT-proBNP [2626 (1280-5958) pg/mL vs. 796 (210-2415) pg/mL, *P* = .003]. P2Y12 inhibitor had a significantly different distribution between the 2 cohorts (*P* = .005). More patients in the bivalirudin cohort used diuretics than that in the UFH cohort (66.7% vs. 39.5%, *P* = .040). The surgical approach was different between the 2 cohorts significantly (*P* = .043). The GRACE score and CRUSADE score were both higher in the bivalirudin group than in the heparin group (163 ± 24 vs. 146 ± 30, *P* = .003 and 48 ± 12 vs. 40 ± 14, *P* = .002) (Table 1).

In-hospital NACE was significantly higher in the bivalirudin cohort (27.3% vs. 11.3%, *P* = .021). The rates of perioperative MI were higher in the bivalirudin cohort than the UFH cohort (15.2% vs. 2.5%, *P* = .010). No statistically significant differences were found for all-cause death during hospitalization, heart failure, and BARC < 3 bleeding (all *P* < .05). No case of TVR or BARC ≥ 3 bleeding was recorded in either cohort. Stent thrombosis was considered in 1 patient in the bivalirudin group and 1 patient in the heparin group; however, they both died during hospitalization in the cohort. In addition, there was no significant difference in all-cause mortality at 23 months (30.3% vs. 20.2%, *P* = .214) (Table 1).

In this study, the univariable analysis revealed that anticoagulant, diagnosis, diuretic, IABP, and procedural complications were independent predictors of NACE (all *P* < .05). Multivariable analysis revealed that procedural complication (OR = 6.14, 95% CI: 1.61-23.38, *P* = .008) was an independent predictor of NACE. Notably, anticoagulant therapy was not associated with NACE (OR = 0.90, 95% CI: 0.18-4.45, *P* = .890) (Table 2).

In this study, the univariable COX analysis revealed that age, diagnosis, glucose, creatinine, high-density lipoprotein, P2Y12 inhibitor, diuretic, IABP, GRACE score, and CRUSADE score were independent predictors of all-cause mortality at 23 months. Multivariable analysis revealed that diuretic (HR = 0.28, 95% CI: 0.08-0.99, *P* = .048) was an independent predictor of all-cause mortality. Notably, anticoagulant therapy was not associated with all-cause mortality at 23 months (HR = 1.01, 95% CI: 0.33-3.15, *P* = .983) (Table 3).

There was no difference in all-cause mortality between the cohorts after an average of 23 (15-29) months follow-up (30.3% vs. 20.2%, *P* = .214) (Table 1); Kaplan–Meier survival curves were presented in Figure 1. The log-rank test demonstrated no significant differences between the 2 cohorts (*P* = .132).

DISCUSSION

Among the total number of patients with ACS undergoing RA treated with anticoagulant drugs, there were 2 cohorts of patients—bivalirudin cohort and UFH cohort. Moreover, NACE during hospitalization and all-cause mortality at 23 months were not significantly different between the 2 cohorts, and it may mean that bivalirudin may exhibit a similar impact as UFH on patients with ACS undergoing RA.

Bivalirudin was a superior anticoagulant for high bleeding risk patients, with distinct pharmacologic advantages that bivalirudin acts as a direct thrombin inhibitor and a reversible, short-acting anticoagulant with a half-life of 25 minutes resulting in lower rates of major bleeding without increasing ischemic complications.[15] In this study, bivalirudin was used perioperatively in 21% of patients, which is a slightly lower proportion than previously reported (23%-33%).[18,19] We found that these patients in the bivalirudin group were older and more of females and had lower HGB, poorer cardiac function, greater use of diuretics, and more use of clopidogrel than ticagrelor and higher CRUSADE score. These findings were concordant with earlier results,[18] meaning that for people with high bleeding risks, bivalirudin as a low risk of bleeding anticoagulants was preferred.[20-23]

This article was the first to report the impact of bivalirudin on patients with RA in ACS. Allali et al[5] investigated the impact of RA on patients presenting with ACS and Kübler et al[6] assessed in-hospital and 1-year outcomes in patients undergoing RA presenting with ACS in comparison to elective RA procedures, and they found the feasibility of performing RA in patients with ACS, but neither article mentioned the proportion of bivalirudin used intraoperatively. Delhaye et al[18] conducted a retrospective cohort study to explain the safety and efficacy of bivalirudin for PCI with RA. They reported that the endpoint and major bleeding were both similar in the bivalirudin and the UFH groups (1.9% vs. 1.7%, *P* = .99; 2.2% vs. 1.7%, *P* = .99), and after adjustment, bivalirudin use was not associated with a reduction in death/Q wave MI/urgent Coronary Artery Bypass Grafting (CABG) and major bleeding compared to UFH. However, one-third of the patients included in their study had a diagnosis of stable angina, leading to little understanding of the impact of bivalirudin on patients diagnosed as ACS undergoing RA. Secondly, in our study, the use of a composite endpoint event—NACE—rather than death/Q wave MI/urgent CABG and major bleeding as the primary outcome was more clinically instructive due to the high risk of bleeding and ischemia in patients with ACS undergoing RA. Thirdly, the present study used perioperative MI rather than Q wave MI as one of the clinical outcome endpoints, mainly because

Table 1. Patients' Demographic, Clinical, and Procedure Characteristics, Procedural Success and Complications, and Outcome During Hospitalization and Follow-up

Patients	UFH (n = 124)	Bivalirudin (n = 33)	*P*
Age, years	71.1 ± 9.2	75.1 ± 7.5	.024
Male	75 (60.5%)	12 (36.4%)	.013
Body mass index, kg/m^2	23.8 ± 3.0	22.9 ± 3.7	.169
Systolic blood pressure on admission, mm Hg	134.9 ± 18.2	135.9 ± 23.4	.788
Diastolic blood pressure on admission, mm Hg	76.6 ± 11.3	74.7 ± 13.2	.418
Heart rate on admission, bpm	77.5 ± 13.8	76.8 ± 10.6	.777
Prior PCI	33 (26.6%)	8 (24.2%)	.783
Hypertension	87 (70.2%)	24 (72.7%)	.773
Diabetes mellitus	45 (36.3%)	12 (36.4%)	.994
Clinical diagnosis			.189
UA	94 (75.8%)	21 (63.6%)	
NSTEMI	27 (21.8%)	9 (27.3%)	
STEMI	3 (2.4%)	3 (9.1%)	
Left ventricle ejection fraction, %	61 (46-67)	52 (42-62)	.087
White blood cell count (10^9/L)	6.13 (4.95-7.77)	6.26 (4.98-7.39)	.900
Hemoglobin count (g/L)	123 (112-130)	114 (103-126)	.014
Platelet count (10^9/L)	191 (151-232)	183 (138-223)	.327
Glucose (mmol/L)	5.12 (4.64-6.14)	5.73 (4.96-6.65)	.082
CK-MB (IU/L)	14 (10-21)	16 (12-22)	.323
Cardiac troponin I (ng/mL)	0.02 (0.01-0.29)	0.85 (0.01-1.95)	.121
NT-proBNP (pg/mL)	796 (210-2415)	2626 (1280-5958)	.001
Creatinine (umol/L)	76 (62-94)	71 (60-123)	.912
Cholesterol (mmol/L)	3.90 (3.06-4.58)	3.98 (3.10-4.86)	.610
Triglyceride (mmol/L)	1.21 (0.98-1.51)	1.14 (0.90-1.47)	.718
High-density lipoprotein (mmol/L)	0.92 (0.79-1.06)	1.03 (0.76-1.36)	.118
Low-density lipoprotein (mmol/L)	1.94 (1.51-2.59)	1.97 (1.57-2.67)	.678
CYP2C19 genotype			.890
Fast metabolism	33 (41.3%)	9 (40.9%)	
Intermediate metabolism	37 (46.3%)	11 (50.0%)	
Poor metabolism	10 (12.5%)	2 (9.1%)	
Medication during hospitalization			
Aspirin	123 (100%)	32 (97%)	.077
P2Y12 inhibitor			.005
Clopidogrel	32 (25.8%)	17 (51.5%)	
Ticagrelor	92 (74.2%)	16 (48.5%)	
Statins	122 (98.4%)	32 (97.0%)	.617
ACEI/ARB	71 (57.3%)	19 (57.6%)	.974
β-Blocker	73 (58.9%)	20 (60.6%)	.857
Diuretic	49 (39.5%)	22 (66.7%)	.005
Nitrates	66 (53.2%)	18 (54.5%)	.893
Target vessel			.746
LM	38 (30.6%)	8 (24.2%)	
LAD	58 (46.8%)	15 (45.5%)	
LCX	4 (3.2%)	2 (6.1%)	
RCA	24 (19.4%)	8 (24.2%)	
Bifurcation	68 (55.3%)	16 (48.5%)	.487
Lesion characteristics			.783
Tortuosity	17 (13.7%)	3 (9.1%)	
Chronic total occlusion	12 (9.7%)	3 (9.1%)	
Ectasia	1 (0.8%)	0	

(*Continued*)

Table 1. Patients' Demographic, Clinical, and Procedure Characteristics, Procedural Success and Complications, and Outcome During Hospitalization and Follow-up (*Continued*)

Patients	UFH (n = 124)	Bivalirudin (n = 33)	*P*
Surgical approach			.043
Radial	100 (81.3%)	28 (84.8%)	
Brachial	18 (14.6%)	1 (3.0%)	
Femoral	5 (4.1%)	4 (12.1%)	
Number of burr			.058
1	115 (92.7%)	27 (81.8%)	
>1	9 (7.3%)	6 (18.2%)	
Size of burr			.463
1.25 mm	27 (21.8%)	8 (24.2%)	
1.5 mm	86 (69.4%)	24 (72.7%)	
1.75 mm	11 (8.9%)	1 (3.0%)	
Times of RA	3 (2-4)	3 (3-5)	.381
Burr speed (10^4/min)	15 (15-16)	15 (15-16)	.122
Direct RA	84 (67.7%)	22 (66.7%)	.907
Number of implanted stents	3 (2-3)	3 (2-4)	.956
Stent diameter	2.94 (2.75-3.17)	3 (2.75-3.19)	.404
Stent length, mm	70 (57-103)	88 (65-102)	.526
IABP	23 (18.5%)	5 (15.2%)	.651
Reason of IABP			.062
Preoperative treatment	1 (4.3%)	2 (40.0%)	
Intraoperative protection	17 (73.9%)	3 (60.0%)	
Bailout therapy	5 (21.7%)	0	
Procedural success	122 (98.4%)	33 (100%)	.330
Procedural complications	31 (25.0%)	11 (33.3%)	.337
Dissection	15 (12.1%)	7 (21.2%)	.199
No/slow reflow	17 (13.7%)	5 (15.2%)	.833
Perforation	3 (2.4%)	0	.232
Atrioventricular block	3 (2.4%)	0	.232
Emergency CABG	2 (1.6%)	0	.330
Reversible slow heart rate	6 (4.8%)	1 (3.0%)	.640
Temporary pacing	1 (0.8%)	0	.491
GRACE score	146 ± 30	163 ± 24	.003
CRUSADE score	40 ± 14	48 ± 12	.002
NACE during hospitalization	14 (11.3%)	9 (27.3%)	.021
All-cause death	6 (4.8%)	1 (3.0%)	.640
MI	3 (2.5%)	5 (15.2%)	.010
Acute stent thrombus	1 (0.8%)	1 (3.0%)	.373
TVR	0	0	
Heart failure	8 (6.7%)	5 (15.6%)	.132
BARC ≥ 3	0	0	
BARC < 3	2 (1.6%)	1 (3.0%)	.614
Follow-up			
All-cause death	25 (20.2%)	10 (30.3%)	.214

P-value for comparison of bivalirudin versus heparin. Data are presented as mean ± SD or median with interquartile ranges, as appropriate for continuous variables, and numbers and percentages for categorical variables.
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; BARC, Bleeding Academic Research Association; CABG, coronary artery bypass grafting; CK-MB, creatine phosphokinase-MB; CYP2C19; cytochrome P450 2C19; IABP, intra-aortic balloon pump; LAD, left anterior descending coronary artery; LCX, left circumflex; LM, left main coronary artery; MI, myocardial infarction; NACE, net adverse clinical events; NSTEMI, non-ST-segment elevation myocardial infarction; NT-proBNP, N-terminal pro-brain natriuretic peptide; PCI, percutaneous coronary intervention; RA, rotational atherectomy; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; TVR, target vessel revascularization; UA, unstable angina; UFH, unfractionated heparin.

Table 2. Multivariable Analysis of In-hospital NACE

	Univariable Analysis			Multivariable Analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Anticoagulant	0.34	0.13-0.88	.025	0.90	0.18-4.45	.890
Age	0.99	0.94-1.04	.729	1.05	0.95-1.16	.317
Gender	0.70	0.29-1.70	.430	0.63	0.14-2.94	.558
Body mass index	1.17	0.99-1.39	.068	1.14	0.89-1.45	.294
Diagnosis			.004			.335
UA	1			1		
NSTEMI	0.22	0.08-0.57	.002	0.32	0.06-1.54	.154
STEMI	0.19	0.03-1.17	.074	0.41	0.02-10.27	.584
Diuretic	5.50	1.93-15.72	.001	2.14	0.41-11.30	.370
Target vessel			.087			.255
LAD	1			1		
LCX	0.53	0.05-5.21	.586	0.42	0.02-7.58	.555
RCA	1.03	0.25 -4.25	.973	0.62	0.09-4.36	.631
LM	0.30	0.11-0.83	.021	0.20	0.04-0.97	.046
IABP	6.31	2.41-16.53	.000	3.30	0.70-15.61	.133
GRACE score	0.98	0.97-1.00	.054	1.00	0.97-1.04	.819
CRUSADE score	0.98	0.94-1.01	.168	0.97	0.91-1.04	.409
Procedural complications	5.89	2.31-15.00	.000	6.14	1.61-23.38	.008

P-value for comparison of bivalirudin versus heparin. Data are presented as numbers and percentages for categorical variables.
IABP, intra-aortic balloon pump; LAD, left anterior descending coronary artery; LCX, left circumflex; LM, left main coronary artery; NACE, net adverse cardiac events; NSTEMI, non-ST-segment elevation myocardial infarction; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

Table 3. Univariate and Multivariate Cox Regression Analysis of All-Cause Mortality at 23 Months

	Univariable Analysis			Multivariable Analysis		
	HR	95% CI	*P*	HR	95% CI	*P*
Anticoagulant	1.75	0.83-3.71	.141	1.01	0.33-3.15	.983
Age	1.05	1.01-1.10	.031	1.00	0.92-1.10	.987
Gender	1.06	0.53-2.09	.879	0.94	0.26-3.40	.927
Body mass index	0.91	0.81-1.02	.108	0.92	0.78-1.09	.340
Diastolic blood pressure on admission	0.98	0.95-1.00	.094	1.00	0.95-1.04	.816
Diagnosis			.009			.616
UA	1			1		
NSTEMI	2.99	1.47-6.08	.002	1.00	0.32-3.16	.996
STEMI	2.46	0.57-10.66	.230	0.27	0.02-3.76	.330
Hemoglobin count	0.98	0.96-1.00	.091	0.99	0.96-1.03	.664
Glucose	1.10	1.01-1.20	.029	1.05	0.90-1.23	.539
Creatinine	1.00	1.00-1.00	.029	1.00	1.00-1.00	.106
High-density lipoprotein	0.19	0.05-0.82	.025	1.07	0.14-7.95	.947
P2Y12 inhibitor						
Clopidogrel	1			1		
Ticagrelor	0.45	0.23-0.90	.023	1.79	0.53-6.00	.349
Diuretic	0.23	0.10-0.51	.001	0.28	0.08-0.99	.048
IABP	0.41	0.20-0.86	.019	0.50	0.19-1.31	.157
GRACE score	1.02	1.01-1.04	.000	1.02	0.99-1.06	.165
CRUSADE score	1.04	1.02-1.07	.002	1.00	0.93-1.07	.904

IABP, intra-aortic balloon pump; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

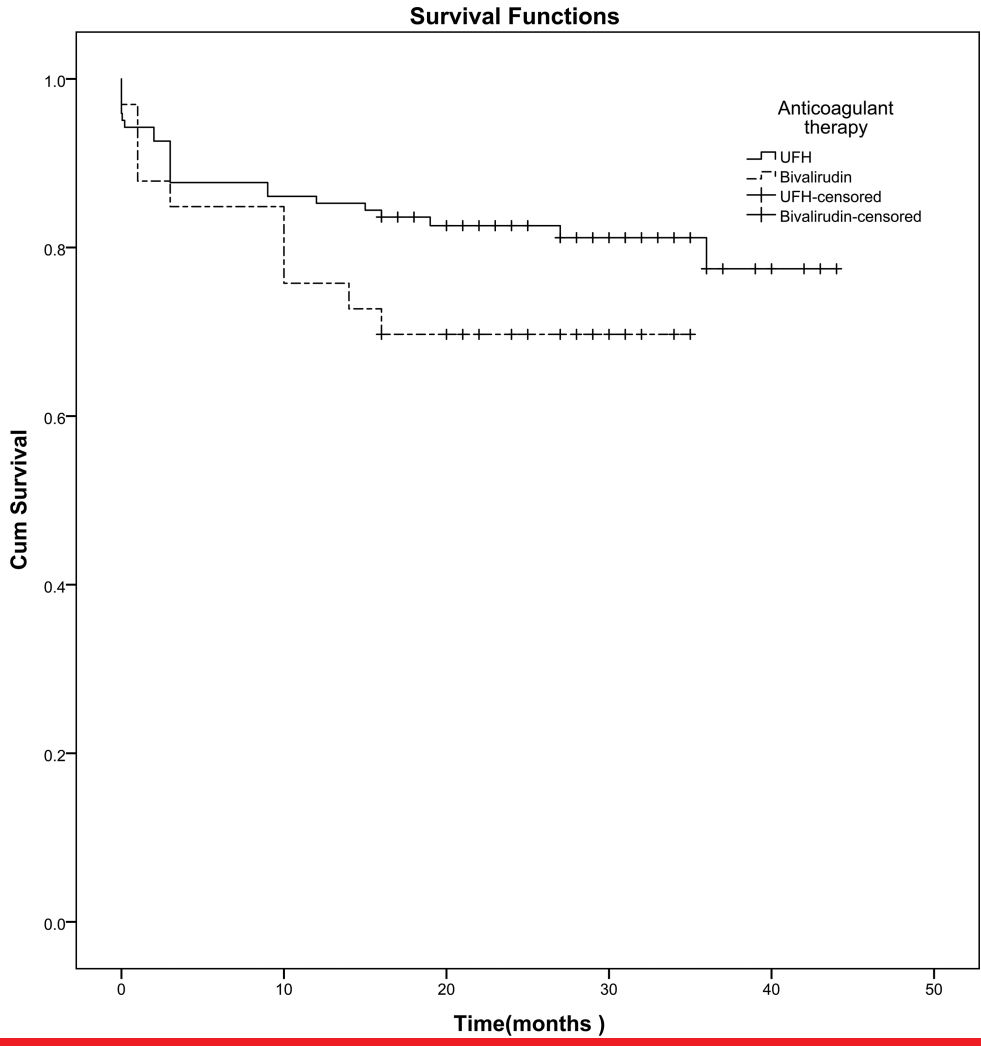

Figure 1. Kaplan–Meier curve of all-cause mortality. Log-rank = 0.132.

we had considered the impact of coronary microembolism and spasm in patients with ACS undergoing RA.

In the present analysis, we found no difference in acute stent thrombosis between the 2 groups (3.0% vs. 1.6%, $P = .373$). We obtained similar results for all-cause mortality, perioperative MI, TVR, and heart failure. These findings are in agreement with previous clinical trials.[18,24,25] The minimizing adverse hemorrhagic events by transradial access site and angioX (MATRIX) clinical trial gets the similar outcomes comparative with the lower rate of acute stent thrombosis in our study.[15] Moreover, from the BRIGHT randomized trial, bivalirudin compared with heparin resulted in similar rates of acute stent thrombosis and low bleeding events.[12]

Regarding bleeding complications, Delhaye et al[18] showed no difference for major bleeding between both bivalirudin and heparin groups (2.2% vs. 1.7%, $P = .99$) and the transfusion rate (5.6% vs. 8.7%, $P = .19$). Similarly, we reach the same conclusion, and there were no bleeding events with BARC ≥ grade 3 in both cohorts.

We found that NACE events were higher in the bivalirudin cohort than the heparin cohort but were not associated with NACE and all-cause mortality at 23 months after multivariable adjustment. This may be related to the fact that the effects of factors (e.g., age, gender, anemia, cardiac function, diuretic use, and choice of antithrombotic drug) on NACE events were counteracted by the effects of anticoagulant drugs.

Therefore, our findings imply that patients with ACS receiving RA do not maintain the advantages of bivalirudin over heparin on the decrease of bleeding events and ischemic events. With the results of this study, we showed theoretical basis for the perioperative use of bivalirudin as an anticoagulant in patients diagnosed with ACS undergoing RA.

Study Limitations

The limitation of this study was a retrospective observational study using data from patients admitted to our single-center with a relatively small sample. Large-scale, multicenter studies were necessary to further confirm our study results. Secondly, only all-cause mortality was followed up for

long-term, and long-term adverse events with bivalirudin use cannot be explored. Thirdly, the use of tirofiban was entirely at the discretion of the operator, and the actual rate of tirofiban usage is not recorded, which might affect the incidence of bleeding events.

CONCLUSIONS

In patients with ACS undergoing RA in a real-world scenario, bivalirudin appeared to have a similar effect as UFH. However, randomized controlled trials with large samples are needed to validate the results in the future.

Data Availability: All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Committee Approval: This study protocol was reviewed and approved by The First Affiliated Hospital of USTC.

Informed Consent: Informed consent was waived due to the retrospective design.

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REFERENCES

1. Uetani T, Amano T. Current status of rotational atherectomy in the drug-eluting stent era. *Circ J*. 2018;82(4):946-947. [CrossRef]
2. Topol EJ, Leya F, Pinkerton CA, et al. A comparison of directional atherectomy with coronary angioplasty in patients with coronary artery disease. The CAVEAT study group. *N Engl J Med*. 1993;329(4):221-227. [CrossRef]
3. Généreux P, Madhavan MV, Mintz GS, et al. Ischemic outcomes after coronary intervention of calcified vessels in acute coronary syndromes. Pooled analysis from the HORIZONS-AMI (Harmonizing Outcomes With revascularization and Stents in acute myocardial infarction) and ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) TRIALS. *J Am Coll Cardiol*. 2014;63(18):1845-1854. [CrossRef]
4. Zimoch WJ, Kubler P, Kosowski M, et al. Patients with acute myocardial infarction and severe target lesion calcifications undergoing percutaneous coronary intervention have poor long-term prognosis. *Kardiol Pol*. 2017;75(9):859-867. [CrossRef]
5. Allali A, Abdelghani M, Mankerious N, Abdel-Wahab M, Richardt G, Toelg R. Feasibility and clinical outcome of rotational atherectomy in patients presenting with an acute coronary syndrome. *Catheter Cardiovasc Interv*. 2019;93(3):382-389. [CrossRef]
6. Kübler P, Zimoch W, Kosowski M, Tomasiewicz B, Telichowski A, Reczuch K. Acute coronary syndrome – Still a valid contraindication to perform rotational atherectomy? Early and one-year outcomes. *J Cardiol*. 2018;71(4):382-388. [CrossRef]
7. Koch KC, Radke PW, Kleinhans E, et al. Mechanisms of myocardial hypoperfusion during rotational atherectomy of de novo coronary artery lesions and stenosed coronary stents: insights from serial myocardial scintigraphy. *J Nucl Cardiol*. 2002;9(3):304-311. [CrossRef]
8. Shenoy C, Harjai KJ. Bivalirudin for mechanical rotational atherectomy: the quest for better outcomes. *J Interv Cardiol*. 2010;23(3):230-232. [CrossRef]
9. Généreux P, Madhavan MV, Mintz GS, et al. Relation between coronary calcium and major bleeding after percutaneous coronary intervention in acute coronary syndromes (from the Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes With revascularization and Stents in acute myocardial infarction Trials). *Am J Cardiol*. 2014;113(6):930-935. [CrossRef]
10. Gargiulo G, Moschovitis A, Windecker S, Valgimigli M. Developing drugs for use before, during and soon after percutaneous coronary intervention. *Expert Opin Pharmacother*. 2016;17(6):803-818. [CrossRef]
11. Mehran R, Lansky AJ, Witzenbichler B, et al. Bivalirudin in patients undergoing primary angioplasty for acute myocardial infarction (HORIZONS-AMI): 1-year results of a randomised controlled trial. *Lancet*. 2009;374(9696):1149-1159. [CrossRef]
12. Han Y, Guo J, Zheng Y, et al. Bivalirudin vs heparin with or without tirofiban during primary percutaneous coronary intervention in acute myocardial infarction: the BRIGHT randomized clinical trial. *JAMA*. 2015;313(13):1336-1346. [CrossRef]
13. Steg PG, van, van 't Hof A, Hamm CW, et al. Bivalirudin started during emergency transport for primary PCI. *N Engl J Med*. 2013;369(23):2207-2217. [CrossRef]
14. Stone GW, White HD, Ohman EM, et al. Bivalirudin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a subgroup analysis from the Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial. *Lancet*. 2007;369(9565):907-919. [CrossRef]
15. Valgimigli M, Frigoli E, Leonardi S, et al. Bivalirudin or unfractionated heparin in acute coronary syndromes. *N Engl J Med*. 2015;373(11):997-1009. [CrossRef]
16. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol*. 2018;72(18):2231-2264. [CrossRef]
17. Leon MB, Piazza N, Nikolsky E, et al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. *Eur Heart J*. 2011;32(2):205-217. [CrossRef]
18. Delhaye C, Wakabayashi K, Maluenda G, et al. Safety and efficacy of Bivalirudin for percutaneous coronary intervention with rotational atherectomy. *J Interv Cardiol*. 2010;23(3):223-229. [CrossRef]
19. Lee MS, Shlofmitz E, Nayeri A, Hollowed J, Kong J, Shlofmitz RA. Comparison of heparin and Bivalirudin in patients undergoing orbital atherectomy. *J Invasive Cardiol*. 2017;29(11):397-400.
20. Subherwal S, Bach RG, Chen AY, et al. Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) Bleeding Score. *Circulation*. 2009;119(14):1873-1882. [CrossRef]
21. Cao D, Mehran R, Dangas G, et al. Validation of the Academic Research Consortium high bleeding risk definition in contemporary PCI patients. *J Am Coll Cardiol*. 2020;75(21):2711-2722. [CrossRef]

22. Pereira NL, Farkouh ME, So D, et al. Effect of genotype-guided oral P2Y12 inhibitor selection vs conventional clopidogrel therapy on ischemic outcomes after percutaneous coronary intervention: the TAILOR-PCI randomized clinical trial. *JAMA*. 2020;324(8):761-771. [CrossRef]
23. Claassens DMF, Vos GJA, Bergmeijer TO, et al. A genotype-guided strategy for oral P2Y(12) inhibitors in primary PCI. *N Engl J Med*. 2019;381(17):1621-1631. [CrossRef]
24. Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med*. 2008;358(21):2218-2230. [CrossRef]
25. Shahzad A, Kemp I, Mars C, et al. Unfractionated heparin versus Bivalirudin in primary percutaneous coronary intervention (HEAT-PPCI): an open-label, single centre, randomised controlled trial. *Lancet*. 2014;384(9957):1849-1858. [CrossRef]