Anticoagulant Use Among Patients With End-Stage Renal Disease Undergoing Percutaneous Coronary Intervention

An Analysis From the National Cardiovascular Data Registry

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Background—Patients with end-stage renal disease undergoing percutaneous coronary intervention (PCI) have largely been excluded from trials of antithrombotic therapies leaving little data to guide agent choice in this population.

Methods and Results—The National Cardiovascular Data Registry CathPCI Registry was used to identify patients with end-stage renal disease undergoing PCI who received monotherapy with either bivalirudin or unfractionated heparin (UFH) (n=71 675). In hospital bleeding and mortality were compared and adjusted using the CathPCI Registry logistic regression models with generalized estimating equations with UFH as the reference. Bivalirudin was used in 51.3% of patients versus 48.7% for UFH. The use of bivalirudin decreased over time, and in 2014, UFH became the most frequently used. Patients receiving UFH were more likely to have an acute coronary syndrome presentation (37.8% versus 27.4%) or have cardiogenic shock (3.74% versus 1.98%). The observed rates for in hospital bleeding (7.0% versus 9.5%; adjusted odds ratio,0.82; 95% confidence interval, 0.76–0.87) and mortality (2.6% versus 4.2%; adjusted odds ratio, 0.87; 95% confidence interval, 0.78–0.97) were lower for patients receiving bivalirudin compared with those receiving UFH.

Conclusions—In patients with end-stage renal disease undergoing PCI, bivalirudin and UFH were used with similar frequency although the patterns of use changed over the enrollment period. Patients with end-stage renal disease undergoing PCI had a lower adjusted risk of in hospital outcomes with bivalirudin; however, given the observational nature of this analysis, a randomized trial is warranted. **(*Circ Cardiovasc Interv*. 2018;11:e005628. DOI: 10.1161/CIRCINTERVENTIONS.117.005628.)**

Key Words: acute coronary syndrome ■ bivalirudin ■ heparin ■ kidney failure, chronic ■ percutaneous coronary intervention

The prevalence of patients with end-stage renal disease (ESRD) in the United States has increased significantly for the past 25 years. Current estimates are that ≈661 000 patients in the United States are enrolled in Medicare-funded ESRD programs, representing an 8-fold increase in program enrollment since 1986.[1] In addition, observations have highlighted the association of renal insufficiency with adverse outcomes in patients with coronary artery disease, including those undergoing percutaneous coronary intervention (PCI), with the highest event rates occurring in those with ESRD.[2–4] In spite of these findings, patients with ESRD have largely been excluded from contemporary randomized trials evaluating antithrombotic therapies in patients undergoing PCI. Although unfractionated heparin (UFH) does not require dose adjustment in patients with renal dysfunction, such patients are at high risk for bleeding, and targeted antithrombin agents like bivalirudin may confer a safety benefit. However, bivalirudin requires dose adjustment in the presence of severe renal dysfunction, has little data in patients with ESRD, and any safety advantage may be negated by the fact that there is delayed clearance of the drug in these patients. Thus, clinicians do not have adequate data to help guide procedural anticoagulant selection in this high-risk group of patients.

To address this evidence gap, we undertook an analysis of a contemporary ongoing PCI registry with the following 2 objectives: (1) to examine the patterns of use of bivalirudin and UFH in patients with ESRD undergoing PCI, and (2) to compare the rates of in hospital bleeding and in hospital mortality associated with the use of each agent.

Methods

The data, analytic methods, and study material will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

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WHAT IS KNOWN

- The presence of end-stage renal disease has been associated with an increased risk for ischemic and bleeding outcomes in patients undergoing percutaneous coronary intervention (PCI).
- In spite of the high-risk nature of these patients, there is a paucity of data from randomized clinical trials to help guide antithrombotic decisions for PCI.

WHAT THE STUDY ADDS

- Unfractionated heparin was more often chosen as the procedural anticoagulant in patients with end-stage renal disease presenting with acute coronary syndrome undergoing PCI.
- The use of bivalirudin was associated with lower rates of in hospital bleeding and mortality compared with unfractionated heparin monotherapy in patients with end-stage renal disease undergoing PCI.
- This analysis highlights the need for a randomized clinical trial of procedural antithrombotic therapy in patients with end-stage renal disease undergoing PCI.

Data Source and Study Sample

The National Cardiovascular Data Registry CathPCI Registry is a nationwide quality improvement program that collects patient and procedural data along with in hospital outcomes on patients undergoing cardiac catheterizations and PCIs at participating sites. All procedures occurring between July 1, 2009, and September 30, 2015, were analyzed, and those conducted in patients with ESRD (defined as receiving chronic hemodialysis) receiving monotherapy with either UFH or bivalirudin were included. Procedures were excluded if a fibrinolytic agent had been administered, an anticoagulant other than UFH or bivalirudin was used (low molecular weight heparin, fondaparinux, and direct thrombin inhibitor other than bivalirudin), a glycoprotein IIb/IIIa receptor antagonist was used, or if both UFH and bivalirudin were used (Figure 1). The Institutional Review Board of Duke University Medical Center approved the study and determined that it met the definition of research not requiring informed consent.

Outcomes and Definitions

The outcome measures were in hospital mortality and in hospital bleeding. In hospital bleeding was based on a previously established registry definition of bleeding that included any of the following occurring within 72 hours after PCI or before hospital discharge (whichever occurred first): site-reported arterial access site bleeding, which may be either external or a hematoma >10 cm for femoral access, >5 cm for brachial access, or >2 cm for radial access; retroperitoneal, gastrointestinal, or genitourinary bleeding; intracranial hemorrhage; cardiac tamponade; postprocedure hemoglobin decrease of 3 g/dL in patients with a preprocedure hemoglobin level ≤16 g/dL; or postprocedure nonbypass surgery–related blood transfusion for patients with a preprocedure hemoglobin level ≥8 g/dL.[5]

Statistical Methods

Patients were categorized according to whether bivalirudin or UFH was used during the PCI procedure. Patient and procedure characteristics, including demographics, history and risk factors, catheterization laboratory visit, diagnostic catheterization procedure, estimate of coronary anatomy, PCI procedure, lesions and devices, laboratories, intra and postprocedure events, discharge, and hospital characteristics, were compared between the groups. Categorical variables are presented as frequencies (percentages), and differences between the groups were assessed using the χ^2 test when the sample size is sufficient, otherwise an exact test was used. Continuous variables are presented as median (Q1, Q3) and were compared using the Kruskal–Wallis test. In addition, to describe hospital variation in use of each agent, we calculated the proportion of patients receiving each agent out of all patients at that hospital and displayed the distribution across hospitals using a histogram.

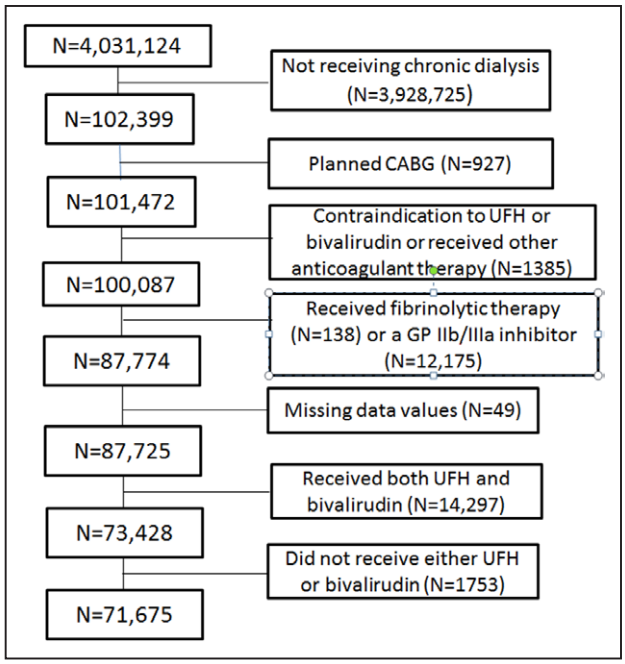

Figure 1. Study sample. CABG indicates coronary artery bypass graft; GP, glycoprotein; and UFH, unfractionated heparin.

Using procedure date to group patients into year and quarter of the study period, we calculated the proportion of patients receiving each agent out of all patients for each quarter of the study period. Temporal trends in the proportion of use of each agent per year and quarter were plotted with a trend line through the observed quarterly proportions. To assess whether the odds of receiving bivalirudin versus UFH changed over time, we fit a logistic regression model for bivalirudin versus UFH adjusted for time (quarters) modeled as a continuous variable and variables selected a priori based on previously developed mortality and bleeding models and clinical expertise.[5,6] Specifically, we adjusted for age, sex, race, time (quarters), body mass index, prior congestive heart failure, cerebrovascular disease, peripheral vascular disease, chronic lung disease, prior PCI, diabetes mellitus (insulin, noninsulin versus none), ejection fraction, preprocedure hemoglobin, heart failure New York Heart Association (NYHA) class within 2 weeks (IV, I/II/III, versus none), Society for Cardiovascular Angiography and Interventions (SCAI) lesion class (II/III, IV, versus I), cardiogenic shock and PCI status (sustained shock and salvage, sustained shock or salvage, transient shock but not salvage, emergency PCI within shock/salvage, urgent PCI without shock/salvage, versus no cardiogenic shock and elective PCI), cardiac arrest within 24 hours, at least 1 previously treated lesion within 1 months with in-stent thrombosis, preprocedure TIMI (Thrombolysis In Myocardial Infarction) flow=no, highest risk lesion segment category proximal left anterior descending , left main, versus other, multivessel disease, and chronic total occlusion. Generalized estimating equations were used to account for within hospital clustering.

Logistic regression models were used to assess the association of bivalirudin versus UFH with in hospital mortality and bleeding. We fit a multivariable model adjusted for the variables described above that were selected a priori based on previously developed mortality and bleeding models and clinical expertise.[5,6] Time (quarters) was included

to account for possible secular trends in outcomes. Generalized estimating equations were used to account for within hospital clustering. As a sensitivity analysis, the models were rerun after excluding sites with <5% or >95% bivalirudin use (n=366 sites and n=11071 patients are excluded). We also refit the models using mixed effects models with random intercepts for hospital instead of generalized estimating equations to account for within hospital clustering. Last, propensity score matching was used as an additional method to account for differences in patient characteristics. The propensity for bivalirudin versus UFH was modeled using a logistic regression model adjusted for the previously stated covariates with the addition of PCI indication. The gmatch macro, publically available from the Mayo Clinic Division of Biomedical Statistics and Informatics website (downloaded on May 13, 2013 from http://mayoresearch.mayo.edu/mayo/research/biostat/sasmacros.cfm), was used to run a computerized matching of bivalirudin to UFH patients. Patients were matched based on the propensity for receiving bivalirudin versus UFH. The gmatch macro performs greedy matching of UFH to bivalirudin patients within a prespecified caliper. If there were no bivalirudin patients with a propensity score within the caliper of a given UFH patient, then that UFH patient was not included in the matched sample. Matching was conducted on the logit of the propensity score and used a caliper width of 0.2× the SD of the logit of the propensity score. Previous research has shown that this approach results in estimates of the treatment effect with lower mean squared error.[7] We assessed for balance of the covariates between the 2 groups using standardized differences[8] (see Appendix in the Data Supplement). To estimate the bivalirudin versus UFH effect on in hospital bleeding and mortality among the propensity-matched sample, the odds ratio (OR) from a conditional logistic regression model is presented. A $P<0.05$ was used to determine statistical significance. Because radial access is known to reduce bleeding, we refit the multivariable logistic regression model with generalized estimating equations adding radial and an interaction term for bivalirudin by radial to assess whether the association of bivalirudin versus UFH on bleeding differed by radial access site. All analyses were performed at the Duke Clinical Research Institute using SAS version 9.4 (Cary, NC)

Results

Patterns of Anticoagulant Use

Between July 1, 2009, and September 30, 2015, a total of 71 675 patients with ESRD undergoing PCI who received monotherapy with either UFH or bivalirudin were identified (Figure 1). Bivalirudin was used in 36 747 (51.3%) patients while UFH was used in 34 928 (48.7%) patients. However, a marked change was observed in the proportional use of each agent during the study period (Figure 2). The odds of bivalirudin use significantly decreased over time (as function of the association of quarterly time increases on the use of bivalirudin), and the decreasing trend was similar after adjustment for the variables in the propensity score model (adjusted OR, 0.97; 95% confidence interval [CI], 0.97–0.98). At the beginning of the study period (third quarter of 2009), UFH was used in 42.1% and bivalirudin in 57.9% of PCI procedures compared with the end of the study period (third quarter of 2015), in which UFH was used in 64% and bivalirudin in 36% of PCI procedures. In addition, significant variance was seen among hospitals for the choice of the preferred anticoagulant in this population (Figure 3). The top quartile of high UFH using institutions used UFH in ≥71.4% of PCI procedures while the bottom quartile of UFH using institutions used UFH in ≤18.6% of cases. Last, given the temporal variations in anticoagulant use, an analysis was conducted to assess the association of increases in time (quarters) on clinical outcomes. No association was observed for increases in time with in hospital mortality (adjusted OR, 1.00; 95% CI, 0.99–1.00; $P=0.27$) although an association was observed for reduced risk of in hospital bleeding (adjusted OR, 0.98; 95% CI, 0.97–0.98; $P\leq0.0001$)

Patient and Procedural Characteristics

Baseline patient characteristics in those receiving UFH and bivalirudin are shown in Table 1. Overall, patients receiving UFH were more likely to have comorbid medical conditions compared with those receiving bivalirudin. Patients receiving UFH were more likely to have had a prior myocardial infarction (43% versus 38%), congestive heart failure (42% versus 37%), peripheral vascular disease 33.3% versus 29.8%), ST-segment–elevation myocardial infarction (STEMI; 5.2% versus 3.9%), or non–STEMI (32.6% versus 23.5%) at presentation. In addition, patients receiving UFH were more likely to have experienced a high-risk clinical event within 24 hours of the PCI, including cardiac arrest (2.5% versus 1.8%) and

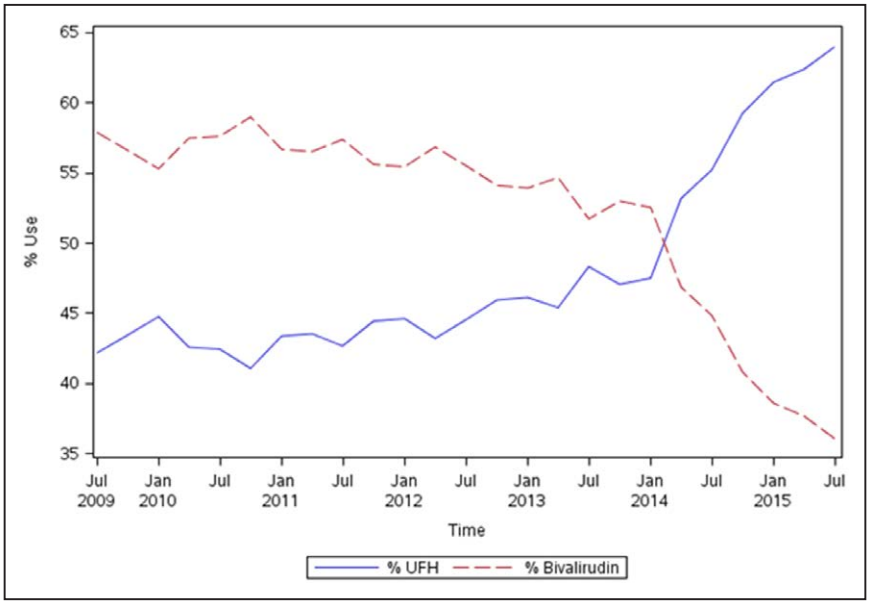

Figure 2. Quarterly proportion of unfractionated heparin (UFH) and bivalirudin use.

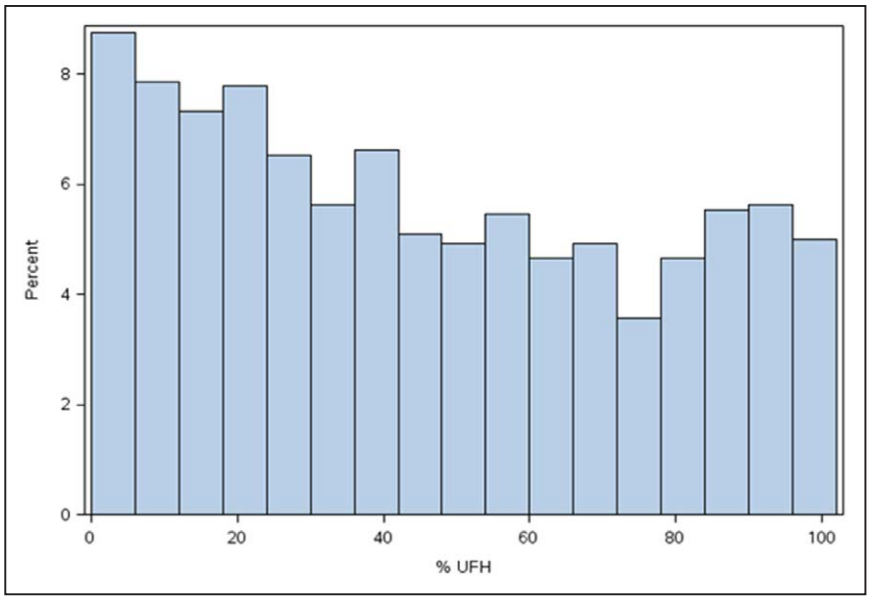

Figure 3. Hospital variation in use of unfractionated heparin (UFH).

cardiogenic shock (4.8% versus 2.6%). At the time of the procedure, patients in the UFH group were more likely to receive aspirin while those in the bivalirudin group were more likely to receive an oral $P2Y_{12}$ inhibitor (Table 2). Radial access was more commonly chosen in patients receiving UFH (9.4% versus 3.1%; $P<0.0001$). Use of intra-aortic balloon pump and other mechanical support devices was observed more often in those receiving UFH.

Table 1. Baseline Patient Characteristics

Variable	Overall (n=71 675)	UFH Alone (n=34 928)	Bivalirudin Alone (n=36 747)	*P* Value
Age	65 (57–73)	65 (57–72)	65 (57–73)	0.6377
Female	38.2%	37.5%	38.8%%	0.0004
Race				
White	65.9%	66.0%	65.9%	0.7256
Black	25.4%	25.8%	25.0%	0.0095
BMI, kg/m^2	28.4 (24.6–33.2)	28.3 (24.5–33.1)	28.5 (24.7–33.3)	0.0005
Previous MI	40.2%	42.8%	37.8%	<0.0001
Previous CHF	39.8%	42.5%	37.3%	<0.0001
Diabetes mellitus	72.8%	73.3%	72.3%	0.0025
Cerebrovascular disease	23.7%	24.4%	23.0%	<0.0001
PVD	31.5%	33.3%	29.8%	<0.0001
Hypertension	95.7%	95.9%	95.6%	0.0673
Current smoker	15.4%	15.8%	14.9%	0.0008
Chronic lung disease	20.5%	21.3%	19.7%	<0.0001
Admission presentation				<0.0001
No symptoms	13.7%	12.6%	14.7%	
Stable angina	13.4%	11.6%	15.1%	
Unstable angina	37.3%	35.1%	39.3%	
NSTEMI	27.9%	32.6%	23.5%	
STEMI	4.5%	5.2%	3.9%	
Cardiogenic shock within 24 h preceding PCI	3.7%	4.8%	2.6%	<0.0001
Cardiac arrest within 24 h preceding PCI	2.1%	2.5%	1.8%	<0.0001

BMI indicates body mass index; CHF, congestive heart failure; MI, myocardial infarction; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; STEMI, ST-segment–elevation myocardial infarction; and UFH, unfractionated heparin.

Table 2. Procedural Characteristics

	Overall (n=71 675)	UFH (n=34 928)	Bivalirudin (n=36 747)	*P* Value
Procedure medications				
Aspirin	86.9%	87.9%	85.8%	<0.0001
Clopidogrel	77.1%	76.5%	77.6%	0.0002
Prasugrel	7.6%	6.6%	8.5%	<0.0001
Ticlopidine	0.2%	0.2%	0.2%	0.34
Arterial access				<0.0001
Femoral	93.3%	90%	96.5%	
Radial	6.1%	9.4%	3.1%	
Highest risk lesion				<0.0001
pRCA/mLAD/pCIRC	38.9%	38.8%	38.9%	
pLAD	15.8%	16.2%	15.5%	
Left main	4.5%	5.2%	3.7%	
Other	40.6%	39.5%	41.7%	
Type of stent				<0.0001
DES placed	68.5%	67.4%	69.6%	
BMS placed	20.5%	20.3%	20.8%	
IABP	2.1%	2.9%	1.4%	<0.0001
Other mechanical support	1.3%	1.8%	0.7%	<0.0001

BMS indicates bare metal stent; DES, drug-eluting stent; IABP, intra-aortic balloon pump; mLAD, mid left anterior descending; pCIRC, proximal circumflex; pLAD, proximal left anterior descending; pRCA, proximal right coronary artery; and UFH, unfractionated heparin.

Outcomes

The observed rate of in hospital bleeding in the overall study population was 8.2%. Bivalirudin use was associated with a lower risk of in hospital bleeding compared with UFH (7.0% with bivalirudin versus 9.5% with UFH; adjusted OR, 0.82; 95% CI, 0.76–0.87; Figure 4). In addition, results using mixed effects models were not materially different (Table I in the Data Supplement). Among propensity-matched patients (n=31 318 matched pairs), similar results were observed (OR, 0.86; 95% CI, 0.81–0.91). Significant differences were observed for site-specific bleeding events, with lower rates of bleeding being observed with bivalirudin for percutaneous access site and gastrointestinal bleeding events (Table 3). A sensitivity analysis was conducted that showed similar results for in hospital bleeding favoring bivalirudin (adjusted OR, 0.83; 95% CI, 0.78–0.90; Figure 4). Given the difference in presentation symptoms between those receiving UFH and those receiving bivalirudin, an analysis was conducted to assess the rates of bleeding based on PCI indication. The rates of bleeding in the overall study population ranged from 5.0% in those with a non–acute coronary syndrome (ACS) indication undergoing PCI to 8.8% in those undergoing PCI for unstable angina/non–STEMI to 20.5% in those undergoing PCI for STEMI. For each indication, lower rates of in hospital bleeding events were observed with bivalirudin compared with UFH (Table 4). No significant interaction was observed between radial access and anticoagulant treatment on in hospital bleeding (adjusted $P_{\text{interaction}}$=0.4875).

The observed rate of in hospital mortality in the overall study population was 3.3%. Rates of in hospital mortality were 4.2% in patients receiving UFH compared with 2.6% in those receiving bivalirudin. After adjustment, bivalirudin was associated with a lower risk of in hospital mortality compared with UFH (adjusted OR, 0.87; 95% CI, 0.78–0.97). Again, results using mixed effects models were not materially different (Table I in the Data Supplement). Similar results were observed in the propensity-matched sample (n=31 318 matched pairs; OR, 0.89; 95% CI, 0.81–0.91). Again, a sensitivity analysis was conducted that produced similar results (adjusted OR, 0.87; 95% CI, 0.77–0.97; Figure 4). The observed mortality rates based on PCI indication in

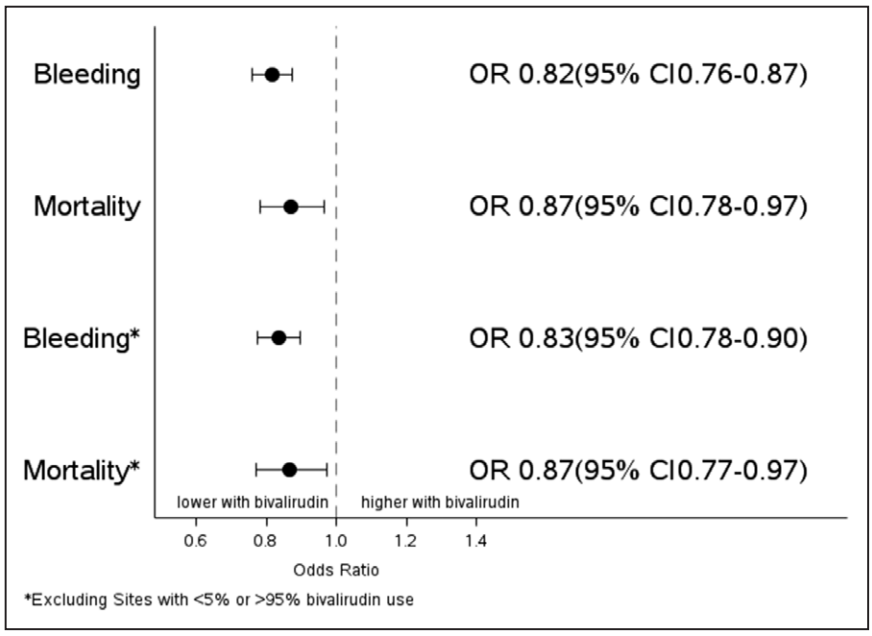

Figure 4. Association of bivalirudin vs unfractionated heparin (UFH) on outcomes. OR indicates odds ratio.

Table 3. Comparison of Site-Specific Bleeding Events

Bleeding Event(s), n (%)	UFH (n=34 928)	Bivalirudin (n=36 747)	*P* Value
Bleeding at percutaneous access site	314 (0.9%)	220 (0.6%)	<0.0001
Hematoma at access site	310 (0.89%)	310 (0.84%)	0.5255
Retroperitoneal bleed	62 (0.18%)	53 (0.14%)	0.2659
Gastrointestinal bleed	156 (0.45%)	127 (0.35%)	0.0311
Genital-urinary bleed	11 (0.03%)	14 (0.04%)	0.6360
Other/unknown	232 (0.66%)	126 (0.34%)	<0.0001

UFH indicates unfractionated heparin.

the overall study population ranged from 1.2% in non-ACS patients to 3.1% in unstable angina/non–STEMI patients to 20.4% in those undergoing PCI for STEMI. For each indication, the observed rates of in hospital mortality were lower in those receiving bivalirudin compared with UFH (Table 4).

Last, the observed rate of in hospital strokes was lower among patients receiving bivalirudin (n=89 [0.24%]) as compared with those receiving UFH (n=133 [0.38%]; *P*=0.0003).

Discussion

In this large contemporary analysis of patients with ESRD undergoing PCI, we observed several major findings. First, although the rates of use of UFH and bivalirudin in patients with ESRD undergoing PCI were similar over the study period, the patterns of use changed over time. Second, patients with ESRD undergoing PCI, especially those with an ACS indication for PCI, are at high risk for adverse outcomes. Third, after adjustment for measured confounders, bivalirudin was associated with lower rates of in hospital bleeding and in hospital mortality compared with UFH.

Bivalirudin and UFH have been the most common anticoagulant therapies studied in contemporary randomized clinical trials of antithrombotic therapies in patients undergoing PCI. However, these clinical trials have largely excluded patients with ESRD. Notably, the pharmacokinetic and pharmacodynamic effects of many of the antithrombotic therapies used in these trials have been shown to have prolonged durations in this group of patients. Product labeling for bivalirudin reports an elimination half-life of 25 minutes for patients without chronic kidney disease which extends to 3.5 hours in patients with ESRD.[9] In addition, chronic kidney disease has been associated with severe, persistent activated partial thromboplastin time prolongations in patients undergoing primary PCI who received UFH.[10] Thus, uncertainty exists on the clinical outcomes which might be associated with the use of these anticoagulants in patients with ESRD undergoing PCI.

To date, limited data have been available to describe the patterns of use of anticoagulant therapies in patients with ESRD undergoing PCI. A previous analysis of the CathPCI registry assessed the use of contraindicated medications in patients with ESRD undergoing PCI but did not describe the use of antithrombotic agents that were not contraindicated.[11] Over the study period of the present analysis (July 2009 to September 2015), we observed an overall similar frequency of use of each agent. However, the patterns of use of each agent changed over time with UFH becoming the more frequently used agent in the second quarter of 2014. Although the reason for this change is unclear, it is possible the presentation and subsequent publication of the HEAT-PPCI trial (How Effective are Antithrombotic Therapies in Primary Percutaneous Coronary Intervention) might have played a role.[12] Although no data on the number or outcomes of patients with ESRD enrolled in this trial have been published to date, the temporal decrease in bivalirudin use we observed is similar to that observed in other populations. Recent publications have described similar decreases in use of bivalirudin in patients with both STEMI and non–STEMI patients undergoing PCI.[13,14] Thus, it is possible that the variations in use observed in the present analysis are simply a reflection of the overall variations observed nationally.

Although previous observations have associated chronic kidney disease with worse outcomes in patients undergoing PCI, this contemporary analysis highlights the increased risks in patients with ESRD. A recent analysis in the overall population from the CathPCI registry reported an in hospital

Table 4. Rates of In Hospital Clinical Outcomes Based on PCI Indication

Variable	Overall (n=71 675)	UFH (n=34 928)	Bivalirudin (n=36 747)	*P* Value
Adverse outcomes				
Overall bleeding	8.2%	9.5%	7.0%	<0.0001
Bleeding among STEMI	20.5%	22.3%	18.3%	0.0043
Bleeding among unstable angina/NSTEMI	8.8%	10.0%	7.6%	<0.0001
Bleeding among non-ACS (no symptoms, atypical chest pain, stable angina)	5.0%	5.8%	4.4%	<0.0001
Overall mortality	3.3%	4.2%	2.6%	<0.0001
Mortality among STEMI	20.4%	23.0%	17.2%	<0.0001
Mortality among unstable angina/NSTEMI	3.1%	3.8%	2.5%	<0.0001
Mortality among non-ACS (no symptoms, atypical chest pain, stable angina)	1.2%	1.4%	1.0%	0.0104

ACS indicates acute coronary syndrome; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and UFH, unfractionated heparin.

bleeding event rate of 1.7%.[15] Comparatively, we observed a rate of 8.2% for this same outcome. In addition, a separate analysis from the CathPCI registry reported in hospital mortality rates for patients undergoing primary PCI for STEMI in the United States to be 5.6%.[13] In the cohort of patients with ESRD undergoing primary PCI for STEMI in this analysis, we observe an in hospital mortality rate of 20.4%. These data underscore the high-risk nature of patients with ESRD undergoing PCI.

In the present analysis, bivalirudin was associated with a lower adjusted risk of in hospital outcomes compared with UFH. Given the differences in the proportion of patients in each anticoagulant group presenting with an ACS indication for PCI, a subgroup analysis based on PCI indication also confirmed this association across indications. These results differ from the results of a single center retrospective analysis of 396 dialysis-dependent patients undergoing PCI who failed to show a significant difference in the rate of bleeding between bivalirudin and UFH (3.4% versus 3.1%, respectively; P=0.9) or a composite cardiovascular end point (1.8% and 0.8%, respectively; P=0.7).[16] One possible reason for the outcomes we observed was the difference in clinical and demographic characteristics between patients who received UFH and those who received bivalirudin. In general, patients who received UFH had a greater burden of comorbid diseases, more often presented with an ACS-related indication for PCI, and more often had high-risk clinical features, including cardiogenic shock and cardiac arrest. The higher acuity in patients receiving UFH is supported by the higher proportion of in hospital deaths that occurred in the catheterization laboratory (9.6% with UFH, 6.8% with bivalirudin; P=0.018). Last, it is important to note that the use of radial access was relatively low in this analysis. Although the reasons for the observed lower rates of radial access are not clear, it may be due, in part, to concerns over the use of radial approach in patients with a planned or present arteriovenous shunt for dialysis.[17]

Given the nonrandomized observational nature of this analysis, several limitations exist for the outcomes observed. As noted above, significant differences were observed between groups with respect to demographic, clinical, and procedural characteristics that might have impacted the results. Although many of these characteristics were covariates in the statistical models used for adjustment, it is possible that we were not able to fully account for these, thereby subjecting the results to possible residual confounding. Second, data on neither the dose of each antithrombotic agent used nor the procedural activated clotting time results were available to be able to assess how the intensity of anticoagulation might have impacted the outcomes observed. In addition, data were also not available on the use of extended anticoagulant infusions postprocedure and therefore limit any conclusions about the use of such a strategy on bleeding or ischemic events in this population. Last, we did not have data for the timing of the initiation of the oral $P2Y_{12}$ inhibitors, which might have impacted the outcomes given the exclusion of concomitant intravenous antithrombotic agents, such as glycoprotein IIb/IIIa inhibitors from this analysis. Finally, not all hospitals participate in the CathPCI registry, and the outcomes described may not apply in those nonparticipating sites.

Conclusions

In this analysis of patients with ESRD undergoing PCI, UFH and bivalirudin were used with similar frequency although the patterns of use changed over the enrollment period. Differences were noted between the 2 groups, with patients receiving UFH being more likely to have comorbid medical conditions and high-risk clinical features, including ACS or cardiogenic shock. Compared with UFH, bivalirudin was associated with lower adjusted risk of in hospital outcomes. However, given the observational nature of this analysis coupled with the ≈4-fold higher rate of in hospital bleeding and mortality in patients with ESRD undergoing PCI compared with the overall population of patients undergoing PCI, a randomized trial of antithrombotic strategies in patients ESRD undergoing PCI is warranted to guide clinical practice.

Disclosures

None.

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Supplemental Material

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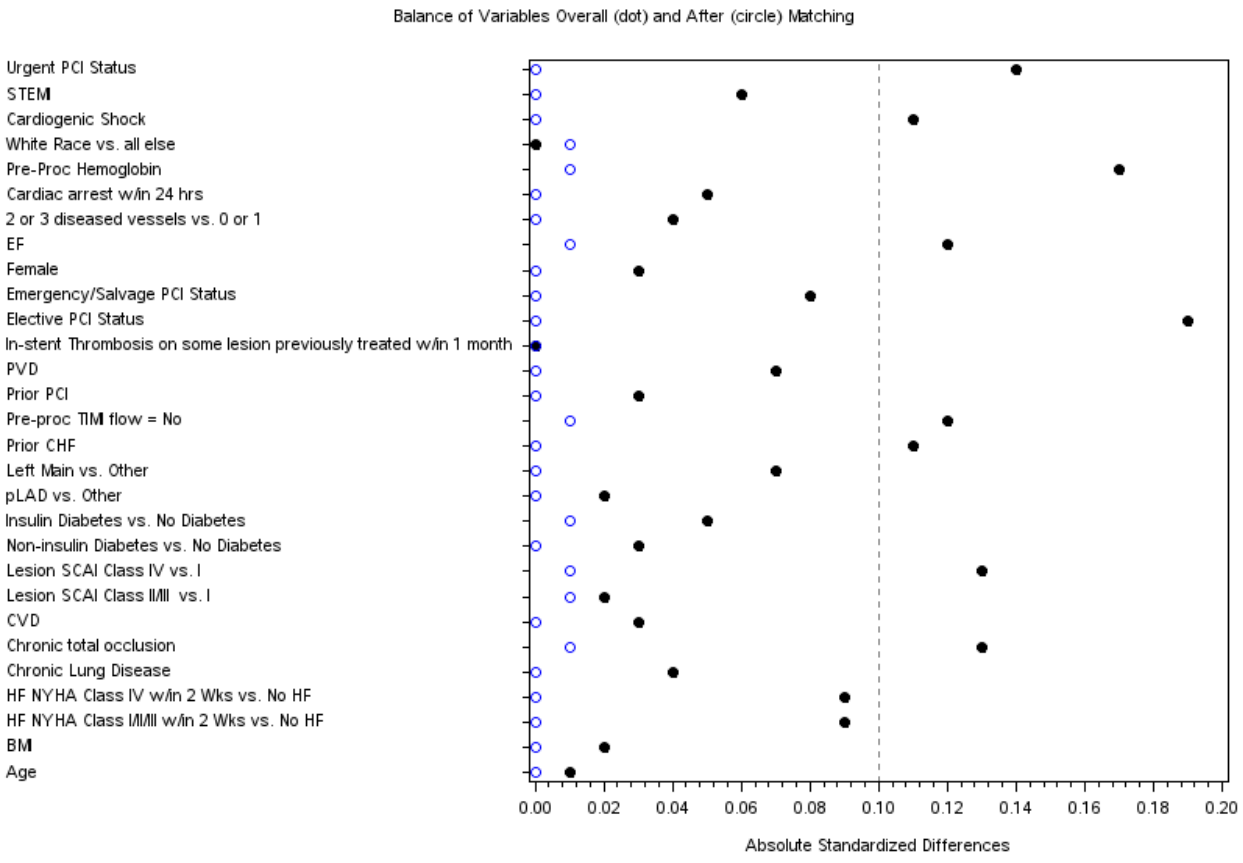
Contents

Supplemental Figure 1: Absolute Standardized Differences of Variables between Bivalirudin and UFH Patients



Supplemental Table 1: Clinical Outcomes in Patients receiving Bivalirudin vs. UFH

		Models with GEE		Models with Random Intercepts for Site	
Outcome	**Effect**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Mortality	Bivalirudin vs. UFH	0.87(0.78, 0.97)	0.0093	0.87(0.78, 0.96)	0.0061
Bleeding	Bivalirudin vs. UFH	0.82(0.76, 0.87)	<.0001	0.82(0.77, 0.88)	<.0001
Mortality: Excluding Sites with <5% or >95% bival use	Bivalirudin vs. UFH	0.87(0.77, 0.97)	0.0147	0.86(0.77, 0.96)	0.0091
Bleeding: Excluding Sites with <5% or >95% bival use	Bivalirudin vs. UFH	0.83(0.78, 0.90)	<.0001	0.84(0.78, 0.90)	<.0001