Safety and Efficacy of Periprocedural Heparin Plus a Short-Term Infusion of Tirofiban Versus Bivalirudin Monotherapy in Patients Who Underwent Percutaneous Coronary Intervention (from the Intermountain Heart Institute STAIR Observational Registry)

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Glycoprotein IIb/IIIa inhibitors, used as a standard intravenous bolus followed by a prolonged infusion for 12 to 18 hours, reduces ischemic complications during percutaneous coronary interventions (PCI) but often at a cost of increased bleeding. Today, when dual oral antiplatelet therapy is routine, heparin use plus short-term (bolus alone or with a <6 hours infusion) glycoprotein IIb/IIIa inhibitors, or bivalirudin monotherapy, have been proposed as potentially superior alternatives. This observational study evaluated the safety and efficacy of heparin plus short-term tirofiban versus bivalirudin monotherapy during PCI. Patients with successful PCI and no cardiogenic shock who were anticoagulated with either of the above regimens were followed for 30-day major bleeding and major adverse cardiovascular events (death, nonfatal myocardial infarction, and urgent target vessel revascularization) at 30 days, 1 year, and long term. A total of 727 patients receiving tirofiban (age = 63 ± 13 years, males = 76%, ACS presentation = 75%, radial access = 51%) and 459 patients receiving bivalirudin, (age = 65 ± 13 years, males = 71%, ACS presentation = 78%, radial access = 18%) were included. Thirty-day major bleeding was 0.7% and 4.1% for tirofiban and bivalirudin, respectively (adjusted odds ratio = 0.17 [0.06, 0.46], p = 0.001). During 30-day, 1-year, and long-term (1.7 ± 0.9 years) follow-up, major adverse cardiovascular events risk did not differ significantly between tirofiban and bivalirudin. However, long-term death was significantly lower in those receiving tirofiban (adjusted hazard ratio = 0.58 [0.34, 1.00], p = 0.05). In conclusion, in this observational study, PCI patients receiving heparin plus short-term tirofiban experienced significantly lower 30-day major bleeding, and improved long-term survival, than those receiving bivalirudin monotherapy. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1927−1934)

Glycoprotein (GP) IIb/IIIa inhibitors are potent antagonists of platelet aggregation proved beneficial in preventing periprocedural ischemic complications after PCI.[1−3] However, use of GP IIb/IIIa inhibitors, especially when given in conjunction with prolonged (12 to 24 hour) infusions, has been associated with increased bleeding complications.[4] The recommendation for prolonged infusions came initially from the *Evaluation of the 7E3 for the Prevention of Ischaemic Complications (EPIC)* trial[1] in which the initial bolus followed by a 12-hour infusion of abciximab was found to be more efficacious than bolus alone. However,

the EPIC trial was before the advent of routine dual anti-platelet therapy (DAPT).[5] It has been proposed that in the setting of DAPT, prolonged infusions of GP IIb/IIIa inhibitors may not be necessary for efficacy and that shortening or eliminating the after-bolus infusion may reduce the risk of bleeding complications.[6] This proposal was tested in patients who underwent elective uncomplicated coronary interventions during the Brief PCI trial,[7] in which it was concluded that in conjunction with DAPT, the postbolus infusion of the GP IIb/IIIa inhibitor eptifibatide could be safely abbreviated from 18 to <2 hours. Short infusion was not inferior to the standard 18-hour infusion in preventing ischemic adverse events, and it was associated with less major bleeding. Studies using tirofiban have also indicated that in the setting of DAPT a bolus alone, or with a short-term infusion of GP IIb/IIIa inhibitor therapy, may be safer and equally effective.[6,8,9] Bivalirudin, a powerful direct thrombin inhibitor,[10] is proposed to be an effective monotherapy alternative to the combination of heparin and GP IIb/IIIa inhibitors.[11−13] Although in most studies patients randomized to bivalirudin as monotherapy were provided

an option to also receive bailout GP IIb/IIIa inhibitors, a meta-analysis of existing data reported that bivalirudin monotherapy resulted in a significant reduction in major bleeding when compared with heparin plus routine use of GP IIb/IIIa inhibitors.[14] How the use of bivalirudin, as described previously, compares with the use of heparin with a bolus and *short-term* infusions of GP IIb/IIIa agents remains unknown. Since January 2013, Intermountain Heart Institute physicians have primarily used heparin, bivalirudin, and/or tirofiban during PCI in any way they feel is best for their patients. The purpose of the *Short Term Aggrastat Infusion Registry* (STAIR) study, therefore, was to determine the comparative safety and efficacy of the use of heparin plus a short-term administration of tirofiban versus bivalirudin monotherapy during PCI.

Methods

Using single-center data from the electronic health record, and without directly contacting patients, we conducted a retrospective, descriptive study of all consecutive patients who underwent successful PCI at Intermountain Medical Center from January 1, 2013 through October 11, 2016. This study was approved by the hospital Institutional Review Board with a waiver of consent. Patients were included if they received either heparin with a planned (initiated before PCI commenced) use of tirofiban, either as an intravenous bolus alone (25 mcg/kg), or a bolus followed by a short (<6 hours) infusion (0.15 mcg/kg/min), or an intravenous bolus of bivalirudin (0.75 mg/kg) followed by a short (for procedure duration or <4 hours postprocedure) infusion (1.75 mg/kg/h) without the planned use of any GP IIb/IIIa agents. Patients were excluded if they presented with cardiogenic shock, received thrombolytic agents within 24 hours of PCI, received heparin monotherapy, or received planned long-term tirofiban infusions.

Baseline clinical and laboratory characteristics, segregated according to the use of tirofiban or bivalirudin, were collected and included age, gender, and presence of any of the following conditions: hypertension, hyperlipidemia, diabetes mellitus, smoking history, family history of coronary artery disease, previous myocardial infarction (MI), previous stroke, previous history of coronary artery disease, renal failure (defined as serum creatinine >1.5 mg/dl), heart failure, history of peripheral vascular disease, atrial fibrillation, history of chronic lung disease, history of sleep apnea, history of previous bleeding, body mass index, clinical presentation (stable angina pectoris, unstable angina pectoris, and MI); medications on admission, and whether or not the patient received a loading dose of aspirin and/or a P2Y12 antiplatelet agent before angiography.

Procedural characteristics collected included type of arterial access (radial or femoral), type of stents used (drug-eluting or bare metal), target vessels treated, number of stents placed, duration of infusions of tirofiban and bivalirudin, and type of P2Y12 inhibitor used.

After completion of the procedure, each patient was followed for safety and efficacy end points to January 1, 2017. The primary end point of the study was the incidence of major bleeding (defined as Thrombolysis in Myocardial Infarction [TIMI] major bleeding[15] or any

blood transfusion). Secondary end points included the safety end point of TIMI minor bleeding[13] (defined as any decrease in hemoglobin between 3 and <5 g/dl or a decrease in hematocrit of between 10% and <15% during the initial hospitalization), and the efficacy end points of major adverse cardiovascular events (MACE), at 30 days, 1 year, and during long-term follow-up, including all-cause death (as determined by state of Utah death certificates, the Social Security death master index, and electronic medical records), non-fatal MI (as determined by ICD-9 code 410.x1 and ICD-10 code I21. x and verified through chart review) and urgent target vessel revascularization (UTVR) (defined as either urgent percutaneous revascularization or coronary artery bypass surgery involving a vessel that had been treated during the index procedure), and combined MACE.

Chi-square statistic and Student's *t* test were used to describe the study population and to examine univariable associations of categorical and continuous variables between the 2 anticoagulation strategies. To confirm the associations determined by univariable analysis, multivariable logistic, and Cox regression analyses (SPSS software, version 13.0, SPSS, Inc., Chicago, Illinois), including all reported baseline and procedural characteristics, were performed to determine odds ratios and hazard ratios, respectively. Models entered variables using forward stepwise regression and forced variable entry with final models entering significant and confounding covariables. To verify results obtained by multivariable adjustment, a propensity analysis was performed. To estimate the propensity score, a logistic regression model was used in which the dependent variable (i.e., bivalirudin or tirofiban) was regressed on by confounders. Two different propensity analyses were performed. First, patients were matched on propensity score (±0.01), resulting in 870 patients (435/group), and evaluated for the end points. In addition, instead of using individual confounders for multivariable modelling, models were adjusted by the propensity score. In all segregated analyses, multivariable adjustments were made using the propensity score because of the lower sample size and thus reduced event rate.[16] Two-tailed p values are presented, with 0.05 designated as nominally significant.

Results

The total numbers of patients who underwent PCI at Intermountain Medical Center during the study period are shown in Figure 1. Almost 40% of all patients were included in this study. Study patient baseline characteristics, segregated by anticoagulation strategy used, are shown in Table 1. In general, patients receiving tirofiban were younger, had a lower prevalence of renal or heart failure, and more often presented with MI. Propensity matched patients resulted in more similarly comparable groups (Supplemental Table 1).

Procedural characteristics are shown in Table 2 and Supplemental Table 2. Radial access was used more frequently in those patients who received tirofiban compared with bivalirudin. More than half of patients had multivessel coronary artery disease in both groups. Drug eluting stents were primarily used in both groups. Tirofiban was given as
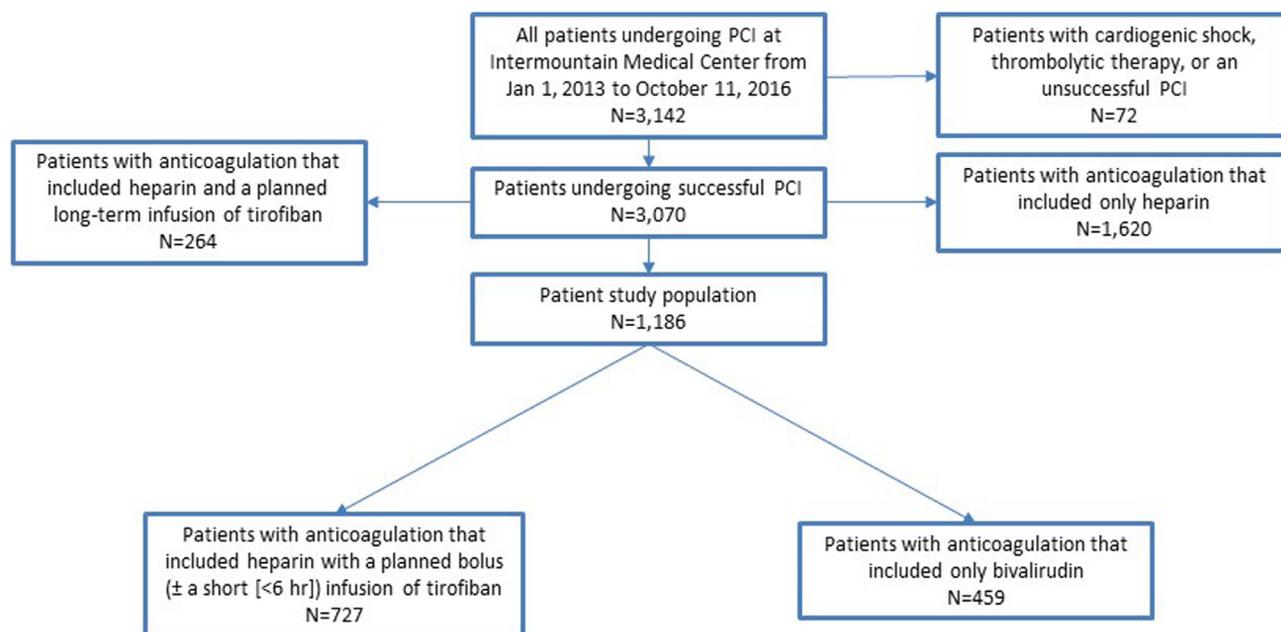
Figure 1. Consort diagram showing categorization of all patients who underwent PCI during the study time-period.

Table 1
Patient baseline clinical characteristics stratified by anticoagulation strategy

Variable	Bivalirudin (n = 459)	Tirofiban* (n = 727)	p value
Age (years)	65.0 ± 12.5	63.3 ± 12.5	0.02
Men	71.2%	75.8%	0.08
Hypertension	63.8%	63.2%	0.82
Hyperlipidemia[†]	66.7%	69.5%	0.31
Diabetes Mellitus	42.5%	39.1%	0.25
Smoker	25.3%	25.7%	0.87
Family history of coronary artery disease (CAD)	37.0%	44.4%	0.01
Prior myocardial infarction	14.6%	17.4%	0.20
Prior stroke	2.4%	3.0%	0.52
Prior CAD	46.4%	43.7%	0.36
Renal failure	4.8%	1.6%	0.002
Heart failure	26.4%	19.8%	0.008
Prior peripheral vascular disease	9.6%	6.0%	0.02
Atrial fibrillation	18.7%	14.1%	0.04
Prior chronic obstructive pulmonary disease	11.8%	10.3%	0.43
Sleep apnea	26.4%	28.6%	0.41
Prior bleeding	18.7%	17.0%	0.45
Prior major bleeding	5.7%	5.8%	0.94
Body mass index (kg/m^2), n = 1083	29.8 ± 6.5	30.4 ± 6.7	0.15
Presentation			<0.0001
Stable angina pectoris	21.8%	24.6%	
Unstable angina pectoris	37.0%	23.1%	
Myocardial infarction	41.2%	52.3%	
Pre-cath Aspirin	64.7%	48.9%	<0.0001
Pre-cath glycoprotein P2Y12 inhibitor	9.1%	7.0%	0.35
Statin	95.2%	90.8%	0.005
Lipid lowering	97.6%	92.6%	<0.0001
Antiplatelet	95.0%	86.2%	<0.0001
Warfarin	5.4%	2.2%	0.003
Calcium channel blocker (CCB)	8.1%	7.3%	0.63
Angiotensin converting enzyme inhibitor (ACEI)	30.9%	39.1%	0.004
Angiotensin receptor blocker (ARB)	8.7%	9.5%	0.65
Diuretic	19.6%	13.1%	0.002

* Tirofiban = bolus heparin with planned short term tirofiban infusion.
[†] Hyperlipidemia was defined as a total cholesterol >200 mg/dl and/or low-density lipoprotein (LDL) cholesterol >130 mg/dl.

Table 2
Percutaneous coronary intervention procedural characteristics stratified by anticoagulation strategy

	Bivalirudin (n = 459)	Tirofiban* (n = 727)	p value
Radial access[†]	18.1%	51.4%	<0.0001
Femoral access[†]	85.2%	51.4%	<0.0001
Drug eluting stent	89.1%	95.7%	<0.0001
Bare metal stent	10.9%	4.3%	<0.0001
Coronary artery disease	99.1%	99.2%	0.93
Number of diseased (≥70%) vessels			0.03
1	43.4%	42.4%	NS
2-4	45.2%	50.4%	NS
≥5	11.5%	7.2%	NS
Max. ACT (median)[‡]	—	248 seconds	—
Procedure glycoprotein P2Y12 inhibitor			
Clopidogrel	66.6%	55.6%	0.0002
Prasugrel	29.4%	39.7%	0.0004
Ticagrelor	4.0 %	4.7%	NS

* Tirofiban = bolus heparin with planned short term tirofiban infusion.

[†] Some patients received vascular access by both the radial and femoral approaches, thus resulting in >100% when added together.

[‡] Max. ACT = maximum procedural activated clotting time after heparin bolus.

a bolus with no further infusion in 448 (61.5%) patients. Of the remaining 280 patients who received both the tirofiban bolus and infusion, the average length of infusion was 3.9 ± 1.3 hours (median: 4.1 [range = 0.3 to 6.0] hours). Of those receiving bivalirudin, the average length of infusion was 0.24 ± 1.74 hours (median: 0.03 [0 to 23.31] hours). Although clopidogrel was mainly used in both groups, prasugrel was used somewhat more commonly in patients receiving tirofiban compared with bivalirudin.

The average length of follow-up was significantly shorter (1.3 ± 0.9 years) in patients treated with the tirofiban strategy than those receiving bivalirudin (2.4 ± 0.9 years). Table 3 shows the univariable outcome frequencies for the primary and secondary end points of the study at 30 days, 1 year, and after long-term follow-up, segregated by anticoagulation strategy. Survival curves for all-cause death, nonfatal MI, and UTVR are shown in Figure 2. The incidence of the primary end point, major bleeding at 30 days, was low in both groups, but significantly lower in patients treated with tirofiban than with bivalirudin. No significant difference in the incidence of in-hospital TIMI minor bleeding was noted between tirofiban and bivalirudin. The univariable outcome frequency of the efficacy end point of MACE was significantly lower in patients treated with tirofiban at 30 days, 1 year, and during long-term follow-up. Additionally, the incidence of all-cause death was lower in patients treated with tirofiban at both 1 year and after long-term follow-up. No significant differences in the frequency of MI and TVR were noted between the 2 strategies of anticoagulation.

Table 3
Univariable outcome frequencies for the primary and secondary end points of the study at 30 days, 1 year, and after long-term follow-up, stratified by anticoagulation strategy

	Bivalirudin	Tirofiban*	p value
30 day TIMI major bleed (including any transfusion)	4.1%	0.7%	<0.0001
MACE (Death, myocardial infarction, UTVR)			
30 day	2.8%	1.2%	0.05
1 year, n = 982	7.9% (36/458)	4.2% (22/524)	0.02
Long-term	17.4%	8.0%	<0.0001
Death			
30 day	1.7%	1.1%	0.35
1 year, n = 982	6.1% (28/458)	2.7% (14/524)	0.008
Long-term	10.7%	3.2%	<0.0001
Myocardial infarction			
30 day	0.4%	0.1%	0.56
1 year, n = 982	0.7% (3/458)	0.4% (2/524)	0.67
Long-term	7.0%	4.4%	0.06
Urgent target vessel revascularization (UTVR)			
30 day	0.7%	0%	0.06
1 year, n = 982	1.3% (6/458)	1.3% (7/524)	1.00
Long-term	2.2%	1.9%	0.76
TIMI minor bleed in hospital	3.5%	4.1%	0.58

MACE = major adverse cardiovascular events; TIMI = thrombolysis in myocardial infarction.

* Tirofiban = bolus heparin with planned short term tirofiban infusion.

Table 4

Multivariable adjusted, propensity matched, and propensity score adjusted odds ratios and hazard ratios for treatment with tirofiban versus bivalirudin (referent)

	Multivariable adjusted	Propensity matched N = 870 (435/group)	Propensity score adjusted
30 day TIMI major bleed (including any transfusion)	OR = 0.17 (0.06, 0.46), p = 0.001	OR = 0.16 (0.05, 0.55), p = 0.004	OR = 0.20 (0.07, 0.54), p = 0.002
TIMI Minor In Hospital	OR = 1.17 (0.62, 2.21), p = 0.64	OR = 1.08 (0.51, 2.26), p = 0.85	OR = 1.21 (0.64, 2.28), p = 0.56
Major adverse cardiovascular event			
30 day	OR = 0.37 (0.14, 0.98), p = 0.04	OR = 0.49 (0.18, 1.33), p = 0.16	OR = 0.56 (0.23, 1.349), p = 0.19
1 year	OR = 0.67 (0.37, 1.22), p = 0.18	OR = 0.45 (0.23, 0.91), p = 0.03	OR = 0.69 (0.39, 1.22), p = 0.21
Long-term	HR = 1.02 (0.71, 1.47), p = 0.92	HR = 0.71 (0.45, 1.12), p = 0.14	HR = 0.99 (0.69, 1.44), p = 0.99
Death			
30 day	OR = 0.76 (0.26, 2.21), p = 0.61	OR = 0.86 (0.29, 2.57), p = 0.78	OR = 0.90 (0.32, 2.50), p = 0.84
1 year	OR = 0.57 (0.27, 1.20), p = 0.14	OR = 0.50 (0.23, 1.09), p = 0.08	OR = 0.64 (0.32, 1.26), p = 0.20
Long-term	HR = 0.58 (0.34, 1.00), p = 0.05	HR = 0.51 (0.28, 0.93), p = 0.03	HR = 0.58 (0.34, 0.98), p = 0.04
Myocardial infarction			
30 day	OR = 0.32 (0.03, 3.77), p = 0.37	*	OR = 0.35 (0.03, 4.15), p = 0.41
1 year	OR = 0.58 (0.10, 3.57), p = 0.56	*	OR = 0.55 (0.09, 3.47), p = 0.53
Long-term	HR = 1.14 (0.68, 1.91), p = 0.61	HR = 0.80 (0.41, 1.55), p = 0.80	HR = 1.16 (0.69, 1.94), p = 0.58
Urgent target vessel revascularization			
30 day	Not enough events	Not enough events	Not enough events
1 year	OR = 0.99 (0.32, 3.01), p = 0.98	OR = 0.45 (0.09, 2.27), p = 0.34	OR = 0.95 (0.31, 2.94), p = 0.93
Long-term	HR = 1.44 (0.61, 3.39), p = 0.40	HR = 0.79 (0.26, 2.35), p = 0.67	HR = 1.33 (0.57, 3.11), p = 0.51

* HR = hazard ratio; OR = odds ratio; TIMI = thrombolysis in myocardial infarction.

Multivariable adjusted, propensity-matched, and propensity score-adjusted ORs and HRs for treatment with tirofiban versus bivalirudin are shown in Table 4. After every method of adjustment, the incidence of major bleeding at 30 days remained significantly lower with the use of tirofiban. However, the propensity-adjusted risk of 30-day, 1-year, and long-term MACE did not differ significantly between the 2 anticoagulation strategies. Likewise, at all time points, the adjusted ORs and HRs associated with the individual MACE components of MI and UTVR did not differ significantly between the 2 groups. However, the adjusted long-term risk of death remained lower in those receiving tirofiban.

The results of multivariable subgroup analyses (adjusted by propensity score) for age, gender, clinical presentation, vascular access, and type of P2Y12 agent used are shown in Figure 3. The reduction in 30-day major bleeding associated with the use of tirofiban was especially apparent in patients over 70 years old and in those presenting with stable or unstable angina pectoris. This reduction persisted regardless of which P2Y12 inhibitor was used. Interestingly, no patient who underwent PCI through a radial access experienced a major bleed. No significant interactions between any of the subgroups analyzed on the effect of tirofiban versus bivalirudin on MACE, death, MI, or UTVR were identified.

Discussion

In this study 2 major observations were made. First, the incidence of 30-day major bleeding was low for both short-term anticoagulation treatment strategies. However when compared, the adjusted incidence of major bleeding was lower in those treated with the tirofiban strategy, especially in patients over the age of 70.

Second, there was no significant difference in the adjusted incidence of 30-day, 1-year, or long-term risk of overall MACE. However, the use of heparin plus short-term tirofiban was associated with a significant reduction in the risk of death during long-term follow-up, a finding that should be considered exploratory. No significant differences in the incidence of non-fatal MI or UTVR were noted between anticoagulation strategies.

In the EPIC trial,[1] the first major clinical study testing GP IIb/IIIa inhibitors during PCI, the incidence of major bleeding was doubled (14% versus 7%) in patients randomized to receive an abciximab bolus plus a 12-hour infusion. In the follow-up *Evaluation in PTCA to Improve Long-term Outcome with abciximab GP IIb/IIIa blockade* (EPILOG) trial,[17,18] abciximab was given with a significantly lower dose of heparin, targeting an ACT of ≥200 seconds, which maintained similar efficacy, but significantly reduced the risk of bleeding.[19,20] Because of the results of EPIC,[1] when the short-acting GP IIb/IIIa agents, tirofiban and eptifibatide, were initially tested, the recommended postprocedural infusion times were 12 to 24 hours.[3,21] In the setting of DAPT, whether a shorter postbolus infusion may provide adequate efficacy but even greater safety[6] was tested and supported in both the BRIEF-PCI[7] and FABULUS PRO[22] trials. Similarly, in our study, short-term tirofiban was associated with a significant reduction in 30-day major bleeding, even when compared with bivalirudin alone.

The use of prolonged postprocedural infusions of GP IIb/IIIa inhibitors during PCI has been shown to reduce the incidence MACE at both 30 days[20,23] and 1 year.[2,24,25] Additionally, in the BRIEF-PCI study[7] patients who underwent PCI randomized to receive heparin plus a brief (versus a prolonged) infusion of eptifibatide showed noninferior MACE efficacy along with significantly improved safety regarding major bleeding.
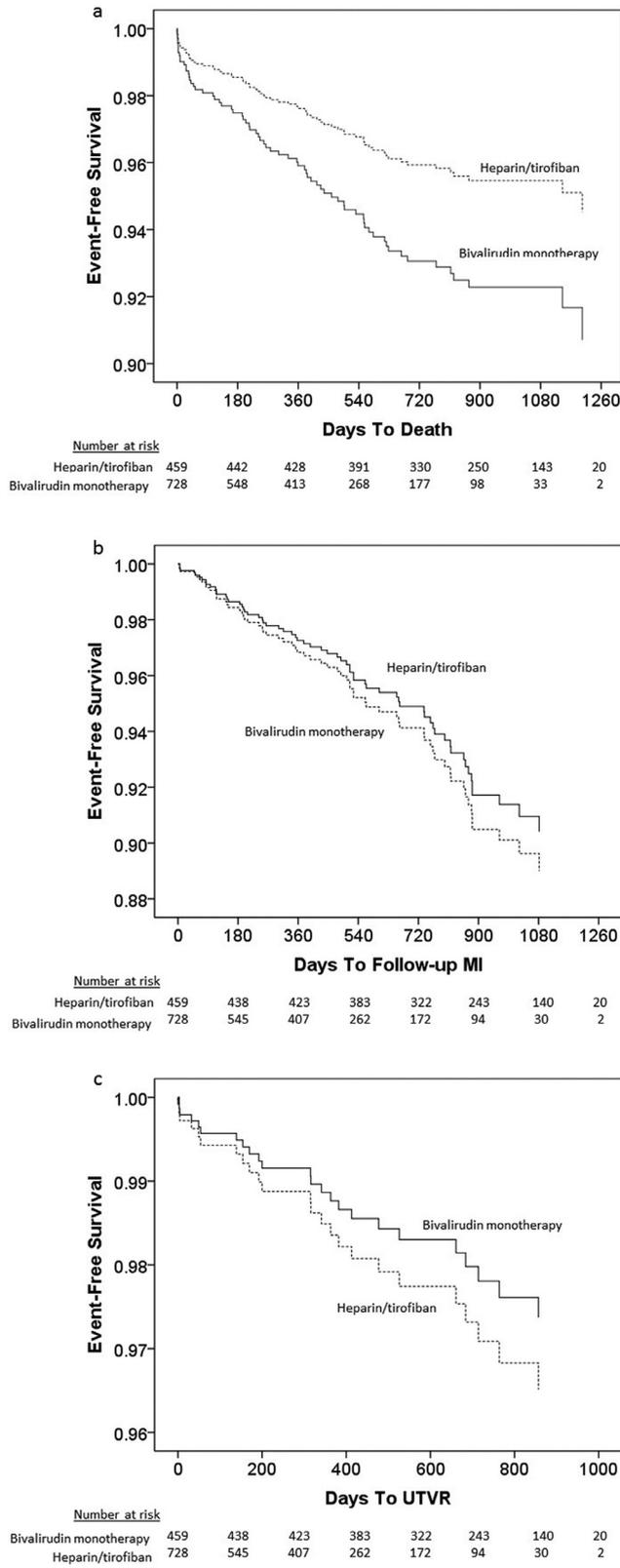
Figure 2. Study patient survival curves for the major adverse cardiovascular events segregated by anticoagulation strategy. (a) Survival curves for all cause death. (b) Survival curves for non-fatal MI. (c) Survival curves for UTVR.
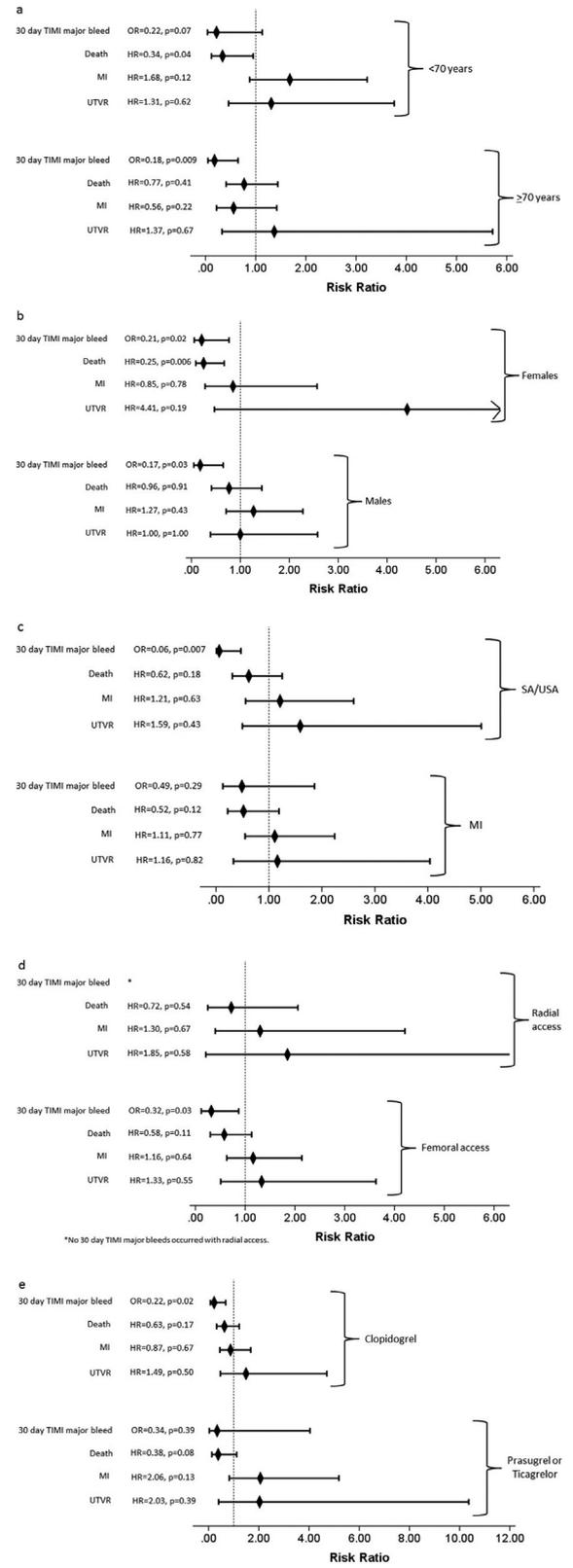
Figure 3. Forest plots depicting hazard ratios for various safety and efficacy end points for the use of tirofiban versus bivalirudin segregated by a variety of baseline subgroups. (a) Segregated by age <70 and ≥70 years. (b) Segregated by gender. (c) Segregated by clinical presentation, MI versus stable/unstable angina (SA/USA). (d) Segregated by vascular access. (e) Segregated by P2Y12 inhibitor used.

Our study evaluated the efficacy of shortened infusions of GP IIb/IIIa inhibitors by comparing the use of heparin plus tirofiban directly to the use of bivalirudin as monotherapy. Bivalirudin, used as monotherapy, has been proposed as an acceptable alternative to the combination of heparin and a GP IIb/IIIa inhibitor.[26−28] This hypothesis has been tested in large clinical trials[11,12] and has always shown noninferior efficacy results. In our observational study, the MACE efficacy of heparin plus short-term tirofiban did not differ significantly from bivalirudin monotherapy. However, our study did show a statistically significant reduction in long-term mortality associated with the use of short-term tirofiban versus bivalirudin monotherapy. This could be a chance finding or due to residual confounding, but it also is consistent with the results of the HORIZONS AMI trial[29] in which an observed 28% reduction in long-term mortality by the use of bivalirudin monotherapy, compared with heparin plus prolonged infusions of GP IIb/IIIa inhibitors, in patients presenting with acute ST elevation MI has been ascribed to the also-observed 36% reduction in major bleeding. In our study, the strategy of short-term tirofiban was associated with an even lower risk of major bleeding than bivalirudin monotherapy. This emphasizes the point that in the HORIZONS-AMI trial, the increased major bleeding risk that resulted from randomization to heparin was almost certainly due to the prolonged (12 to 18 hours) infusion of GP IIb/IIIa inhibitor used, a risk that can be eliminated by simply shortening the length of the infusion.

Because of bleeding risks during PCI, it is proposed that GP IIb/IIIa inhibitors should be reserved for use in "high-risk" patients or as "bailout" therapy.[30] Our present study provides evidence for a method of routinely using GP IIb/IIIa inhibitors during PCI, which may optimize efficacy and also minimize major bleeding.

This observational study may be limited by unadjusted selection biases. However, every effort was made to appropriately adjust for all known baseline differences. The ongoing randomized open-label *Shortened Aggrastat versus Integrilin in Percutaneous Coronary Intervention (SAVI-PCI)* trial, comparing short-term tirofiban versus long-term tirofiban versus label-recommended eptifibatide, should shed a potentially less-biased light on the safety and efficacy of tirofiban. (https://clinicaltrials.gov/ct2/show/NCT01522417).

In this observational study of patients who underwent successful PCI, those who were selected to receive periprocedural anticoagulation with heparin plus short-term tirofiban experienced lower 30-day major bleeding than those selected to receive bivalirudin monotherapy. Over-all MACE did not differ between groups, but long-term survival was observed in those who received tirofiban. Our results suggest that the routine use of GP IIb/IIIa inhibitors in this way may provide improved safety and long-term efficacy in patients who underwent percutaneous coronary interventions.

Declarations of Interest

Dr. Muhlestein reports that he participated in a consultancy dinner meeting sponsored by Medicure. Dr. May reports modest consulting for Medicure unrelated to the present study. No other potential conflicts of interest exist.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.03.025.

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