

Comparison of Safety and Efficacy of Bivalirudin Versus Unfractionated Heparin in Percutaneous Peripheral Intervention

A Single-Center Experience

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Objectives The aim of this study was to determine the efficacy and safety of bivalirudin versus low-dose unfractionated heparin (UFH) in percutaneous peripheral intervention (PPI).

Background Anticoagulation strategies used in PPI are based primarily on studies of percutaneous coronary intervention where higher doses of heparin are used usually in combination with a glycoprotein IIb/IIIa inhibitor. There are no studies comparing bivalirudin alone versus low-dose heparin in PPI.

Methods Consecutive patients who underwent PPI at our institution were treated with either bivalirudin or low-dose UFH. Patients were assessed prospectively during index hospital stay for procedural success and bleeding complications. Of 236 patients, 111 were dosed with UFH at 50 U/kg (goal activated clotting time of 180 to 240 s), and 125 were dosed with bivalirudin at 0.75-mg/kg/h bolus followed by a 1.75-mg/kg infusion. Procedural success was defined as <20% post-procedure residual stenosis with no flow-limiting dissections or intravascular thrombus formation and major bleeding as intracranial or retroperitoneal hemorrhage or a fall in hemoglobin ≥ 5 g/dl. Anticoagulation cost analysis was conducted.

Results Procedural success and major bleeding rates were similar with bivalirudin versus heparin (98% vs. 99% and 2.4% vs. 0.9%, respectively). There were no differences in minor bleeding, time to ambulation, and length of hospital stay. The hospital cost for bivalirudin was \$547 and <\$1.22 for heparin (10,000 U). Two activated clotting time levels cost \$4.00.

Conclusions Low-dose UFH is as effective and safe as bivalirudin when used as an anticoagulation strategy in patients undergoing PPI, and low-dose UFH is less costly than bivalirudin. Larger randomized studies are required to further evaluate these findings. (J Am Coll Cardiol Intv 2009;2: 871–6) © 2009 by the American College of Cardiology Foundation

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Approximately 14 to 16 million Americans suffer from peripheral arterial disease (1), some of whom will require intervention. The goal of any percutaneous peripheral intervention (PPI) is not only to achieve immediate procedural success but also to avoid any post-procedure complications. Patients with peripheral arterial disease undergoing PPI are at high risk for thrombotic complications. This risk is reduced with the use of anticoagulation during the procedure. However, anticoagulation itself leads to higher post-procedure bleeding rates. An ideal anticoagulation strategy would be one that reduces thrombosis risk with little or no increase in bleeding rates.

Currently, there are no American College of Cardiology/American Heart Association guidelines for anticoagulation in PPI. Anticoagulation strategies used during PPI are based primarily on studies conducted for percutaneous coronary intervention (PCI), in which the safety and efficacy of unfractionated heparin (UFH) and bivalirudin have been clearly defined (2–6). Some studies have suggested that bivalirudin offers the same efficacy as UFH but with reduced ischemic and bleeding complication rates (5–7). However, in these studies, relatively higher doses (up to 70 to 175 U/kg) of heparin were used, usually in combination with a glycoprotein (GP) IIb/IIIa receptor inhibitor. Large-scale randomized studies directly comparing in-hospital efficacy and complication rates of low-dose heparin versus bivalirudin in PPI have not been conducted. In this prospective cohort study, we compared the in-hospital efficacy and safety of low-dose UFH versus bivalirudin in patients undergoing PPI.

Abbreviations and Acronyms

ACT = activated clotting time

GP = glycoprotein

PCI = percutaneous coronary intervention

PPI = percutaneous peripheral intervention

PRBC = packed red blood cells

UFH = unfractionated heparin

in-hospital efficacy and safety of low-dose UFH versus bivalirudin in patients undergoing PPI.

Methods

Consecutive patients undergoing PPI at Aurora Sinai and Aurora St. Luke's Medical Centers in Milwaukee were studied in a nonblinded, prospective fashion between March and July 2008. Patients over the age of 18 requiring noncoronary/noncarotid PPI met the inclusion criteria. The exclusion criteria included: 1) acute limb ischemia; 2) use of fibrinolytic agents or GP IIb/IIIa receptor inhibitors; 3) myocardial infarction or stroke in the last 6 months; and 4) contraindication to use of bivalirudin or heparin. A total of 236 patients were enrolled. Eight operators alternated the use of bivalirudin and heparin in consecutive patients; 125 received bivalirudin and 111 received heparin. The institutional review board approved the protocol.

Study protocol. Bivalirudin was used at the standard dose of 0.75-mg/kg bolus and 1.75-mg/kg/h infusion. Bivalirudin

infusion was discontinued at the end of the procedure. Heparin was given as a bolus of 50 U/kg with additional boluses given to maintain an activated clotting time (ACT) between 180 and 240 s. The ACT levels were checked at 5 and 30 min after the bolus. Femoral sheaths were removed 2 h after bivalirudin infusion was discontinued in patients with normal renal function and at ACT <160 s in patients receiving heparin. Patients were put on bed rest for 4 to 6 h after sheath removal in both groups. Please see Table 1 for the number of patients receiving pre-procedure acetylsalicylic acid (ASA), clopidogrel, and warfarin. Of the patients taking warfarin in each group, only 1 bivalirudin patient (pre-procedural international normalized ratio 1.6) suffered a minor bleed. Daily dosing of lifelong ASA 325 mg and 1 month of clopidogrel 75 mg were given to the majority of patients. Exceptions included superficial femoral artery or below-the-knee intervention, in which case clopidogrel dosing was increased to 6 to 12 months, or if the patient was taking warfarin (for any other medical indication), in which case the ASA dose was decreased to 81 mg daily and duration of clopidogrel dosing was decreased to 2 weeks.

Duration of procedure, largest sheath size used, baseline renal function, international normalized ratio, and complete blood count before and after the procedure were all recorded. Signs or symptoms of acute thrombosis were monitored, and a duplex ultrasound was performed if clinically indicated. Patients were followed while they were in the hospital to check for any signs or symptoms of bleeding. Time of sheath removal, time to ambulation, and length of hospital stay were documented. The overall cost per patient was calculated for both the heparin and the bivalirudin groups. **Study end points.** Primary study end points included immediate procedural success and in-hospital major bleeding. Procedural success was defined as residual stenosis of <20% in the

Table 1. Baseline Demographic Data and Clinical Characteristics

Variable	Bivalirudin (n = 125)	UFH (n = 111)	p Value
Age (yrs)	69.9 ± 10.43	71.2 ± 11.88	0.3724
Male	71 (56.8%)	51 (46.0%)	0.1250
CAD	98 (78.4%)	90 (81.1%)	0.7271
Diabetes mellitus	56 (44.8%)	45 (40.5%)	0.5975
Hypertension	96 (76.8%)	82 (73.9%)	0.7114
Dyslipidemia	78 (62.4%)	74 (66.7%)	0.5837
Obesity (BMI >30 kg/m ²)	70 (56.0%)	54 (48.7%)	0.3183
Current cigarette smoker	35 (28.0%)	28 (25.2%)	0.7391
Medications (pre-procedure)			
ASA	113 (90.4%)	103 (92.8%)	0.6716
Clopidogrel	46 (36.8%)	45 (40.5%)	0.6491
Warfarin	10 (8.0%)	3 (2.7%)	0.1349

ASA = acetylsalicylic acid; BMI = body mass index; CAD = coronary artery disease; UFH = unfractionated heparin.

target vessel with no flow-limiting dissections or intravascular thrombus formation as estimated by the operator after the intervention. Patients were monitored for in-hospital adverse events, such as unplanned percutaneous or surgical revascularization for acute limb ischemia, subacute thrombosis, amputation before discharge, myocardial infarction, cerebrovascular accident, or death. These adverse events were considered procedure failures. The TIMI-1 trial (Thrombolysis In Myocardial Infarction Trial-Phase 1) definition of major bleeding was adopted and included intracranial or retroperitoneal hemorrhage, a fall in hemoglobin of >5 g/dl, and/or transfusion of ≥2 U of packed red blood cells (PRBCs) for any reason (8). Secondary end points included minor bleeding (bleeding that did not meet the aforementioned criteria), time to sheath removal, time to ambulation, length of hospital stay, and cost analysis.

Statistical analysis. To achieve 80% power, assuming alpha = 0.5 and 2-tail, the study would require an excess of 769 subjects/group. This number is not feasible, given the resources at our facility. Therefore, our study will be underpowered to detect group differences (35% power). The objective of this study is to demonstrate statistical nonsignificance between groups. Continuous variables were presented by either mean ± SD or median with the 25th (Q1) and 75th (Q3) percentiles and compared by the Mann-Whitney *U* test. Categorical variables were presented as counts and percentages and compared by chi-square test and Fisher exact test. All *p* values are 2-tailed, and statistical significance was considered as *p* < 0.05. All analyses were performed with SAS version 9.1 (SAS Institute, Inc., Raleigh, North Carolina).

Results

Baseline demographic data and clinical characteristics of both groups are shown in Table 1. Various peripheral vascular interventions were performed (Table 2). Sheath sizes, number of closure devices, and ACT values are shown in Table 2.

Procedural success was achieved in 98% (n = 122) of the 125 patients receiving bivalirudin versus 99% (n = 110) of the 111 patients with low-dose UFH (*p* = NS). Of the 3 patients in the bivalirudin group with unsuccessful procedures, 1 had in-stent restenosis and 2 had post-procedural residual stenosis of >20%. The patient with in-stent restenosis underwent successful repeat angioplasty, and 1 of the patients with post-procedural residual stenosis of >20% underwent amputation for osteomyelitis. One patient in the UFH group showed only minimal improvement of blood flow after percutaneous manual thrombectomy; therefore, surgical thrombectomy was recommended. Duration of procedure was 61.4 ± 31.3 min for bivalirudin and 50 ± 20.9 min for UFH. Major bleeding occurred in 2.4% (n = 3) of the patients with bivalirudin versus 0.9% (n = 1) with

Table 2. Target Artery Sheath Sizes, Closure Devices, and ACT Values

	Bivalirudin (n = 125)	UFH (n = 111)	<i>p</i> Value
Artery			
Subclavian	1 (0.8%)	4 (3.6%)	0.2993
Renal	17 (13.6%)	16 (14.4%)	0.9928
Iliacs	41 (32.8%)	34 (30.6%)	0.8282
Femoral	9 (7.2%)	8 (7.2%)	0.8034
Profunda	2 (1.6%)	2 (1.8%)	0.6995
SFA	65 (52.0%)	45 (40.5%)	0.1029
Popliteal	19 (15.2%)	9 (8.1%)	0.1389
Below the knee	14 (11.2%)	18 (16.2%)	0.3503
Celiac	0 (0.8%)	1 (0.9%)	0.5300
SMA	2 (1.6%)	1 (0.9%)	0.9180
Sheath sizes used			
5-F	8 (6.4%)	8 (7.2%)	0.9904
6-F	65 (52.0%)	73 (65.8%)	0.0444
7-F	43 (34.4%)	24 (21.6%)	0.0425
8-F	9 (7.2%)	6 (5.4%)	0.7680
Closure devices used			
	11 (8.8%)	5 (4.5%)	0.2928
ACT values			
5 min	328 ± 68.7	236 ± 61.4	<0.001
30 min	325 ± 67.6	223 ± 56.4	<0.001

ACT = activated clotting time; SFA = superficial femoral artery; SMA = superior mesenteric artery; UFH = unfractionated heparin.

UFH (*p* = NS). Two patients in the bivalirudin group required a transfusion of 2 U of PRBCs with no obvious source of bleeding, and 1 suffered a gastrointestinal bleed requiring a transfusion of 3 U of blood. This patient had baseline hemoglobin of 10 and hematocrit of 30.3, which were reduced after the procedure to 8.4 and 25.2, respectively. Heme-positive stools were noted, and the patient elected outpatient gastroenterologic work-up, which he failed to complete. He returned to the hospital 2 weeks later with hemoglobin of 6.6. Endoscopy revealed intestinal arteriovenous malformations, and the patient was treated per gastroenterology's recommendations. One patient in the UFH group sustained a major bleed secondary to retroperitoneal hemorrhage and required 5 U of PRBCs. This patient unfortunately did not have documented ACT levels, an arterial closure device was not used, and therefore the exact reason for the hemorrhage can only be postulated to be a high arterial access; antegrade approach was used for PPI; however, on fluoroscopy the femoral head was not recorded on cine to estimate the location of the arterial access. Table 3 shows the primary end points.

Minor bleeding occurred in 11 patients in each group. One bivalirudin patient sustained a pseudoaneurysm, which was treated successfully with a thrombin injection. Ten bivalirudin and 11 heparin patients were observed to have puncture-site oozing and/or a small hematoma (<4 cm diameter), requiring prolonged bed rest and/or 2 to 4 h of femoral-stop placement (*p* = NS). Secondary outcomes

	Bivalirudin (n = 125)	UFH (n = 111)	p Value
Primary end points			
Procedure success	122 (97.6%)	110 (99.1%)	0.6245
Secondary end points			
Major bleeding	4 (3.2%)	1 (0.9%)	0.3741
Minor bleeding	11 (8.8%)	10 (9.0%)	0.9551
Time to sheath removal (h)	2.15 ± 0.77	2.49 ± 1.13	0.0065
Time to ambulation (h)	6.19 ± 1.75	6.1 ± 1.37	0.7384
Median duration of hospital stay (h)	24.0 (Q1-Q3: 18.5-36.0)	24.0 (Q1-Q3: 20.0-40.0)	0.3819

UFH = unfractionated heparin.

(i.e., minor bleeding, time to ambulation, and the average hospital course duration) were also similar ($p = \text{NS}$) (Table 3). Time to ambulation was 6.14 ± 1.83 h vs. 6.12 ± 1.37 h and duration of hospital stay was 45.33 vs. 44.26 average hours in the bivalirudin and UFH groups, respectively. Time to sheath removal was 2.15 ± 0.77 h vs. 2.49 ± 1.33 h ($p = 0.0065$) in the bivalirudin and UFH groups, respectively.

The hospital costs for bivalirudin and UFH are dramatically different. The cost for bivalirudin in our facilities is \$547 for a 250-mg vial. Renal dosing adjustments made no difference in cost, because the minimum charge for bivalirudin was for 1 vial; and no patient in the study required more than 1 vial. Weight-based dosing of UFH varied per patient, with a basic hospital cost of \$0.61/1-ml vial of 5,000 U; and no patient in the study required more than 2 vials of UFH. The hospital cost for an ACT level is \$2.00.

Discussion

Unfractionated heparin historically has been the primary anticoagulant used in percutaneous interventions, and in many instances, it is now being replaced with bivalirudin. There are no randomized trials directly comparing bivalirudin to UFH in PPI. The results of multiple coronary studies demonstrating the procedural success and bleeding/ischemic complications have been extrapolated into anticoagulation strategies used currently in PPI. No American College of Cardiology/American Heart Association guidelines exist specifying the anticoagulation strategy in peripheral intervention (1).

Procedural success with either anticoagulant has been established as similar in multiple coronary and peripheral studies (5-7,9-12). Regarding long-term success, Allie et al. (12) showed that, in addition to similar rates of initial procedural success, the 6-month ultrasound follow-up rates of >50% restenosis in 4% to 5% of patients were also similar between both anticoagulant groups in renal and iliac intervention. Our study also showed procedural success rates of 98% vs. 99% in bivalirudin and UFH, respectively. Thus, it seems that neither anticoagulant provides additional benefit

with achieving immediate or long-term procedural success. However, whether either anticoagulant will provide benefit in maintaining a luminal diameter will require studies with long-term follow-up.

Major and minor bleeding complication rates after PCI have been reported to be as high as 13% and 26% with UFH, versus 4% and 9% with bivalirudin, respectively (5-7,10-13). There are a number of factors that might have contributed to these results, such as higher dosing of UFH and the use of UFH in combination with GP IIb/IIIa inhibitors. When high doses of bivalirudin (1-mg/kg bolus, 4-h infusion at 2.5 mg/kg/h and then up to 20-h infusion at 0.2 mg/kg/h) and UFH (175-U/kg bolus followed by 15 U/kg/h for up to 24 h) were used, major bleeding was found to be 3.5% vs. 9.3%, respectively (6). In the REPLACE-2 (Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events) trial (5), lower doses of bivalirudin (0.75-mg/kg bolus/1.75 mg/kg/h) and UFH (65-U/kg bolus, ACT >225 s) administered with a GP IIb/IIIa inhibitor resulted in reduced rates of major bleeding at 2.4% vs. 4.1%, respectively. The ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial (7) reported no statistically significant differences in major or minor bleeding rates when the use of bivalirudin alone was compared with the use of UFH; however, when UFH was used in combination with a GP IIb/IIIa inhibitor, significant differences in major (3% vs. 5.7%, $p < 0.001$) and minor (3.7% vs. 6.4%, $p < 0.001$) bleeding were found. A small, retrospective PPI study showed no statistical differences in rates of major and minor bleeding when bivalirudin was compared with low-dose UFH (10). Therefore, the higher bleeding complications seen in the coronary studies mentioned might be secondary to the higher doses of UFH used and/or the use of GP IIb/IIIa inhibitors. Similarly, our study showed no statistical difference in major and minor bleeding rates when bivalirudin alone was compared with low-dose UFH in PPI.

Activated clotting time is used to follow the level of anticoagulation during interventions, but the optimal ACT or UFH dosing during peripheral vascular interventions has

not been defined. In a meta-analysis (14), an ACT of approximately 375 s was defined as optimal to prevent ischemic complications when UFH was used for PCI. However, this degree of anticoagulation is associated with increased risk of bleeding, specifically in patients undergoing complex peripheral arterial procedures. In 2006, Capuano et al. (15) demonstrated the safety and efficacy of an ACT <200 s in conjunction with the use of standard antiplatelet therapy in patients undergoing PCI. In-hospital complication rates after percutaneous angioplasty have been reported at a range of 3.5% to 32.7% in PPI (11). Shammas et al. (9) reported an overall complication rate of 9.2% in patients who received anticoagulation with heparin during PPI. In their study, they acknowledged that ACTs were not available in all patients; however, their measured ACTs were relatively high, with 42.1% of patients having an ACT >400 s (9). There was no correlation in our study among ACT levels, sheath size, or time to sheath removal and bleeding risk. No published data attribute a causative relationship between these factors and higher rates of bleeding complications. Prior publications do link higher dosages of UFH with a trend toward higher rates of complications (9). In our study, ACTs averaged approximately 330 and 230 s in the bivalirudin and UFH groups, respectively, with much lower rates of major and minor bleeding. There was no correlation between ACT levels and major/minor bleeding.

Time to sheath removal, measured from the time of procedure completion, was 2.15 ± 0.77 h vs. 2.49 ± 1.33 h ($p = 0.0065$) in the bivalirudin and UFH groups, respectively. This difference can theoretically be accounted for by the fact that UFH half-life is 3 times that of bivalirudin and is possibly due to nursing delays in obtaining the required ACT <160 s before sheath removal. Per protocol, the bivalirudin patients had their sheaths removed 2 h after procedure completion. The fact that time to ambulation and overall duration of hospital course was not statistically significant suggests that time to sheath removal is clinically relevant only with regard to patient comfort, secondary to duration of required bed rest.

In our study, the cost of bivalirudin at \$547 is hard to justify, because similar procedural success and in-hospital complication rates are seen when using UFH at a cost less than approximately \$6.00 (2 vials of UFH [10,000 U] and 2 ACT level checks). The limitations of UFH use are well-recognized. They include activation of platelets, unpredictable dosing, and the potential for heparin-induced thrombocytopenia (16). Multiple coronary studies have shown decreased ischemic and bleeding complication with bivalirudin (5-7). However, as mentioned earlier, these results might have been secondary to higher doses of UFH used and/or because UFH was used in combination with a GP IIb/IIIa inhibitor. If further studies reveal there is no sustained long-term ischemic benefit associated with the use

of bivalirudin in peripheral intervention in addition to no in-hospital benefit, then the cost of bivalirudin can only be justified if the use of a GP IIb/IIIa inhibitor is required or there is a contraindication to heparin, such as allergy or a history of heparin-induced thrombocytopenia. An additional advantage to choosing UFH during PPI is that protamine sulfate is readily available to reverse the anticoagulation, if necessary.

Study limitations. The study was small, nonblind, and nonrandomized. To prove noninferiority between both groups regarding procedural success and bleeding complications, it would be necessary to study a cohort of at least 770 patients in each group so that the study would be sufficiently powered. Unfortunately, due to the limitations of resources at our facility, we were not able to conduct a study of this magnitude. And the question remains: Does either anticoagulant provide long-term benefit?

Conclusions

Low-dose UFH is equally as effective and safe as bivalirudin when used as an anticoagulation strategy in patients undergoing PPI. In addition, use of low-dose UFH is less costly than bivalirudin. Larger randomized studies are required to further evaluate these findings.

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REFERENCES

1. Hirsch AT, Haskal ZJ, Hertzner NR, et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *J Am Coll Cardiol* 2006;47:1239-312.
2. Gardiner GA Jr., Meyerovitz MF, Stokes KR, Clouse ME, Harrington DP, Bettmann MA. Complications of transluminal angioplasty. *Radiology* 1986;159:201-8.
3. Dick P, Barth B, Mlekusch W, et al. Complications after peripheral vascular interventions in octogenarians. *J Endovasc Ther* 2008;15: 383-9.

4. Stone GW, McLaurin BT, Cox DA, et al. Bivalirudin for patients with acute coronary syndromes. *N Engl J Med* 2006;355:2203-16.
5. Lincoff AM, Bittl JA, Harrington RA, et al. Bivalirudin and provisional glycoprotein IIb/IIIa blockade compared with heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary intervention: REPLACE-2 randomized trial. *JAMA* 2003;289:1638.
6. Bittl JA, Chaitman BR, Feit F, Kimball W, Topol EJ. Bivalirudin versus heparin during coronary angioplasty for unstable or postinfarction angina: Final report reanalysis of the Bivalirudin Angioplasty Study. *Am Heart J* 2001;142:952-9.
7. Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med* 2008;358:2218-30.
8. Rao AK, Pratt C, Berke A, et al. TIMI Trial—phase I: hemorrhagic manifestations and changes in plasma fibrinogen and the fibrinolytic system in patients treated with recombinant tissue plasminogen activator and streptokinase. *J Am Coll Cardiol* 1988;11:1-11.
9. Shammass NW, Lemke JH, Dippel EJ, et al. In-hospital complications of peripheral vascular interventions using unfractionated heparin as the primary anticoagulant. *J Invasive Cardiol* 2003;15:242-6.
10. Hallak O, Shams SA, Broce M, et al. Similar success rates with bivalirudin and unfractionated heparin in bare-metal stent implantation. *Cardiovasc Intervent Radiol* 2007;30:906-11.
11. Allie DE, Hall P, Shammass NW, et al. The APPROVE trial: in-hospital and 30-day results. *J Invasive Cardiol* 2004;16:651-6.
12. Allie DE, Lirtzman MD, Wyatt CH, et al. Bivalirudin as a foundation anticoagulant in peripheral vascular disease: a safe and feasible alternative for renal and iliac interventions. *J Invasive Cardiol* 2003;15:334-342.
13. Eres A. Use of bivalirudin as the foundation anticoagulant during percutaneous peripheral intervention. *J Invasive Cardiol* 2006;18:125-8.
14. Chew DP, Bhatt DL, Lincoff AM, et al. Defining the optimal activated clotting time during percutaneous coronary intervention: aggregate results from 6 randomized, controlled trials. *Circulation* 2001;103:961-6.
15. Capuano C, Sesana M, Leonzi O, Cuccia C. Safety and efficacy of low-dose unfractionated heparin during percutaneous coronary revascularisation and the relationship between activated clotting time and haemorrhagic or ischaemic complications: our results. *J Cardiovasc Med (Hagerstown)* 2006;7:866-71.
16. Warkentin TE, Levine MN, Hirsh J, et al. Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. *N Engl J Med* 1995;332:1330-5.

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