Original Article

In-hospital Outcome of Use of Low Molecular Weight Heparin in Patients Undergoing Percutaneous Coronary Intervention

Tariq Ahmed Chowdhury[1], Mustafizul Aziz[2], Iftekhar Alam[3], Abuduz Zaher[4], Sayed Azizul Haque[5], Abdul Wadud Chowdhury[6]

Abstract:

This prospective observational study was carried out in the Department of Cardiology of national institute of cardiovascular diseases (NICVD), Dhaka to assess the safety of low molecular weight heparin (LMWH) in patients undergoing percutaneous coronary intervention (PCI).

Safety of low molecular weight heparin in comparison to unfractionated heparin (UFH) was observed in this study. In total data from 100 patients undergoing elective PCI was evaluated. Among them 50 patients in group I received I mg/kg intra-arterial LMWH and rest in group II received UFH.

Demographic profile of individuals in both groups was almost similar. There was no significant difference in major coronary risk factors between the two groups. Patients were monitored during their stay in hospital for any complications like bleeding, haematoma, myocardial infraction and death. No death was observed in any group. Minor bleeding in group I and II (6% vs 105), Major bleeding (2% vs4%) and haematoma (6% vs 10%). Myocardial infraction no incidence in group I and 4% in group II. So complications was more prevalent in group II who were treated with UFH, but those were not statistically significant.

The intra-arterial administration of LMWH in patients undergoing PCI is safe. The risk of acute and sub-acute coronary events and bleeding complications are similar in both groups and in hospital outcome there is less complication with LMWH used during PCI.

Key words: Percutaneous Coronary Intervention, Heparin, Low-Molecular-Weight.

(Bangladesh Heart Journal 2018; 33(1): 22-27)

Introduction:

Unfractionated heparin is the standard choice of anticoagulant used during percutaneous coronary intervention (PCI). There are several recommendation regarding the use of intravenous unfractionated heparin with dose adjusted activated clotting time during PCI.[1, 2] Considering limitations of unfractionated heparin, which include it is sometimes difficult to manage effects of heparin on coagulation, the need for repeated monitoring of coagulation, the narrow therapeutic window, the potential induction of platelet activation, and the risk of thrombocytopenia better anticoagulation regimens are needed for PCI.[3]

As compared with unfractionated heparin, low-molecular-weight heparins (LMWHs) are considered to induce a more stable and predictable anticoagulant dose response thus removing the necessity for coagulation monitoring. LMWH have a longer half-life and a greater ratio of anti–factor Xa activity to anti–factor IIa activity, which reduces the generation

1 Assistant Professor of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.

2 Associate Professor of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.

3 Junior Consultant of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.

4 Professor of Cardiology, Lab Aid Cardiac Hospital, Dhaka, Bangladesh.

5 Professor of Cardiology, Medinova Medical Services, Dhaka, Bangladesh.

6 Professor of Cardiology, Dhaka Medical College, Dhaka, Bangladesh.

Address of Correspondence: Dr. Tariq Ahmed Chowdhury, Assistant Professor of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh. Mobile: +8801819156927, E-mail: tariq.achy@gmail.com

DOI: http://dx.doi.org/10.3329/bhj.v33i1.37020

and activation of thrombin.[3] The important pharmacologic characteristics that distinguish LMWH from UFH include: greater bioavailability; minimal plasma protein and vessel wall binding; more predictable anticoagulant response; ease of subcutaneous and intravenous administration; and inhibition of acute phase release of von-Willebrand factor in acute coronary syndrome.[4]

LMWH have earned their place and established their superiority over UFH in the management of post-surgical deep vein thrombosis[5] and acute coronary syndrome (ACS) including unstable angina (UA) and non ST elevated myocardial infarction (NSTEMI).[6] The efficacy and safety of subcutaneous Enoxaparin a LMWH used in NSTEMI showed enoxaparin plus aspirin was superior to UFH plus aspirin in patients with ACS. The need for urgent revascularization was significantly lower in enoxaparin group. LMWH represent a major advancement in the management of patients with ACS or as part of the strategy in candidates undergoing coronary interventions.[7]

Several trials have shown that the LMWH enoxaparin offer the practical and potential pharmacologic advantages over UFH in multiple applications and logically should also provide a similar benefit during percutaneous coronary intervention (PCI).[8] However, during coronary and non-coronary interventions, UFH is conventionally used more frequently than LMWH. Data from randomized, controlled clinical trials support the administration of LMWH and/or platelet GP IIb/IIIa inhibitor in patients who represent with non ST elevation ACS.[9, 10]

Small or noncomparative trials have evaluated a single intravenous bolus of enoxaparin in different doses form, such as:1 mg, 0.75 mg or 0.5 mg[11, 12] per kilogram of body weight, in patients undergoing PCI with or without the administration of glycoprotein IIb/IIIa inhibitors. However, these uncontrolled studies have not allowed definite conclusions to be drawn about the efficacy of enoxaparin as compared with that of standard anticoagulation regimens involving unfractionated heparin. In a meta-analysis of data from randomized studies comparing intravenous low-molecular-weight heparins and intravenous unfractionated heparin in patients undergoing PCI, there was a nonsignificant trend toward a reduction in major bleeding with LMWHs and no difference between groups in the occurrence of ischemic events. In an additional analysis, a dose of less than 1 mg of enoxaparin per kilogram resulted in fewer ischemic and bleeding events than a dose of 1 mg per kilogram.[13]

The use of LMWH eliminates the need for continuous intravenous infusion, anticoagulation monitoring and dose adjustment associated with UFH.[8] Despite evidence-based support for administering LMWH and/or GP IIb/IIIa receptor blocker to patients undergoing PCI and those presenting with ACS, algorithms for integrating these agents into clinical practice have not been determined. The NICE trials have evaluated this issue in details and the results of these trials are likely to have a major impact on the choice of adjunctive therapy during PCI.[8]

The ease of intravenous use, good & predictable anticoagulation response and absence of monitoring need make LMWH enoxaparin a very affective choice for heparinization

during PCI. So this study is undertaken to assess the suitability and safety of intravenous LMWH to that of unfractionated heparin in patients undergoing elective PCI and to determine in hospital outcome regarding complications of UFH.

Method:

This prospective observational study was done in the department of cardiology of the national institute of Cardiovascular diseases (NICVD) during May 2004 to December 2004. Approval for the study was obtained from the institutional review board. All patients gave written informed consent. Patients undergoing percutaneous coronary intervention at NICVD were included in the study and depending on the type of heparin used patients were divided in two groups. In group I 50 patients were included who received intra-arterial LMWH e.g. Enoxaparine 1mg/kg during PCI. In group II 50 patients were included who received conventional UFH. Patients with Creatinine >2 mg/dl, Platelet count <100000 / mm^3 and with Liver disease (INR> 1.3) were excluded from the study.

All patients initially evaluated by history, physical examination, 12 Lead ECG, CK-MB, and echocardiography. Pre catheterization investigations including CBC, Clotting time, bleeding time, HBsAg, VDRL, anti HCV, anti HIV was done as required. Diagnostic angiogram and PCI was done as standard method. Patients were randomly assigned to receive an intravenous bolus of unfractionated heparin, adjusted for activated clotting time according to current guidelines or intravenous enoxaparin at a dose of 1mg per kilogram.[1] All patients received aspirin (300mg) and thienopyridines two hours prior to the procedure. Patients who were assigned to enoxaparin group received a single intravenous bolus of enoxaparin, without anticoagulation monitoring, after sheath insertion and immediately before PCI. When procedures were prolonged by more than 2 hours, an additional bolus of enoxaparin (half the original dose) was used.[14] Patients who were randomly assigned to receive unfractionated heparin were given an initial intravenous bolus of 10,000 IU after crossing the lesion with

guide wire to achieve a target activated clotting time of 300 to 350 seconds. Unfractionated heparin was re-administered during the procedure when measurements of activated clotting time dropped below the recommended range. Activated clotting time was measured with a standardized Hemochron device (ITC). Sheath removal was done in UFH group at an activated clotting time between 150 and 180 seconds, 4 to 6 hours after the end of PCI. In group I who received 1 mg of enoxaparin per kilogram no monitoring of anticoagulation was required before sheath removal and sheath was removed within 2 to 4 hours after the procedure.[15]

Post PCI continuous monitoring done during the whole hospitalization period. Follow-up for ischemic complication, bleeding events, abrupt closure, vascular events and death was monitored. The occurrence of major or minor bleeding during the first 48 hours after the index PCI, according to pre-specified definitions. Major bleeding: Fatal bleeding. Retroperitoneal, intracranial, or intraocular bleeding. Bleeding that causes hemodynamic compromise requiring specific treatment. Bleeding that requires intervention or decompression of a closed space to stop or control the event. Clinically overt bleeding, requiring any transfusion of ≥1 unit of packed red cells or whole blood, causing a decrease in hemoglobin of ≥3 g/dl or a decrease in hematocrit of ≥10%.

Minor bleeding: Gross hematuria not associated with trauma. Epistaxis that is prolonged, repeated, or requires plugging or intervention. Gastrointestinal hemorrhage Hemoptysis. Subconjunctival hemorrhage. Clinically overt bleeding, causing a decrease in hemoglobin of 2 to 3 g/dl. Hematoma >5 cm or leading to prolonged or new hospitalization. Death from any cause, nonfatal myocardial infarction (defined by a new Q wave in two or more leads or a total creatine kinase level or creatine kinase MB fraction that was ≥3 times the upper limit of the normal range during hospitalization for the index PCI or that was ≥2 times the upper limit of the normal range after discharge), or urgent target-vessel revascularization after the index PCI.[16]

All clinical, angiographic, procedural and follow-up data were prospectively recorded on pre-designed data collection sheet. The numerical data obtained from the study were analyzed and significance of difference was estimated by using the statistical methods. Data were expressed in frequency, percentage, mean and standard deviation as applicable. Comparison between groups was done by unpaired student's test, chi-square test, and Fisher's exact test as applicable. Data were analyzed by using computer based SPSS program (version 11.5). Probability less than 0.05 were considered significant.

Result:

In this study mean age of the patients in Group I was 57.04±9.27 years and Group II was 52.18 ± 9.40 years (P value > 0.05). The commonest age group of study patients for group I was 55-64 years age group and for the group II 44-54 years.

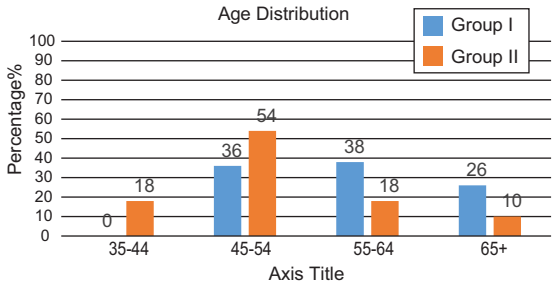

Fig.-1: *Age distribution of study population in percentage among the groups*

Smoking was the most common risk factor among the groups. Incidence of other risk factors were similar in between the groups.

Table-I

Distribution of risk factors in between the groups

Risk factors	Group I		Group II		P value
	n =50	%	n =50	%	
Hypertension	14	28	20	40	0.15^{NS}
Diabetes	10	20	05	10	0.13^{NS}
Smoking	44	88	37	74	0.06^{NS}
Family History of CAD	10	20	10	20	0.60^{NS}
Dyslipidemia	02	04	07	14	0.08^{NS}

Diagnosis of patients among group I was asymptomatic 6 (16%), chronic stable angina 12(24%), unstable angina 8(16%), NSTEMI 10(20%) and STEMI 12(24%).

Table-II

Distribution of groups on the basis of clinical diagnosis

Clinical Diagnosis	Group I		Group II		P value
	n =50	%	n =50	%	
Asymptomatic	08	16	07	14	0.20^{NS}
Chronic Stable Angina	12	24	23	46	0.08^{NS}
Unstable Angina	08	16	04	08	0.07^{NS}
NSTEMI	10	20	08	16	0.19^{NS}
STEMI	12	24	08	16	0.15^{NS}

Whereas in group II asymptomatic 7(14%), chronic stable angina 12(24%), unstable angina 4(8%), NSTEMI 10(20%) and STEMI 17(34%). There is no statistical difference between the groups (P value> 0.05).

In both the groups single vessel was treated in 75 patients and double vessel treated in 21 patients and triple vessel disease was treated in 4 patients.

Table-III

Distribution of the groups on the basis of involvement of number of coronary arteries

Coronary Artery	Group I		Group II	
	n =50	%	n =50	%
LM	00	—	02	04
LAD	25	50	23	46
LCX	04	08	06	12
RCA	14	28	11	22
RCA+LCX	01	02	01	02
LAD+RCA	05	10	05	10
LAD+LCX	01	02	02	04

Among single vessel treated in group I, most common vessel was LAD 25(50%) followed by RCA 14(28%) LCX 4(8%), and in group II, most common vessel was LAD 23(46%) followed by RCA 11 (22%), LCX 6 (12%) and LM 2(4%). Among the double vessel treated in group I, most common vessels were LAD & RCA 5(10%), LAD & LCX 1 (2%), RCA & LCX I (2%) and in group II, most common vessels were LAD & RCA 5(10%), LAD & LCX 2 (4%) and RCA & LCX 1(2%) (P value> 0.05).

In group I single stent was used in 38 (76%) patients double stents were used in 11(22%) and no stent was used in 1(2%) patients.

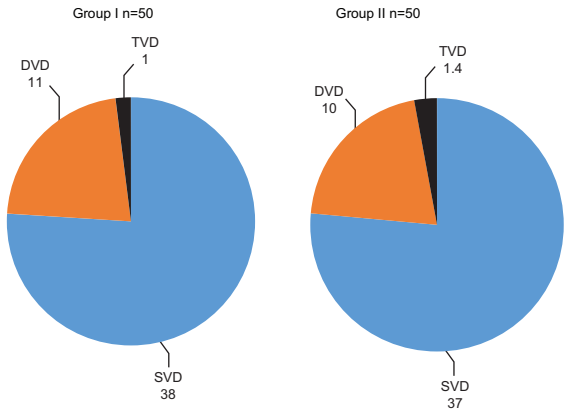

Fig.-2: *Distribution of the groups on the basis of number of coronary arteries treated with stents during PCI.*

However in group II single stent was used in 36(72%) patients, double stents were used in 12(24%) and triple stents were used in 2 (4%) patients. There is no statistical difference between the groups (P value> 0.05).

The incidence of post PCI complications was more prevalent in group II then group I. there was no incidence of death during the study period among the groups.

Table-IV

Distribution of the groups on the basis of post PCI complications

Clinical Diagnosis	Group I		Group II		P value
	n =50	%	n =50	%	
Minor Bleeding	03	06	05	10	0.35^{NS}
Major Bleeding	01	02	02	04	0.50^{NS}
Haematoma	03	06	05	10	0.35^{NS}
Myocardial infraction	00	00	02	04	0.35^{NS}
Death	00	00	00	00	—

None of the patients in group I suffered post PCI myocardial infarction but in group II 08 (16%) patients suffered from post PCI infarction. The prevalence of minor and major bleeding, haematoma was higher in group II compared to group I. There is no statistical dissimilarity between the groups (P value> 0.05).

Discussion:

This was a prospective observational study conducted in the department of cardiology, national Institute of Cardiovascular Disease, Dhaka. There was no published data in Bangladesh comparing effects of two types of heparin in PCI. Hence the result of this study was not possible to be compared with any other Bangladeshi studies but the results have shown similarity with studies done abroad.

Similar pattern of age distribution were reported by Jakub Drozd et.al. There was similar type of risk factor distribution like hypertension, smoking, dyslipidaemia, diabetes mellitus and Family history of CAD in both groups. Similar observation was found by Jakub Drozd et.al.[17]

Heparin has always been used during PCI and in spite of the progress which took place in interventional cardiology it still remains a standard treatment during and after this procedure. The goal of heparin treatment is to decrease the risk of acute restenosis of a vessel undergoing PCI and to prevent thrombo-embolic complications associated with introduction of instruments into the cardio-vascular system. The risk of acute restenosis may be as high as 11%. Acute reocclusion may be complicated by such severe events as death, MI or urgent need for redo PCI. The main limitations of heparin therapy are not fully predictable effects of this agent on the coagulation system due to variable binding to serum protein, platelets and endothelial cells. Therefore, the continuous monitoring of blood coagulation parameters is mandatory. At present, no generally accepted scheme of heparin administration prior to PCI exists. Usually a bolus of

10,000 iu of heparin is given, followed by serial ACT measurements every several minutes. This regimen has two limitations. First, the standard dose *of* heparin is not effective in some patients whereas in some others it is too high. Second, the costs of serial ACT measurements are not negligible. Ogilby et.al.[18] revealed that 11 % of patients had ACT <300 seconds following 10,000 iu of heparin. Doughenty et.al. have demonstrated a very wide range of ACT <250 seconds was measured in 58% of patients, ACT 250-275 seconds in 17%, ACT 275-300 seconds in 12% and >300 seconds in 13% of patients.[19]

The ESSENCE studies have documented the advantages of enoxaparin over standard heparin in patients with acute coronary events resulting in lower risk of death, MI or the need for revascularization.[20] Similar encouraging results were obtained by the TIMI IIB investigations. The promising results of the above mentioned studies encourage the use of LMWH during PCI.[21] Data in literature concerning this topic are very scant. The safety of enoxaparin administration (1 mg/kg) before PCI was examined in the open-label study.[22] The rate of acute coronary complications was 4.9% whereas the rate of bleeding complications- 0.6%. The randomized study REDUCE[23] compared 10,000 iu bolus of standard heparin with reviparin (LMWH) administered at a dose of 7,000 iu anti Xa. A significant reduction in the coronary event rates during the first three days following PCI was documented in the reviparin group (8.2% vs. 3.9%, respectively).[24] Randomized patients to enoxaparin (1 mg/kg) or UFH 10.000 iu, given before PCI. The rate of coronary events, haemorrhage and local bleeding complications was similar in both analyzed groups, however, 30% of patients receiving UFH required additional doses of heparin to achieve the target ACT(>300 s). A study conducted in Poland revealed that in patients with acute coronary events enoxaparin given at a dose of 1mg/kg prior to PCI was equally safe as standard heparin titrated according to ACT.[25]

Safety of enoxaparin in comparison to UFH observed in this study was evaluated in 100 patients. Among them, 50 received enoxaparin and similar number received UFH. Demographic profile of individuals in both groups was almost similar. There was no significant difference of major coronary risk factors between the two treatment groups. Patients were monitored up to hospitalized period for observation of any complications. No death was observed in any group. Major and minor complications was comparatively similar in both groups but relatively there was better outcome in LMWH group.

Study Limitations

Although the results of this study support the hypothesis there are some facts to be considered which might affect the results:

1. The study was a non-randomized and observational study.

2. Number of study population was limited.

3. Duration of follow up period was short.

Conclusion:

The intra-arterial administration of 1 mg/kg of enoxaparin in patients undergoing PCI is

safe. The risk of acute and sub-acute coronary events and bleeding complications are

similar in patients treated with UFH. The study was a non-randomized study with small number of patients. So further comparative study which will be randomized, with larger group will give a clear picture of clinical outcome between patients having enoxaparin and UFH in PCI.

References:

1 Smith SC Jr, Dove JT, Jacobs AK, et al. ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines) — executive summary: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1993 Guidelines for Percutaneous Transluminal Coronary Angioplasty). J Am Coll Cardiol 2001;37:2215-39.

2 Silber S, Albertsson P, Aviles FF. Guidelines for percutaneous coronary interventions: the Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Eur Heart J 2005; 26:804-47.

3 Cohen M. The role of low-molecular weight heparin in the management of acute coronary syndromes. J Am Coll Cardiol 2003;41:Suppl 4:55S-61S.

4 Melandri, G., Seuprini, F., Cervi, V., Candiotti, N., Branzi, A., Palazzini, E., et al. Comparison of efficacy of low molecular weight heparin with that of unfractionated heparin in the presence of activated platelets in healthy subjects. Am J Cardiol 1993, vol. 72: 450-454.

5 Leizoroviez A. Comparison of the efficacy and safety of low molecular weight heparins and unfractionated heparin in the initial treatment of deep venous thrombosis - An updated meta-analysis. Drugs 1996, Vol. 52 (Suppl): 30-37.

6 Antman, E.M., McCabe, C.H., Gurfinkel, E.P. at.al. Exoxaparin prevents death and cardiac Ischemic events in unstable angina/non-Q-wave myocardial infarction. Results of the thrombolysis in myocardial infarction (TIMI) IIB trail. Circulation1999. Vol. 100: 1593-1601.

7 Cohen M., Blaber R., Demers C. at.al. The Essence Trial: Efficacy and Safety of Subcutaneous Enoxaparin in Unstable Angina and Non-Q-Wave MI: A Double-Blind, Randomized, Parallel-Group, Multicenter Study Comparing Enoxaparin and Intravenous Unfractionated Heparin: Methods and Design. Journal of Thrombosis and Thrombolysis, June 1997, Volume 4, Issue 2: 271–274.

8 Young JJ, Kereiakes DJ, Grines CL. Low-molecular-weight heparin therapy in percutaneous coronary intervention: the NICE 1 and NICE 4 trials. National Investigators Collaborating on Enoxaparin Investigators. J Invasive Cardiol, Dec 2000;12 Suppl E:E14-8;discussion E25-8.

9 Deutsch, E. The emerging role of Low-molecular weight heparin and anti platelet therapies in the Cardiac Catheterization laboratory. Am Heart J 1999, vol. 138: S577-S585.

10 Kereiakes, D.J., Grines, C., Fry, F. et.al. Abeiximab-enoxaparin interaction during percutaneous Coronary intervention, Results of NICE 1 and 4 trials [Abstr].' JAM Coll 'Cardiol 2000, vol. 35: 92A.

11 Choussat R, Montalescot G, Collet JP, et al. A unique, low dose of intravenous enoxaparin in elective percutaneous coronary intervention. J Am Coll Cardiol 2002; 40:1943-50.

12 Miller L, Gupta A, Bertolet BD. Use of clopidogrel loading, enoxaparin, and double-bolus eptifibatide in the setting of early percutaneous coronary intervention for acute coronary syndromes. J Invasive Cardiol 2002;14:247-50.

13 Borentain M, Montalescot G, Bouzamondo A, Choussat R, Hulot JS, Lechat P. Low-molecular-weight heparin vs. unfractionated heparin in percutaneous coronary intervention: a combined analysis. Catheter Cardiovasc Interv 2005;65:212-21.

14 Sanchez-Pena P, Hulot JS, Urien S, et al. Anti-factor Xa kinetics after intravenous enoxaparin in patients undergoing percutaneous coronary intervention: a population model analysis. Br J Clin Pharmacol 2005;60:364-73.

15 Popma JJ, Berger P, Ohman EM, Harrington RA, Grines C, Weitz JI. Antithrombotic therapy during percutaneous coronary intervention: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126:Suppl 3: 567S-599S.

16 Enoxaparin versus unfractionated heparin in elective percutaneous coronary intervention. Montalescot G[1], White HD, Gallo R, et.al. N Engl J Med. 2006 Sep 7;355(10):1006-17.

17 Drozd J., Wójcik J., OpaliDska E., Zapolski T., Widomska T. Percutaneous angioplasty of chronically occluded coronary arteries: long-term clinical follow-up. Kardiol Pol 2006; 64: 667-673

18 Ogilby, J.B., Kogelman, H. A., Klein, L. W. Adequate heparinization during PCI assessment using activated clotting times. Cathet Cardivasc Diagn 1989, vol. 18: 206-209.

19 Daugherty, K. S., Goas, C. M., Bush, H. S. Activated clotting times and activated partial thromboplastin times in patients undergoing coronary J angioplasty who receive bolus doses of heparin. Cathet Cardiovasc Diagn 1992, vol.26: 260-263.

20 Cohen,M., Demers, C., Gurfinkel, E.P. A Comparison of low-molecular - weight heparin with unfractionated heparin for unstable coronary artery disease. N.Eng. J Med 1997, Vol, 337: 447-452.

21 Fared, J., Jeske, W., Hoppensteadt, D., Clarizio, R., Walenga, J.M. Low molecular weight heparins: Pharmacologic profile and product differentiation. Am J Cardiol 1998, vol.82: 3L- 10L.

22 Ferguson JJ, Antman EM, Bates ER, Cohen M, Every NR, Harrington RA, et al. The use of enoxaparin and IIb/IIIa antagonists in acute coronary syndromes, including PCI: final results of the National Investigators Collaborating on Enoxaparin-3 (NICE 3) study. Am Heart J 2003; 146:628–34.

23 Karsch KR, Preisack MB, Baildon R, Eschenfelder V, Foley D, Garcia EJ, et al. Low molecular weight heparin (reviparin) in percutaneous transluminal coronary angioplasty. Results of a randomized, double-blind, unfractionated heparin and placebo-controlled, multicenter trial (REDUCE trial). Reduction of Restenosis After PCI, Early Administration of Reviparin in a Double-Blind Unfractionated Heparin and Placebo-Controlled Evaluation. J Am Coll Cardiol 1996; 28(6):1437–43.

24 Rabah MM, Premmereur J, Graham M, Fareed J, Hoppensteadt DA, Grines LL, Grines CL. Usefulness of intravenous enoxaparin for percutaneous coronary intervention in stable angina pectoris. Am J Cardiol 1999; 84:1391–5.

25 Dudek, D., Dabrowski, M., Ochala, A. Multicenter, prospective, double blind randomized comparison of enoxaparin versus unfractionated heparin for percutaneous coronary interventions'. Am J Cardiol 2000, vol.86(Suppl 8A), TCT-34, 15i.