

Assessment of Safety and Efficacy of Conventional Heparin Dose in Percutaneous Coronary Interventions Characterized by Means of Activated Clotting Time

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Abstract

Background- Percutaneous coronary intervention (PCI) is an invasive procedure which traumatizes the coronary vessel wall and serves as a potent stimulus for thrombus formation. Unfractionated heparin is used routinely during the procedures to reduce the likelihood of acute thrombotic complications. Activated clotting time (ACT) is the preferred assay to determine the degree of anticoagulation during PCI. Our aim was to assess ACT values during PCI after administering heparin with conventional dose (10000 u) and determining ischemic and bleeding complications.

Methods- Coronary artery disease (CAD) patients (N=205) receiving conventional heparin dose and undergoing PCI were included in this study. ACT was assessed 10 minutes after heparin injection. Demographic data and cardiovascular risk factors were registered in the forms and the patients were followed up for about one month for complications.

Results- ACT range 10 minutes after heparin injection was 160 – 682 sec (mean 353 sec, SD: 94.5 sec). ACT was lower than 250 in 12.7% of patients (95% CI: 8.2%-17.2%). ACT had a range of 250-350 seconds in 37% of patients. Overall, 21 patients (10.3%) had ischemic complications (including chest pain, new ischemic changes in EKG, unstable angina and 2 deaths) and 3 patients (1.5%) had bleeding complications. Ischemic complications were significantly higher in smokers (16%) versus nonsmokers (6%, $P=0.038$) and in patients with ≥ 2 risk factors (12%) versus those with ≤ 1 risk factor (4%, $P=0.046$). All three patients with bleeding complications were hypertensive ($P=0.02$).

Conclusion- Although this study shows relative safety of conventional heparin dose in PCI, but only about one third of our patients reached desired ACT values (250-350 sec). So it seems appropriate to use weight adjusted heparin doses (e.g. 100u/kg) instead of conventional dose and to assess ACT in all patients and use additional heparin doses to maintain ACT at optimal levels (*Iranian Heart Journal 2008; 9 (1): 18-21*).

Key words: activated clotting time ■ heparin ■ percutaneous coronary intervention

Arterial injury at the site of percutaneous transluminal coronary intervention serves as a potent stimulus for thrombus formation. So anticoagulant and antiplatelet agents are administered routinely during the procedure to reduce the likelihood of acute thrombotic complications.¹

Despite the continued evolution of antithrombotic therapies, unfractionated heparin remains an attractive option given its relatively low cost, the availability of a rapid “point of care” test for dose individualization (activated clotting time, ACT) and a known

Received Apr ,22 2007; Accepted for publication Apr 24, 2008.

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antagonist that allows the prompt reversal of antithrombin activity (protamine sulphate).² During the early experience with balloon angioplasty, heparin was typically administered via an empirically derived, fixed-dosing schedule, and the degree of anticoagulation was not monitored.¹ This strategy is still being applied in our cath labs in spite of much evidence about the usefulness of ACT assay to monitor and more precisely titrate the degree of heparin anticoagulation during angioplasty.²⁻⁵ Our aim in this study was to assess ACT values during PCI after administering heparin with conventional dose (10000 u) and determining ischemic and bleeding complications, in our population.

Methods

This was an observational, analytic study with a case-series design. Patients with coronary artery disease (n=205) receiving conventional heparin dose and undergoing PCI at our center were included in this study. ACT was assessed with HemoTec kit (Medtronic, Englewood, CO) 10 minutes after heparin injection. Demographic data and cardiovascular risk factors were registered in the forms and the patients were followed for about one month for complications.

Results

The patients had an age range of 33-81 years (mean 54.5 y; SD 9.7 y). Of the 205 patients, 148 (72.2%) were male, and 57 (27.8%) were female. Weight range was 44-126 kg (mean 75.6 kg, SD 11.7 kg). Eleven cases (5.4%) had a CABG surgery history and 22 (10.7%) had previous PCI. In 118 cases (57.6%), PCI was done on LAD or its branches; in 48 (23.4%) on LCX or its branches; in 63 patients (30.7%) on RCA; in one patient (0.5%) on LIMA; and in another one (0.5%) on saphenous vein graft (SVG).

Table I shows the frequency of cardiovascular risk factors among our cases and Table II demonstrates the number of risk factors.

Most of our patients had chronic stable angina (n=188; 91.7%); 16 patients (7.8%) were unstable and one case (0.5%) was in acute phase of myocardial infarction.

Table 1: Frequency of cardiovascular risk factors

Risk Factor	Frequency	Percent
TG > 200 mg/dl	61	29.7
Chol > 200 mg/dl	96	46.8
HTN	77	37.6
DLP *	155	75.6
LDL > 100 mg/dl	100	48.8
HDL < 40 mg/dl	48	23.4
Current smoker	50	24.4
Ex-smoker	23	11.2
Diabetes	57	27.8

*DLP included high TG, Chol, LDL or low HDL

Table II. Number of risk factors

Number	Frequency	Percent	Cumulative Percent
0	11	5.4	5.4
1	68	33.2	38.5
2	82	40.0	78.5
3	40	19.5	98.0
4	4	2.0	100.0
Total	205	100.0	

In the majority of our cases, lesions were type C (n=122; 59.5%); 59 cases (28.8%) had type B, and 24 patients (11.7%) had type A lesions. In 179 cases (87.3%), PCI was done on a single vessel; in 25 cases (12.2%) on two vessels; and in one case (0.5%) on 3 vessels. ACT values are shown in Figure 1. ACT range was between 160-682 seconds (mean 353 sec, SD 94 sec). Of the total patients, 179 (87.3%) had no complications. Two patients (1%) died¹; 19 cases (9.3%) had chest pain; two cases (1%) had a small hematoma at the

¹ One in the first week and another in the first month, possibly not related to the procedure directly.

arterial puncture site; one patient (0.5%) had neuropathic pain; one (0.5%) had GI bleeding; and one (0.5%) had transient ischemic attack.

Figure 2 shows the frequency of ischemic complications following PCI (including chest pain, unstable angina, MI, rise of CKMB>3 times normal, new ST-T changes) in each group.

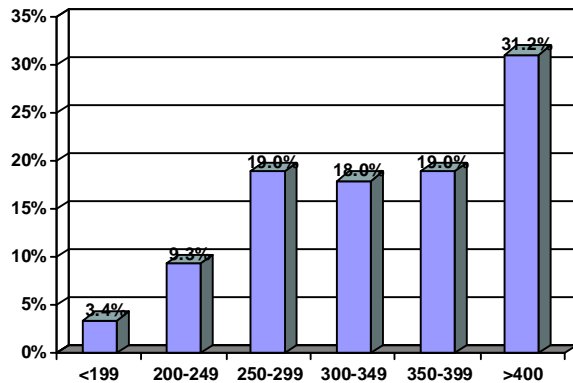


Fig. 1. Frequency of ACT values.

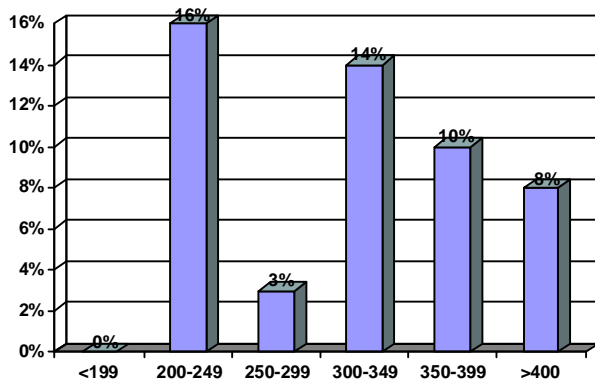


Fig. 2. Frequency of ischemic complications in each ACT group.

ANOVA¹ method was used to compare the means of ACT values in different subgroups and also complications according to different variables. Mean ACT was 350 in women and 355 in men without any significant difference. The difference between incidence of ischemic and bleeding complications were insignificant between men and women. Similarly mean ACT values did not change significantly in

patients with or without high TG, high cholesterol, hypertension, diabetes, high LDL, low HDL, smoking, angina syndrome, history of CABG or PCI, lesion type or number of vessels undergoing PCI.

The incidence of ischemic complications was not correlated with the above variables except smoking compared with nonsmokers (16% vs. 6%, $P=0.038$); and in patients with ≥ 2 risk factors compared with those with ≤ 1 risk factor (12% vs. 4%, $P=0.046$). Considering bleeding complications, the only significant difference observed was with hypertension; all of the 3 cases with bleeding events were hypertensive ($P=0.02$). Mean ACT in these patients was 450.

12.7% of patients had ACT values lower than 250 which was considered suboptimal (95% CI: 8.2%-17.2%).

Linear regression model was used to correlate ACT values and weight. In this model the correlation coefficient was 0.16:

$$\text{ACT} = 451 - 1.29 \times \text{weight}$$

Discussion

The standard test for assessment of the degree of anticoagulation activity is aPTT² but it needs laboratory equipment and trained staff, and it can not be done as a bedside test. On the other hand, high doses of heparin used in PCI, produce on aPTT beyond the measurable range.⁶ ACT does not have these disadvantages, but there has been much controversy over the level of “optimal ACT” for PCI. Early studies showed a linear relationship between heparin dose and ACT values, but the slope of this line varies from patient to patient.⁷ Thus, in most cath labs, it has become routine to assess ACT during PCI and administer added heparin doses according to ACT results instead of administering a single bolus of conventional heparin dose. Current recommended ACT values in PCI are 300-375 seconds with Hemochron kit (International Technidyne Corporation,

¹ ANOVA: analysis of variance

² aPPT: activated partial thromboplastin time

Edison, NJ), and 250-350 seconds with HemoTec kit (Medtronic, Englewood, CO).¹⁻³ In our cath lab, it is not routine to assess ACT in patients undergoing PCI. In this study ACT values had a wide range of 160-682 seconds, although all the patients received a single 10000u heparin dose. This underscores previous studies which showed dependency of ACT upon many factors (weight, sex, angina syndrome, etc). Of the total number of patients, 21 (10.3%) experienced ischemic complications, mostly chest pain and unstable angina. In this study, patient with ≥ 2 cardiovascular risk factors (especially smoking) had a higher risk of ischemic complications following PCI. Therefore, more accurate titration of heparin dose for "optimal ACT" can be invaluable in these patients. On the other hand, occurrence of bleeding complications in hypertensive patients alone, underscores the necessity of cautious titration of heparin in these cases.

There was no significant relation between ACT values and ischemic complications in our study, but as depicted in Fig. 3, we saw a trend toward lower incidence of ischemic complications with higher ACT values. Previous studies did not recommend ACT values lower than 250 sec in PCI. In this study, only 26 patients (12.7%) had ACT lower than 250 sec (95% CI: 8.2%-17.2%) which seems a good result, but only 37% of patients had ACT values between 250-350 seconds which is the current recommended value.

In our linear regression model correlating weight and ACT, there was much dispersion of data around the line, reducing goodness of fit. But it can be used as a simple tool to predict ACT value at every weight-adjusted heparin dose, (e.g. ACT about 322 sec with heparin dose of 100 u/kg).

Conclusion

Although this study shows the relative safety of conventional heparin dose in PCI, but only about one third of our patients achieved the

desired ACT values (250-350 sec). So it seems appropriate to use weight-adjusted heparin doses (e.g. 100 u/kg) instead of the conventional dose and to assess ACT in all patients and administer added heparin doses to maintain ACT at optimal levels. This strategy is particularly suitable for patients with multiple risk factors (especially smoking and hypertension).

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