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Comparison of low dose versus standard dose heparin for radial approach in elective coronary angiography?

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ABSTRACT

Objective: The aim of this study is to evaluate the efficacy and safety of two doses of heparin, a low dose (2500 IU) and a standard dose (5000 IU) in patients who underwent transradial coronary angiography (TRCAG).
Methods: A total of 459 consecutive patients were included in the present study, 217 in the 2500-IU heparin group and 242 in the 5000-IU heparin group. Radial artery patency was evaluated one month after the TRCAG with Doppler ultrasonography.
Results: The RAO was observed in 15 (3.3%) patients. The RAO was significantly higher in 2500 IU heparin group than 5000 IU heparin group (5.5% vs 1.2% $p = 0.010$, respectively). Female gender (Odds ratio (OR) = 66.135, $p = 0.002$, 95% confidence interval (CI) = 4.584–954.131), sheath removal time (OR = 1.496, $p < 0.001$, 95% CI = 1.254–1.784) and administration of 2500 IU heparin (OR = 9.758, $p = 0.034$, 95% CI = 1.195–79.695) were the independent predictors of RAO in multivariate regression analysis. While the presence of hypertension was independently associated with radial artery patency in multivariate regression analysis (OR = 0.022, $p = 0.005$, 95% CI = 0.002–0.307).
Conclusion: The patients in the standard dose heparin group had lower RAO rates compared to low dose group in this study. This suggests that using the current technique, standard dose of heparin is still required for transradial diagnostic angiography.

1. Introduction

Radial artery occlusion (RAO) is usually silent but an undesired complication of transradial coronary angiography (TRCAG). The reported incidence of RAO is varying [1]. The incidence of RAO is affected by many factors including patient weight, the ratio between the radial artery diameter and sheath size, repeated procedures, prolonged cannulation time, compression method, and heparin dose (1). Greater incidence of RAO was reported with the combination of low doses of heparin and occlusive radial artery compression [2,3]. However, the usage of patent hemostasis method reduces the incidence of RAO [4]. Various studies reported an association between heparin dosage and RAO. However the optimal dose of heparin administration was still debatable. In the present study, we evaluated the incidence of RAO with 2 doses of heparin, a low dose (2500 IU) and a standard dose (5000 IU) in patients who underwent TRCAG.

2. Methods

This prospective study was conducted at our clinic between March 2013 and November 2013. We enrolled 744 consecutive patients and randomized in a 1:1 ratio before cardiac diagnostic catheterization from the right radial artery to a low (2500 IU) or standard (5000 IU) dose of unfractionated heparin. All patients had a good pulsating radial artery and normal oximetry–plethysmography testing before TRCAG. Patients taking warfarin, with acute coronary syndrome, admitted for elective percutaneous coronary intervention, had previous TRCAG were not enrolled in this study. A total of 285 patients were excluded after diagnostic angiography when a different final dose of heparin had been administered owing to ad hoc angioplasty or in the case of conversion to another artery approach. A total of 459 patients were included in the present study, 217 in the 2500-IU group and 242 in the 5000-IU group. Informed consent was obtained from all subjects, and the investigation conforms to the principles outlined in the Declaration of Helsinki. The study protocol was approved by ethics committee.

After palmar arch permeability assessment and randomization, sterile preparation and local anesthesia with 1 ml of 2% prilocain was performed. The radial artery was cannulated with 6Fr hydrophilic 10-cm-

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long sheaths (Glidesheath introducer, Terumo, Tokyo, Japan). After sheath insertion, a radial cocktail containing 2 mg of diltiazem, 200 mcg nitroglycerin and heparin 2500 or 5000 IU diluted in a 10-ml syringe was injected gradually through the sheath side arm into the radial artery. Coronary angiography was preferentially performed using a 6Fr Judkins left and right catheters (Boston Scientific). On completion of the diagnostic procedure, the radial sheaths were removed, and the inflatable hemostatic device was applied at the access site and after transfer to the recovery room, the initial compression was further reduced to maintain radial artery patency. Radial artery patent hemostasis was verified, first by placing a pulse oximeter on the thumb, and then observing the continuous plethysmographic signal on the monitor during manual compression of the ulnar artery just proximal to the pisiform bone. Great care was taken to obtain radial artery hemostasis while maintaining minimal pressure with the band. The band was left in place until hemostasis was completed, usually within <2 h. All patients were discharged at the same day. The radial artery patency was verified by duplex ultrasonography (Mindray M7 ultrasound system, MİndRay, Inc, Shenzen, PRC, 7L4S linear probe [5–10 mHz]) one month after the procedure.

All coronary angiograms were performed by 2 interventional cardiologists with large experience in radial access. Duplex ultrasonography assessment of the radial artery was performed by 2 experienced physicians who remained unaware of the heparin dosing.

Weights of the patients, in light clothes and without shoes, were measured in kilograms, and their heights were also measured. Body mass index (BMI) was calculated by dividing body weight in kilograms by the square of body height in meters. Glomerular filtration rate (GFR) was calculated according to modification in diet in renal disease formula.

Hypertension was defined by a previous diagnosis of hypertension or the presence of systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg (mean of two consecutive measurements). Diabetes was defined as fasting plasma glucose ≥126 mg/dl or plasma glucose level ≥200 mg/dl 2 h after the 75 mg oral glucose tolerance test or symptoms of hyperglycemia accompanied by casual plasma glucose ≥200 mg/dl or HbA1C ≥6.5% or patients using antidiabetic medications. Dyslipidemia was defined as total cholesterol value >200 mh/dl or usage of statin and/or fibrate.

Patients who self-reported as having smoked during the previous six months were classified as smokers. Venous blood samples were drawn after a 12-hour overnight fast. Serum glucose and triglycerides were determined using standard automatic enzymatic methods. High density lipoprotein (HDL) cholesterol was determined after specific precipitation and low density lipoprotein (LDL) cholesterol was determined by the Friedewald formula.

2.1. Statistical analysis

SPSS 17.0 statistical software (SPSS Inc., Chicago, Ill., USA) was used for statistical analysis. Continuous variables were expressed as means ± SD, and categorical variables were expressed as percentages. The Kolmogorov–Smirnov test was used to test the normality of distribution of continuous variables. Group means for continuous variables were compared using Student's t test and the Mann–Whitney U test as appropriate. Categorical variables were compared using the Chi square test. Multivariate logistic regression analysis was performed to find the independent predictors of RAO. Sex, presence of hypertension and dyslipidemia, sheath removal time and heparin group were entered to multivariate regression analysis. A value of $p < 0.05$ was considered statistically significant.

3. Results

A total of 459 (355 male) patients were included in the present study, 217 (160 male) in the 2500-IU group and 242 (195 male) in the 5000-IU group. The characteristics of patients are shown in Table 1. The mean age of the patients was similar in both groups. Prevalence of hypertension, diabetes mellitus, dyslipidemia and smoking in both groups were similar. The procedure time, fluoroscopy time and sheath removal time were similar in both groups. While the fasting glucose, HDL, triglyceride, creatinine and eGFR levels were similar in both groups, the LDL cholesterol levels were significantly higher in the 5000 IU heparin group than in the 2500 IU heparin group (147.86 ± 42.03 mg/dl vs 138.70 ± 41.89 mg/dl). The RAO was observed in 15 (3.3%) patients. The RAO was significantly higher in the 2500 IU heparin group than in the 5000 IU heparin group (5.5% vs 1.2% $p = 0.010$ respectively). None of the patients had major bleeding.

Table 2 summarizes the procedural and clinical data for radial artery patent (RAP) and RAO groups. Prevalence of diabetes mellitus, dyslipidemia and smoking in both groups were similar. The mean age, laboratory data, procedure time and fluoroscopy time were similar in both groups. There were significantly more women in the RAO group than in the RAP group (53.3% vs 21.6%, $p = 0.008$, respectively). Hypertension was significantly common among patients in the RAP than in the RAO group (54.3% vs. 26.7%, $p = 0.035$, respectively) while the dyslipidemia was significantly lower (59.5% vs 86.7%, $p = 0.034$). Sheath removal time was significantly longer in the RAO group than in the RAP group (12 (5) min vs 33 (14) min, $p < 0.001$, respectively). Heparin dose was also significantly different for the two groups. (See Table 3.)

Female gender (Odds ratio (OR) = 66.135, $p = 0.002$, 95% confidence interval (CI) = 4.584–954.131), sheath removal time (OR = 1.496, $p < 0.001$, 95% CI = 1.254–1.784) and administration of 2500 IU heparin (OR = 9.758, $p = 0.034$, 95% CI = 1.195–79.695) were the independent predictors of RAO in multivariate regression analysis. While the presence of hypertension was independently associated with radial artery patency in multivariate regression analysis (OR = 0.022, $p = 0.005$, 95% CI = 0.002–0.307).

4. Discussion

In the present study we have shown that female sex, sheath removal time and heparin dosage were the independent predictors of RAO. While the presence of hypertension was associated with radial artery patency.

Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL) and radial versus femoral randomized investigation in ST-elevation acute coronary

Table 1
The patient characteristics.

Variable	2500 IU Heparin n = 217	5000 IU Heparin n = 242	p
Male, n%	160 (73.7%)	195 (80.6%)	0.080
Age, year	58.85 ± 9.82	60.72 ± 10.63	0.052
Body mass index, kg/m^2	27.35 ± 4.24	27.65 ± 4.19	0.445
Hypertension, n%	119 (54.8%)	126 (52.1%)	0.552
Dyslipidemia, n%	121 (55.8%)	156 (64.5%)	0.057
Diabetes Mellitus, n%	40 (18.4%)	54 (22.3%)	0.304
Smoking, n%	84 (38.7%)	104 (43%)	0.354
Glucose, mg/dl	103 (20)	103 (22)	0.696
High density lipoprotein cholesterol, mg/dl	43.08 ± 10.85	42.28 ± 9.68	0.408
Low density lipoprotein cholesterol, mg/dl	138.70 ± 41.89	147.86 ± 42.03	0.020
Triglyceride, mg/dl	140 (98)	142.5 (84)	0.850
Creatinine, mg/dl	0.89 ± 0.23	0.90 ± 0.26	0.449
Glomerular filtration rate, ml/min	90.4 (30.7)	90.3 (34.5)	0.982
Fluoroscopy time, sc	150 (79.5)	142.5 (75.3)	0.065
Procedure time, min	7 (2)	6.5 (2)	0.391
Sheath removal time, min	12 (5)	12 (7)	0.732
Hematoma, n%	0	5 (2.1%)	0.063
Radial artery occlusion, n%	12 (5.5%)	3 (1.2%)	0.010