The effect of low dose versus standard dose of arterial heparin on vascular complications following transradial coronary angiography: Randomized controlled clinical trial

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Original Article

Abstract

BACKGROUND: The potential risk of vascular complications associated with heparin, the dose of heparin therapy has not been exactly examined in patients undergoing transradial angiography. Thus, this study was aimed to compare referral arterial thrombosis, hematoma and hemorrhagic complications with 2500 and 5000 IU arterial heparin and the association of these complications with predictors in patients undergoing diagnostic angiography.

METHODS: This prospective, randomized, double-blind controlled trial was carried out on 441 patients aged ≥ 18-year-old in Isfahan, Iran. They were referred for diagnostic coronary angiography with radial access. First participants were randomized into to inject either 2500 IU (group A) or 5000 IU (group B) of heparin. Study's primary endpoints were thrombosis, hematoma, and hemorrhage.

RESULTS: The frequency of thrombosis was 25.5% in group A vs. 2.3% in group B ($P < 0.001$), while the frequency of hematoma had no significant differences in group A and B. None of patients in both groups had hemorrhage. Using 5000 IU of heparin protected the occurrence of thrombosis by 95% [odds ratio (OR): 0.05, 95% confidence interval (CI): 0.02-012] after adjustment for confounders.

CONCLUSION: The low dose (2500 IU) versus standard dose (5000 IU) of heparin use increased the risk of thrombosis following trans-radial diagnostic coronary angiography, with no effect on hematoma and bleeding.

Keywords: Coronary Angiography; Thrombosis; Hemorrhage; Hematoma

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Introduction

Cardiovascular diseases (CVDs) are the first leading cause of mortality in Iran and worldwide over the last decades.[1,2] The improving in primary and secondary prevention approaches and more access to invasive and non-invasive treatments have reduced CVD mortality in developed countries.[3] However, definite diagnosis is suggested before doing any coronary aggressive treatment. The most precise technique for final interpretation of coronary diseases is coronary angiography.[4] Although the transfemoral approach (TFA) has some vascular complications including bleeding, hematoma and arteriovenous fistula or pseudoaneurysm, it is the first option for diagnostic and therapeutic percutaneous coronary intervention (PCI).[5] Transradial approach (TRA) which was initiated by Campeau[6] in 1989 for a diagnostic procedure and improved by Kiemeneij and Laarman[7] for PCI, is the next alternative.

The radial artery is an increasingly utilized access site for coronary arteriography, now used in up to 20% of diagnostic procedures in the United States.[4] Although it is routine to use intense antiplatelet and anticoagulant treatment in coronary angiography via TRA, this approach is as safe as TFA,[8] and vascular access site complications are less common than TFA.[9] On the other hand, the prevalence of radial artery occlusion (RAO) was 2-18% in some studies after TRA coronary procedures.[10] Several factors including gender, body weight, the duration of procedure and compression, the dose of the

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anticoagulation agent and catheter numbers are can effect on vascular complication with TRA.[11] However, the potential risk of vascular complications associated with heparin. The dose of heparin therapy has not been exactly examined in patients undergoing TRA. Thus, this study was performed to evaluate the incidence and comparing the arterial thrombosis and hemorrhagic complications with 2500 and 5000 IU atrial heparin and the association of these complications with predictors in patients who underwent diagnostic angiography.

Materials and Methods

This was a two-center prospective, randomized, double-blind controlled trial (RCT) registered in Iranian Randomized Clinical Trial Center by ID number of IRCT138905124497N1. This study had a parallel design which was done in two specialized governmental and referral hospitals including Chamran and Nour on 441 subjects in Isfahan, Iran, from April 2014 to March 2015. The sample size was determined based on 95% confidence interval (CI), 80% power of the test and the frequency of thrombosis in low and a high dose of heparin in the same previous study[12] and 10% of effect size was estimated about 200 samples in each group. We recruited subjects aged > 18-year-old, who referred for diagnostic coronary angiography with radial access by nonprobability sampling method. The indications for angiography were intermediate to high risk in non-invasive test, stable ischemic heart disease with severe angina, deposit of optimal treatment and left ventricle (LV) dysfunction (LV ejection fraction < 50) with ischemic heart disease in noninvasive tests. The participants were randomized based on simple randomization using flipping a coin method. The randomization was done by a statistician, who was unaware of the different treatment. We excluded participants who patients were suggested to urgent angiography, angioplasty, having bleeding disorders, prior radial intervention, pathological Allen tests and chronic renal failure. Patient undergoing radial angiography the average fluoroscopy duration (from the first to the last rays radiation) was 8 minutes but the average whole TRA duration was 18 minutes.

The Ethics Committee of Isfahan University of Medical Sciences was approved and followed of the Declaration of Helsinki (Ethic Committee Code: 394080). Written informed consents were obtained from subjects.

All subjects underwent a medical history and clinical examination. Socio-economic demographic data including gender, age, and occupation as well as smoking status were obtained by a physician of treatment group. Physician acquired medical history such as acute coronary syndrome and peripheral vascular diseases and CVD risk factors including diabetes mellitus (DM) and using relevant drugs. Height and weight were measured using standard methods. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). A trained nurse measured blood pressure (BP) with a mercury sphygmomanometer according to a standard protocol,[13] twice each from right and left arms in sitting position after 5 minutes of rest. The first Korotkoff sound was recorded as the systolic BP (SBP) and the disappearance of the sounds (V phase) was considered as the diastolic BP (DBP). The values of BP used in the analysis were the recorded mean level of measured BP in the higher arm. According to the Joint National Committee (JNC) and World Health Organization (WHO) guideline criteria, hypertension was defined as an SBP ≥ 140 mmHg and/or a DBP ≥ 90.[14] In addition, sheath size, the number of catheters, procedure duration, and compression time after the procedure are some factors associated with RAO and hemorrhagic complication were reported.

Transradial catheterization procedure: Under sterile conditions, local anesthesia was achieved by an injection of 2% lidocaine at the puncture site. A 20-gauge needle was used to puncture the radial artery 2-3 cm proximal to the crease of the wrist. On appearance of pulsatile flow, a wire (0.025 inch, 45 cm) was advanced into the radial artery lumen. A glide sheath (Merit's) was then advanced over the wire into the radial artery using Seldinger technique in this study. For diagnostic coronary catheterization, a 5-French sheath system was used in all patients. Total 200 µg of nitroglycerin and 2.5 mg verapamil and 2500 (group A) or 5000 IU (group B) unfractionated heparin was injected via the arterial sheet before the wire into the radial artery through the sheath. Diagnostic angiography was performed with 5-French standard diagnostic coronary catheters (tiger).

Patients were randomized to receive either 2500 IU (group A) or 5000 IU (group B) of unfractionated heparin by another staff that was unaware of the patient's history.

Homeostasis procedures: All introducer sheaths were immediately removed following the angiography. A radial compression device (TR band, Terumo Europe, Leuven, Belgium) was

placed tightly around the wrist. The band was inflated with 15 ml air after removal of the sheath to obtain homeostasis.

Inflation pressure was reduced after 15, 30 and 60 minutes by removing 3-5 ml of air of the inflation chamber of the TR band, respectively. The band was left in place for at least 1 hour. A light dressing was applied to the site after removal of the compression device.

Endpoints: Study's primary end points were thrombosis, hematoma and hemorrhage record by one cardiology resident who was unaware of the study group. Thrombosis was assessed by patient's pulse Q30 minute until 4 hour (time of discharge) and then 24 hours after angiography and patient with radial pulseless investigated by color Doppler sonography. Radial artery flow was assessed at the access site at the wrist and the complete forearm up to the brachial artery in the cross section and in the longitudinal axis. The absence of radial artery flow was defined as complete occlusion. The partial flow was defined as a reduced flow velocity in a partial occluded vascular lumen in the distal, middle and/or proximal part of the radial artery. The hematoma was examined in 4 and 24 hours and hemorrhage in 1 and 4 hour after angiography. We defined hematoma as localized swelling and bruising in place of sheath and hemorrhage as active bleeding in place of the sheath. To achieve double-blind condition, the patients and the physician who examined the endpoints were unaware of the treatment.

The data normality of data was checked and approved. For the descriptive data analysis, categorical variables were expressed as absolute frequencies and percentages and were compared using the chi-square test. Continuous variables were expressed as the mean and standard deviation (SD) and compared using Student's t-test. Primary endpoints were compared between groups A and B by chi-square test. Logistic regression was utilized to examine odds ratio (OR) (95% CI) of any complications and some indicators including, age (year), gender (male/female), BMI (kg/m^2), current smoking status (yes/no), DM (yes/no), hypertension (yes/no), number of catheters (1/2 or 3), fluoroscopy duration (minute) and heparin use (2500 or 5000 IU). SPSS software (version 18, SPSS Inc., Chicago, IL, USA) was used for the statistical analyses, and $P < 0.050$ was considered statistically significant.

Results

We recruited 512 patients who were a candidate for TRA diagnostic angiography. Of total 71 were excluded because of not meeting inclusion criteria (n = 49) or refused to participate (n = 22). The flow chart showing number of eligible and excluded participants, the number of participants allocated to 2500 and 5000 IU of heparin is presented in figure 1.

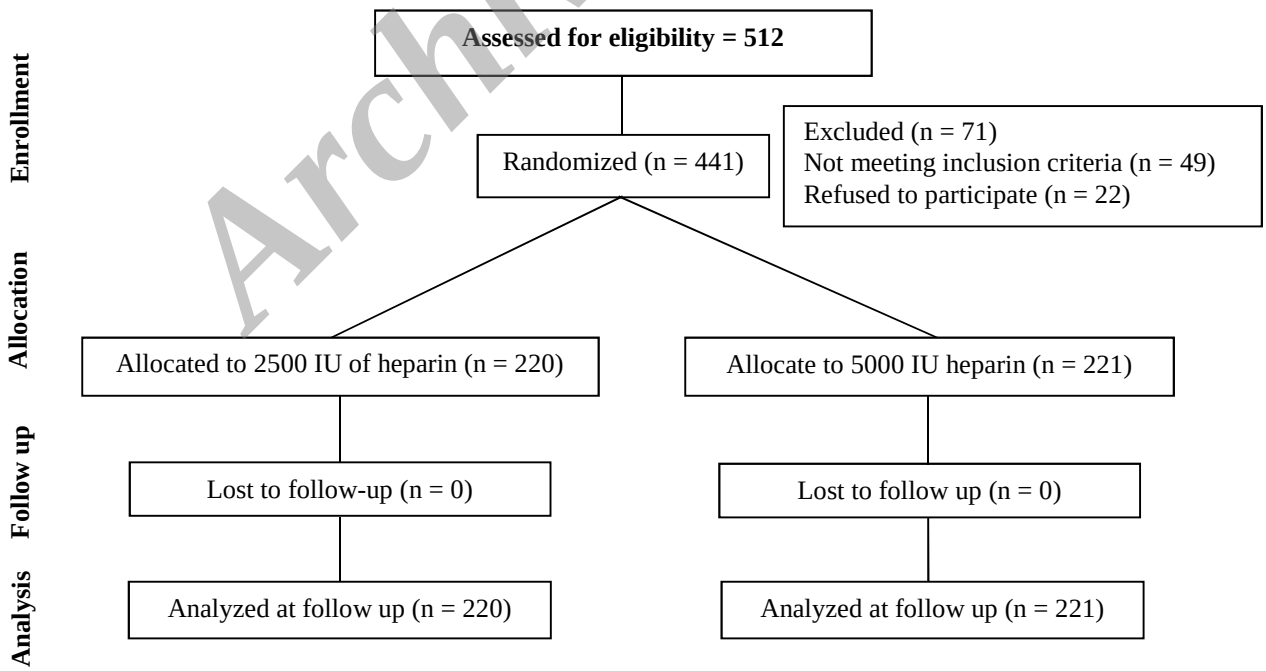

Figure 1. Flow chart showing number of eligible and excluded participants, number of participants allocated to 2500 and 5000 IU of heparin

Table 1 shows baseline characteristics and procedure status of patients based on study groups. Of 441 patients participated in this study 220 and 221 subjects were in group A and B, respectively. There is no significant differences in mean age and BMI of participants in group A vs. group B (P = 0.149 and P = 0.066, respectively). Totally 240 patients were male in both groups, however, there was no significant difference between two groups (P = 0.567). The frequency of hypertension, DM and smoking status were similar in both groups (all P more than 0.050).

The frequency of patients in group A, who had one catheter in the procedure was significantly less than group B [182 (82.7) vs. 202 (91.4); P = 0.007], while the fluoroscopy duration had no significant difference between two groups (P = 0.059). The baseline characteristics of patients were compared in subjects with and without events including thrombosis and hematoma based on the dose of heparin. This comparison shows the thrombosis was more frequent in female gender and smokers (P < 0.001 and P = 0.001, respectively). In addition, the hematoma was more frequent in diabetic patients (P = 0.047). There were no significant differences in the other variables between the patients with and without thrombosis and hematoma.

Table 2 demonstrates that injecting 2500 IU of heparin increased the occurrence of thrombosis in unadjusted and after adjustment for all potential confounders were more than 14 and 21 times than standard heparin dose (OR: 14.75, 95% CI: 5.78-37.65; P < 0.001) and [21.87 (8.12-56.93); P < 0.001], respectively. The risk of thrombosis was 2.25 times more in female than male (OR: 2.25, 95% CI: 1.02-4.94). After adjustment of potential confounders, hypertension, DM, current smoking, a number of catheters and fluoroscopy duration increased the risk of thrombosis by 2.11, 1.79, 2.281.12 and 2.84 times, respectively. However, the BMI inversely associated with incidence of thrombosis [0.82 (0.72-0.93); P = 0.002] (Table 3). However, there is no association of the amount of injected heparin as well as other risk factors with hematoma incidence (Table 3). The frequency of thrombosis was 25.5 against 2.3% in group A vs. group B (P < 0.001), while the frequency of hematoma had no significant differences in group A and B (Figure 2). Furthermore, there was no bleeding occurrence in patients of both groups.

Discussion

In this two-center RCT study, we examined the incidence of RAOs following TRA access coronary angiography with 2500 against 5000 IU heparin injection. TRA access occlusions are often asymptomatic and consequently underdiagnosed, thus it seems logical, that anticoagulant therapy should be used to decline these events.[14] We found that the risk of thrombosis was more than 21 times in low dose group versus standard dose. However, the risk of hematoma had no difference in low and standard dose of heparin injection. Furthermore, there was no minor and major bleeding incidence after 1 and 4 hours in both groups. Our findings were consistent with Mohandes et al.[15] and the accumulating evidence which suggests TR access is associated with significant reductions in bleeding compared with a TFA.[14,16,17] Patients' baseline and angiographic characteristics were well balanced in two groups and had no significant differences except for the number of catheters which was less in high dose group.

Table 1. Baseline characteristics and procedural data of the study population based on study group

Characteristics	Group		P
	Group A* (n = 220)	Group B** (n = 221)	
Age (year) (mean ± SD)	62.87 ± 9.10	62.48 ± 9.40	0.149
BMI (kg/m²) (mean ± SD)	26.09 ± 3.60	25.59 ± 3.10	0.066
Gender (female) [n (%)]	97 (44.1)	104 (47.1)	0.567
Hypertension [n (%)]	48 (21.8)	43 (19.5)	0.558
DM [n (%)]	29 (13.2)	20 (9.0)	0.176
Smoking [n (%)]	39 (17.9)	35 (15.8)	0.611
Number of catheters [n (%)]			0.007
1	182 (82.7)	202 (91.4)	
2 or 3	38 (17.3)	19 (8.6)	
Fluoroscopy duration (min) (mean ± SD)	8.11 ± 0.70	8.23 ± 0.47	0.059

*Group A: Group who injected 2500 IU heparin, **Group B: Group who injected 5000 IU heparin. Categorical variables were analyzed by chi-square test and continuous variables by independent t-test.
BMI: Body mass index; DM: Diabetes mellitus; SD: Standard deviation

Table 2. Odds ratio and 95% confidence interval of thrombosis and hematoma according to different characteristics

Characteristics	Thrombosis		Hematoma	
	OR (95% CI)	P	OR (95% CI)	P
Crude				
Heparin*	14.75 (5.78-37.65)	< 0.001	0.82 (0.13-4.97)	0.819
Age (year)	0.99 (0.96-1.02)	0.674	1.02 (0.93-1.13)	0.621
BMI (kg/m²)	0.82 (0.74-0.91)	< 0.001	1.02 (0.79-1.31)	0.882
Gender (female)**	2.94 (1.58-5.45)	0.001	2.85 (0.31-25.79)	0.351
Hypertension (no/yes)	1.93 (1.06-3.52)	0.031	5.76 (0.94-35.16)	0.058
DM (no/yes)	2.27 (1.11-4.65)	0.025	5.35 (0.87-33.08)	0.071
Current smoker (no/yes)	2.92 (1.59-5.37)	0.001	3.29 (0.29-37.10)	0.334
Number of catheters (2 or more)***	1.39 (0.66-2.92)	0.386	9.16 (1.49-56.28)	0.017
Fluoroscopy duration (minutes)	2.00 (1.04-3.08)	0.001	5.26 (1.26-21.95)	0.023
Adjusted†				
Heparin	21.87 (8.12-56.93)	< 0.001	0.26 (0.01-3.99)	0.332
Age (year)	0.99 (0.96-1.03)	0.784	1.08 (0.91-1.30)	0.375
BMI (kg/m²)	0.82 (0.72-0.93)	0.002	1.06 (0.67-1.69)	0.794
Gender (female)	2.25 (1.02-4.94)	0.044	7.04 (0.05-20.34)	0.443
Hypertension (no/yes)	2.11 (1.02-4.39)	0.045	2.54 (0.36-12.02)	0.206
DM (no/yes)	1.79 (1.04-4.53)	0.021	3.38 (0.32-14.51)	0.181
Current smoker (no/yes)	2.28 (1.03-5.07)	0.043	3.9 (0.13-15.92)	0.277
Number of catheters (2 or more)	1.12 (1.01-1.14)	0.048	4.5 (0.70-16.23)	0.078
Fluoroscopy duration (minutes)	2.84 (1.58-5.10)	< 0.001	1.86 (0.13-10.67)	0.649

*Group B, who injected 5000 IU heparin considered as a reference group, **The reference group was male gender, ***The reference group was using 1 catheter, †Each variable was adjusted by the others one
BMI: Body mass index; CI: Confidence interval; OR: Odds ratio; DM: Diabetes mellitus

Table 3. Baseline characteristics and procedural data in patients with and without thrombosis and hematoma based on study group

Characteristics	With thrombosis	Without thrombosis	P	With hematoma	Without hematoma	P
Group A*						
Age (year) (mean ± SD)	62.89 ± 10.30	62.86 ± 8.70	0.186	66.00 ± 2.10	62.81 ± 9.20	0.070
BMI (kg/m²) (mean ± SD)	24.33 ± 2.70	26.69 ± 3.70	0.016	26.37 ± 2.60	26.08 ± 3.60	0.419
Gender (Female) [n (%)]	29 (51.8)	35 (21.4)	< 0.001	2 (66.7)	93 (43.1)	0.083
Hypertension [n (%)]	17 (30.4)	31 (18.9)	0.057	2 (66.7)	46 (21.3)	0.122
DM [n (%)]	11 (19.6)	18 (11)	0.080	2 (66.7)	27 (12.5)	0.047
Smoking [n (%)]	19 (33.9)	20 (12.3)	0.001	1 (33)	39 (18.1)	0.820
Number of catheters (2 or 3) [n (%)]	8 (14.3)	30 (18.3)	0.322	1 (33)	37 (17.1)	0.437
Fluoroscopy duration (minutes) (mean ± SD)	8.27 ± 0.49	8.21 ± 0.40	0.204	8.19 ± 0.56	8.24 ± 0.43	0.224
Group B**						
Age (year) (mean ± SD)	54.60 ± 8.20	62.67 ± 9.40	0.393	64.50 ± 3.50	64.29 ± 9.50	0.094
BMI (kg/m²) (mean ± SD)	24.42 ± 2.30	25.6 ± 3.1	0.514	25.79 ± 2.70	25.59 ± 3.10	0.684
Gender (female) [n (%)]	2 (60)	101 (46.8)	0.444	102 (86.4)	1 (50)	0.264
Hypertension [n (%)]	41 (19)	2 (40)	0.251	1 (50)	23 (19.5)	0.361
DM [n (%)]	1(20)	19 (8.8)	0.381	1 (50)	10 (8.5)	0.140
Smoking [n (%)]	1(20)	34 (15.7)	0.581	5 (4.2)	1 (50)	0.098
Number of catheters (2 or 3) [n (%)]	8 (14.3)	30 (18.3)	0.322	1 (50)	10 (8.5)	0.140
Fluoroscopy duration (minutes) (mean ± SD)	8.08 ± 0.69	8.12 ± 0.61	0.213	8.17 ± 0.72	8.10 ± 0.64	0.237

*Group A: Group who injected 2500 IU heparin, **Group B: Group who injected 5000 IU heparin, Categorical variables were analyzed by chi-square test and continuous variables independent t-test.
BMI: Body mass index; SD: Standard deviation; DM: Diabetes mellitus

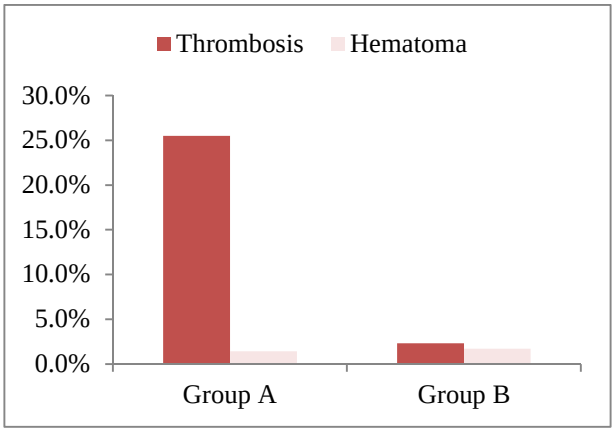

Figure 2. Comparison of the incidence of thrombosis and hematoma in group A (2500 IU heparin injection) and group B (5000 IU heparin injection)

Although TRA has some advantages against TFA, increasing fluoroscopy duration lead to fluoroscopy and radiation time extension which is the TRA disadvantages.[18] The average of fluoroscopy duration was more than 8 minutes in both groups in the current study, which was higher than previous studies.[19,20]

Thrombosis risk following TRA access diagnostic and interventional coronary procedures raged between 1 and 5%.[7,20] Thrombolytic therapy on ischemic hand symptoms after right atrium cannulation had a favorable effect in Geschwind et al. study.[21] In our study, this post-procedural symptom following TRA diagnostic angiography was higher than previous studies in low dose, but not in the high dose heparin group. Moreover, the incidence rate of RAO, as the most common post-procedural complication of TRA ranged from 2 to 18% event in evidence.[22-25] It seems that creation of thrombus involves in the early RAO occurrence.[26]

Consistent to our study, Moody et al.[14] reported that application of higher dose of heparin (100 IU/kg body weight) against 5000 IU in the patients who underwent coronary angiography led to less rate of RAO development. They proposed that the using higher heparin doses with average of 9000 IU inversely associated with the occurrence of RAO.[14] In addition, Spaulding et al.[27] found that RAO rates were 24 vs. 4.3% in the patients with 2000-3000 and 5000 IU of heparin use, respectively, which was similar to the incidence of post-procedural thrombosis in our study. In another study of RAO incidence was 30% in patients receiving 1000 IU of heparin during diagnostic angiography.[28] However, in the study of Manoukian et al.[29] with TRA access, the incidence of RAO had no difference between two groups with 50 IU/kg and 5000 IU heparin.

No anticoagulant therapy, increased pressure of the radial artery compression, low ratio of radial artery to sheath and smoking are some important risk factors of RAO development.[22-24]

The risk of thrombosis positively associated to female gender, hypertension, DM, current smoking, number of catheters and procedure duration while inversely had relationship with BMI. Contrary to our findings, several studies reported that RAO occlusion was associated with body weight, however, these studies had similar results about gender.[22,23,30] Gender difference might be due to less radial artery to sheath diameter ratio in females.[14] However, in line with our results Plante et al.[31] found inverse association between body weight and RAO occurrence. They believed that body weight could be as effective as heparin in RAO risk reduction.[31,32] Furthermore inconsistent to our findings Moody et al.[14] found no association between hypertension and the smoking status with RAO development.

Limitations

Our strength was examining three events including thrombosis, hematoma, and hemorrhage at the same time. In addition, determining the potential confounders consist of age, gender, number of the catheter, BMI, presence of DM and hypertension. This study had some limitations. First, study sample size was small, thus, we could not conduct subgroup analysis; Not performing this study as a multi-center RCT was our second limitation.The other limitation was using only 2 heparin doses for all patients with no consideration of their weights.

Conclusion

The low dose (2500 IU) of heparin use against standard dose (5000 IU) increased the risk of thrombosis following TRA diagnosis coronary angiography. While, it had not any influence on hematoma and hemorrhagic complications. Further studies in multi-center with more study population are required to confirm our observations.

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Conflict of Interests

Authors have no conflict of interests.

References

1. Talaei M, Sarrafzadegan N, Sadeghi M, Oveisgharan S, Marshall T, Thomas GN, et al. Incidence of cardiovascular diseases in an Iranian population: the Isfahan Cohort Study. Arch Iran Med 2013; 16(3): 138-44.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006; 3(11): e442.
3. Capewell S, Beaglehole R, Seddon M, McMurray J. Explanation for the decline in coronary heart disease mortality rates in Auckland, New Zealand, between 1982 and 1993. Circulation 2000; 102(13): 1511-6.
4. Mann DL, Zipes DP, Libby P, Bonow RO, Braunwald E. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. Philadelphia, PA: Elsevier/Saunders; 2015. p. 392, 397.
5. Cevik C, Izgi C, Nugent K. Radial artery access as an emerging factor for decreasing mortality in cardiovascular interventions. J Interv Cardiol 2010; 23(1): 95-9.
6. Campeau L. Percutaneous radial artery approach for coronary angiography. Cathet Cardiovasc Diagn 1989; 16(1): 3-7.
7. Kiemeneij F, Laarman GJ. Percutaneous transradial artery approach for coronary stent implantation. Cathet Cardiovasc Diagn 1993; 30(2): 173-8.
8. Ziakas A, Gomma A, McDonald J, Klinke P, Hilton D. A comparison of the radial and the femoral approaches in primary or rescue percutaneous coronary intervention for acute myocardial infarction in the elderly. Acute Card Care 2007; 9(2): 93-6.
9. Jolly SS, Amlani S, Hamon M, Yusuf S, Mehta SR. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. Am Heart J 2009; 157(1): 132-40.
10. Pancholy SB. Transradial access in an occluded radial artery: new technique. J Invasive Cardiol 2007; 19(12): 541-4.
11. Pancholy SB, Patel TM. Effect of duration of hemostatic compression on radial artery occlusion after transradial access. Catheter Cardiovasc Interv 2012; 79(1): 78-81.
12. Hahalis G, Xathopoulou I, Tsigkas G, Almpanis G, Christodoulou I, Grapsas N, et al. A comparison of low versus standard heparin dose for prevention of forearm artery occlusion after 5 French coronary angiography. Int J Cardiol 2015; 187: 404-10.
13. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42(6): 1206-52.
14. Moody WE, Chue CD, Ludman PF, Chan YK, Narayan G, Millington JM, et al. Bleeding outcomes after routine transradial primary angioplasty for acute myocardial infarction using eptifibatide and unfractionated heparin: a single-center experience following the HORIZONS-AMI trial. Catheter Cardiovasc Interv 2013; 82(3): E138-E147.
15. Mohandes M, Colomer I, De Castro R, Guarinos J, Rojas S, Fernandez F, et al. Safety of diagnostic coronary angiogram by radial approach in patients on chronic anticoagulation therapy with coumarin derivatives. Int Cardiovasc Res J 2012; 6(2): 36-9.
16. Louvard Y, Lefevre T, Morice MC. Radial approach: what about the learning curve? Cathet Cardiovasc Diagn 1997; 42(4): 467-8.
17. Ziakas AG, Koskinas KC, Gavrilidis S, Giannoglou GD, Hadjimiltiades S, Gourassas I, et al. Radial versus femoral access for orally anticoagulated patients. Catheter Cardiovasc Interv 2010; 76(4): 493-9.
18. Gurm HS, Smith DE, Collins JS, Share D, Riba A, Carter AJ, et al. The relative safety and efficacy of abciximab and eptifibatide in patients undergoing primary percutaneous coronary intervention: insights from a large regional registry of contemporary percutaneous coronary intervention. J Am Coll Cardiol 2008; 51(5): 529-35.
19. Madan M, Kereiakes DJ, Hermiller JB, Rund MM, Tudor G, Anderson L, et al. Efficacy of abciximab readministration in coronary intervention. Am J Cardiol 2000; 85(4): 435-40.
20. Mann T, Cubeddu G, Bowen J, Schneider JE, Arrowood M, Newman WN, et al. Stenting in acute coronary syndromes: a comparison of radial versus femoral access sites. J Am Coll Cardiol 1998; 32(3): 572-6.
21. Geschwind JF, Dagli MS, Lambert DL, Kobeiter H. Thrombolytic therapy in the setting of arterial line-induced ischemia. J Endovasc Ther 2003; 10(3): 590-4.
22. Nagai S, Abe S, Sato T, Hozawa K, Yuki K, Hanashima K, et al. Ultrasonic assessment of vascular complications in coronary angiography and angioplasty after transradial approach. Am J Cardiol 1999; 83(2): 180-6.
23. Yoo BS, Lee SH, Ko JY, Lee BK, Kim SN, Lee MO, et al. Procedural outcomes of repeated transradial coronary procedure. Catheter Cardiovasc Interv 2003; 58(3): 301-4.
24. Sanmartin M, Gomez M, Rumoroso JR, Sadaba M, Martinez M, Baz JA, et al. Interruption of blood flow during compression and radial artery occlusion after transradial catheterization. Catheter Cardiovasc Interv 2007; 70(2): 185-9.
25. Stella PR, Kiemeneij F, Laarman GJ, Odekerken D, Slagboom T, van der Wieken R. Incidence and outcome of radial artery occlusion following

transradial artery coronary angioplasty. Cathet Cardiovasc Diagn 1997; 40(2): 156-8.
26. Agostoni P, Biondi-Zoccai GG, de Benedictis ML, Rigattieri S, Turri M, Anselmi M, et al. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures; Systematic overview and meta-analysis of randomized trials. J Am Coll Cardiol 2004; 44(2): 349-56.
27. Spaulding C, Lefevre T, Funck F, Thebault B, Chauveau M, Ben HK, et al. Left radial approach for coronary angiography: results of a prospective study. Cathet Cardiovasc Diagn 1996; 39(4): 365-70.
28. Lefrevre T, Thebault B, Spaulding C. Radial approach patency after percutaneous left radial artery approach for coronary angiography. The role of heparin. Eur Heart J 1995; 16: 293.
29. Manoukian SV, Feit F, Mehran R, Voeltz MD, Ebrahimi R, Hamon M, et al. Impact of major bleeding on 30-day mortality and clinical outcomes in patients with acute coronary syndromes: an analysis from the ACUITY Trial. J Am Coll Cardiol 2007; 49(12): 1362-8.
30. Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation 2006; 114(8): 774-82.
31. Plante S, Cantor WJ, Goldman L, Miner S, Quesnelle A, Ganapathy A, et al. Comparison of bivalirudin versus heparin on radial artery occlusion after transradial catheterization. Catheter Cardiovasc Interv 2010; 76(5): 654-8.
32. Feray H, Izgi C, Cetiner D, Men EE, Saltan Y, Baltay A, et al. Effectiveness of enoxaparin for prevention of radial artery occlusion after transradial cardiac catheterization. J Thromb Thrombolysis 2010; 29(3): 322-5.

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