Safety of diagnostic coronary angiogram by radial approach in patients on chronic anticoagulation therapy with coumarin derivatives

Mohsen Mohandes*, Ingrid Colomer, Ramón De Castro, Jordi Guarinos, Sergio Rojas, Francisco Fernández, Alfredo Bardaji

Interventional Cardiology Unit, Cardiology Division, Joan XXIII University Hospital. IISPV. Universitat Rovira i Virgili, Tarragona , Spain

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ABSTRACT

Background: The use of radial access for diagnostic coronary angiogram and percutaneous coronary intervention (PCI) has increased during the last few years, especially due to its benefit regarding reduction in site vascular complication compared with femoral approach.

Objectives: To evaluate the safety and feasibility of diagnostic coronary angiography in patients on chronic anticoagulation therapy without drug interruption and to study the impact of this strategy in terms of bleeding complication as first endpoint and length of hospitalisation as second endpoint.

Methods: This is a retrospective study of 53 patients on chronic anticoagulation therapy with coumarin derivatives who underwent diagnostic coronary angiography in our centre between January 2003 and July 2011, compared with a control group of 53 patients without anitcoagulation therapy. The international normalised ratio (INR) in the anticoagulated group with uninterrupted anticoagulation therapy was >2. Thrombolysis In Myocardial Infarction (TIMI) classification was used for the evaluation of bleeding complication. Hospitalisation stay was also compared between two groups.

Results: Baseline characteristics were similar in both groups except for diagnostic which motivated coronary angiogram and INR level during the procedure. A minimal bleeding occurred in the acenocoumarol group compared with 0 event in control group (1.9% vs. 0%, *P*=NS). The average of hospitalisation was 6±4.9 days in the acenocoumarol group and 6.3 ±4.1 in the control group (*P*=NS).

Conclusions: This study reveals that diagnostic coronary angiography by radial approach in patients on chronic coumarin derivative therapy without drug interruption is a safe strategy and is not associated with a significant increase in bleeding complication and length of hospitalisation.

►*Implication for health policy/practice/research/medical education:*

This study is designed to show the safety of diagnostic coronary angiogram by radial approach in the subgroup of patients on chronic anticoagulation therapy in term of bleeding complication.

►*Please cite this paper as:*

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Introduction

Coronary angiogram continues to be the gold standard method for the study of coronary artery anatomy and evaluation of coronary diseases. The femoral approach is still the most common access worldwide for both diagnostic and therapeutic procedures. Although vascular complication and patient discomfort are not uncommon with femoral access most interventionalists consider radial approach as a second or third option to initiate the procedure

if both right and left femoral access attempts fail (1). Transradial approach has gained progressive acceptance since its first introduction by Campeau in 1989 for diagnostic coronary angiography (2) and its improvement by Kiemeneij and Laarman (3) for percutaneous coronary intervention (PCI). The main reason for transradial access among interventional cardiologists in many countries is that radial approach is associated with a clear reduction in entry site complication compared with femoral approach (4). Besides, average age in patients undergoing coronary angiogram and PCI has increased considerably taking into account the inconvenience of potentially higher risk for bleeding complication in elderly patients as opposed

* *Corresponding author:* Mohsen Mohandes, Interventional Cardiology Unit, Cardiology Division, Joan XXIII University Hospital. IISPV. Universitat Rovira i Virgili, Tarragona, Spain, Tel: 0034-627888935, Email: mohandesmohsen@hotmail.com

to younger people. The benefit of transradial acces in reducing site vascular complication in this subgroup of patients has been tested in a few studies (5).

Training curve in radial is longer than femoral approach and a gentler catheter management is needed when the transradial access is used. The unique radial anatomy and its susceptibility to spasm can be a limitation to finishing the procedure in some cases. This is the reason why vasodilator agents like verapamil should be systematically administered through sheath introducer to reduce the radial spasm (6).

Although the success rate of the radial access is very high in experienced hands both in diagnostic and therapeutic cases, some particular anatomic variations like radioulnar loop and retroesophageal origin of subclavian artery (lusoria), all determined by angiography in high load centres are more frequently associated with procedural failure (7).

There is a group of patients on long-term acenocoumarol treatment due to history of atrial fibrillation, valvular prosthesis or cerebrovascular accident in whom durg interruption or not should be carefully evaluated prior to the procedure. Acenocoumarol interruption could have its inconvenience in this group of patients with potential thromboembolic events and longer hospitalisation. On the other hand coronary angiogram in patients on oral anticoagulation therapy can increase potential risk of bleeding complications. The common recommendation in patients on oral anticoagulation therapy who undergo diagnostic coronary angiography is to reach an INR less than 2 before arterial puncture, when using femoral artery access and up to 2.5 INR regarding transradial procedure. Patients with high risk of systemic thromboembolism on withdrawal of warfarin, such as those with atrial fibrillation, mitral valve disease or prior history of systemic thromboembolism, may be treated with intravenous unfractionated heparin or subcutaneous low-molecular-weight-heparin in the periprocedural period (8).

The safety of coronary angiography by radial approach without acenocoumarol interruption has been compared with drug interruption and substitution for unfractionated heparin 48 hours prior to the procedure (9).

The first endpoint of this study is to compare bleeding complication and the second endpoint is to evaluate hospitalisation period with the strategy of uninterrupted anticoagulation therapy between acenocoumarol and control group.

Patients and methods

This study is a retrospective analysis of 75 patients on chronic oral anticoagulation therapy with acenocoumarol referred to our cath lab between January 2003 and July 2011 for diagnostic coronary angiogram using radial approach with uninterrupted anticoagulation therapy. Considering INR>2 as threshold, 22 patients with INR less than 2 from anticoagulation therapy group were thus excluded from the study. The remaining 53 patients in acenocoumarol group, matched with 53 patients without oral anticoagulation therapy, underwent diagnostic coronary angiography by radial approach during the same period.

TIMI bleeding classification was used for major bleeding if associated with an intracranial hemorrhage or ≥ 5 g/dl decrease in either haemoglobin concentration or $\geq 15\%$ absolute reduction in the hematocrit. Minor bleeding consisted of observed blood loss ≥ 3 g/dl decrease in the hemoglobin concentration, or $\geq 10\%$ reduction in the hematocrit or no observed blood loss ≥ 4 g/dl decrease in the hemoglobin concentration or $\geq 12\%$ decrease in the hematocrit. Finally minimal bleeding according to TIMI classification is defined as any clinically overt sign of hemorrhage that is associated with reduction in haemoglobin concentration of less than 3 g/dl or less than 9% decrease in the hematocrit. (10)

Before starting the procedure the radial pulse appropriateness and normal Allen's test were verified in all patients. Patients with abnormal Allen's test were excluded from catheterization by radial approach. Local anesthesia with mepivacaine was used before radial puncture and sheath introducer positioning. Verapamil 2 mg, as a vasodilator agent was administered through sheath introducer immediately after its positioning into radial artery. The preference access was right radial artery in order to achieve a more operator comfort. Diagnostic catheters used were 4, 5 or 6 French at the physician's discretion. Judkins left 3.5 for left coronary artery system and Judkins right 5 for right coronary artery engagement were used if the access was right radial artery and Judkins left 4 and Judkins right 4 were utilized in case of left radial artery access. In oral anticoagulant therapy group the heparin was not administered and in control group 50-70 units per kg of intravenous unfractionated heparin was administered according to operator criteria.

All arterial sheaths were removed immediately after the procedure in both groups and hemostasis was performed with a compressed bandage consisting of a gauze swab and an adhesive elastic bandage for a minimum of 2 hours.

Statistical Analysis

Continuous variables were expressed as mean value ± SD. Differences between groups were assessed by bilateral unpaired student's t-test or Mann-Whitney U test, as appropriate. Categorical variables were expressed as count and percentage and were tested with X2 test or Fisher's exact test, as appropriate. Statistical significance was considered as P-value <0.05. All data were introduced and analysed with SPSS 15 version (SPSS Chicago, IL).

Results

Table 1 shows baseline characteristics of patients. Of 106 patients analysed in this study 58 (54.7%) were males. In the acenocoumarol group 27 (50.9%) were males against 31(58.5%) in the control group (*P*=0.44). The mean age was 65.8±11.9 years in the oral anticoagulation group and 63.7±11.2 years in the control group (*P*=0.35). In both groups 35(66%) patients had hypertension (*P*=NS). The number of patients exhibiting dyslipidemia were about 20 (37.7%) and 22 (41.5%) in the acenocoumarol and control groups respectively (*P*=0.69). Diabetes was present in 14(26.4%) in the oral anticoagulation group and 18(34%) in the control group (*P*=0.4). There were 20(37.7%)

Table 1. Baseline characteristics in acenocoumarol and control group

Characteristics		Acenocoumarol (n=53	Control (n=53)	P value
Age		65.8± 11.9	63.7± 11.2	0.35
Male		27 (50.9%)	31 (58.5%)	0.44
Hypertension		35 (66%)	35 (66%)	-
Diabetes Mellitus		14 (26.4%)	18 (34%)	0.4
Dyslipidemia		20 (37.7%)	25 (48%)	0.28
Smoking habit		20 (37.7%)	25 (48%)	0.28
Diagnosis	Unstable angina	21 (39.6%)	42 (79.3%)	
	Valvulopathy	22 (41.5%)	5 (9.4%)	< 0.001
	Others	10 (18.9%)	6(11.3%)	
Catheter size	4F	22 (41.6%)	16 (30.2%)	
	5F	19 (35.8%)	17 (32.1%)	0.22
	6F	12 (22.6%)	20 (37.7%)	
INR		2.74±0.56	0.99±0.28	< 0.001

smoker or previous smoker in the acenocoumarol group and 25(48%) in the control group (*P*=0.28). The reason for performing coronary angiogram was unstable angina in 21 (39.6%) patients of acenocoumarol group and 42 (79.3%) in control group, valvular heart disease in 22 (41.5%) and 5 (9.4%) and other diagnosis in 10 (18.9%) and 6 (11.3%) in acenocoumarol and control groups respectively (*P*<0.001). In 22 (41.6%) vs 16 (30.2%) 4F catheter was used, and in 19 (35.8%) vs 17(32.1%) 5F catheter was utilized and finally 6F catheter was employed for coronary angiogram in 12 (22.6%) vs 20 (37.7%) in acenocoumarol and control groups respectively (*P*=0.22). INR mean value was 2.74±0.56 in the acenocoumarol group compared with 0.99±0.28 in the control group (*P*<0.001). A minimal bleeding consisting of a local hematoma was detected in oral anticoagulation group compared with 0 in control group, the difference which is not statistically significant (1.9% vs. 0%, *P*=NS). There was not any minor and major bleeding complication in any group. The average hospitalisation was 6±4.9 days versus 6.3±4.1 days (*P*=NS) in acenocoumarol and control groups respectively.

Discussion

Although femoral artery continues to be the main approach in many cath labs worldwide for both diagnostic coronary angiogram and PCI, there is a lot of evidence favouring radial access in regard to reduced bleeding complication associated with the procedure (11).This advantage becomes more attractive in the era of antiplatelet and antithrombotic therapy in patients with coronary artery disease especially in the elderly patients in whom the risk of site vascular and bleeding complication is higher (12).

This study analyses a subgroup of patients on chronic anticoagulation therapy undergoing diagnostic coronary angiography for different reasons using radial approach. The interruption of oral anticoagulation therapy and the need of its substitution with heparin could eventually produce a few inconveniences such as prolonged hospitalisation and could ultimately increase the risk of thromboembolic events. The possibility of performing a diagnostic coronary angiogram by radial access with uninterrupted anticoagulation therapy strategy makes this approach attractive and can avoid a few problems associated

with therapy interruption. We have already indicated a need for a particular training for diagnostic coronary angiogram and PCI by radial approach (13) .In our cath lab we usually perform around 90% of all procedures by radial approach and the results of our study in the subgroup of patients on chronic anticoagulation therapy did not show any significant increase in bleeding and site vascular complication compared with a control group. This was of especial interest to many patients coming from other hospitals to be catheterized in our centre with immediate ambulation after the diagnostic procedure performed by radial approach. The patient with access site hematoma had an INR 2.87. This site vascular complication was resolved by standard compression and the patient did not need blood transfusion. One patient in acenocoumarol group with an INR 2.94 received transfusion after the procedure. Haemoglobin level before and after the procedure in this patient was 8.6 g/dl and 7.7 g/dl respectively and there was no evidence of site vascular complication or overt sign of hemorrhage. Besides this patient had a previous history of anaemia of digestive origin which needed more blood trasnsfusions a few months ago, so the patient did not fulfil the criteria for TIMI bleeding classification.

In our study the INR ranged from 2 to 4.26 in the acecoumarol group. Antti-Pekka Annala et al. in a retrospective study concluded that access site complication in patients undergoing diagnostic coronary angiography with uninterrupted Warfarin treatment and a supratherapeutic anticoagulation (INR>3) is more common compared with therapeutic (INR 2-3) or subtherapeutic (INR<2) periprocedural anticoagulation respectively(14). Although in this study femoral approach significantly predicted access site complication in the entire study population this association was not significant in the Warfarin group.

We thus believe that performing diagnostic coronary angiogram by radial approach in patients on chronic anticoagulation therapy with acenocoumarol derivatives with an uninterrupted anticoagulation strategy is safe and did not significantly increase the risk of bleeding complications. Uninterrupted anticoagulation therapy strategy with an INR in therapeutic rang during a diagnostic coronary angiogram by radial approach can avoid many

inconveniences derived from therapy interruption and can provide a similar hospitalisation regarding control group.

Finally this is a retrospective study with acenocoumarol derivatives as oral anticoagulation therapy and further investigation are needed before extrapolating our results to other populations. In this context, other prospective and randomised studies are needed before arriving at definitive conclusion.

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