

# Predictors of local venous complications resulting from electrophysiological procedures

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## Abstract

**Background:** *Thromboembolic complications resulting from radiofrequency catheter ablation (RFCA) have an overall incidence of 0.6%. Multiple intracardiac catheters are often necessary for electrophysiological study and RFCA therapy. Therefore, the placement of multiple venous sheaths in one femoral vein is always required for multiple intracardiac catheter insertion. The safety of the placement of multiple separate venous sheaths has been studied previously in a non-randomized study, but the placement of multiple sheaths via one venous line has not been fully studied.*

**Methods and Results:** *A randomized clinical trial was conducted with a total of 200 patients. We studied the safety of placing multiple sheaths via one venous line, and the effect of heparin on deep vein thrombosis (DVT) and on in situ thrombosis. DVT was not seen in our patients. We observed a significant decrease in the rate of in situ thrombosis in patients who received heparin during the procedure (28% vs 11%,  $p = 0.04$ ). The type of cannulation changed the in situ thrombosis rate independently of the heparinization protocol. The rate of in situ thrombosis was higher when placing sheaths via one venous line regardless of the heparinization protocol used (16% vs 6%,  $p = 0.1$  for the group on heparin, and 38% vs 18%,  $p = 0.04$  for the other group). In the group cannulated with only one venous line (100 patients), heparinization significantly decreased the rate of in situ thrombosis (16% vs 38%,  $p = 0.023$ ), but there was an insignificant decrease in the separate cannulation group (6% vs 18%,  $p = 0.12$ ). Advanced age had no effect on thrombosis. Surprisingly, there was a significantly greater rate of in situ thrombosis (not DVT) among women than among men (26% vs 11%,  $p = 0.01$ ), regardless of the heparinization protocol or the type of cannulation.*

**Conclusions:** *Given the local venous complications and DVT after electrophysiological procedures, heparinization is not necessary for right-sided electrophysiological procedures. In situ thrombosis is a minor complication that can be reduced by heparinization in patients undergoing one-line cannulation and in women during longer procedures. (Cardiol J 2012; 19, 1: 15–19)*

**Key words:** deep vein thrombosis, local venous complications, electrophysiological procedures

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Received: 22.11.2010

Accepted: 12.05.2011

## Introduction

Radiofrequency catheter ablation (RFCA) is an established effective therapy for the treatment of many cardiac tachyarrhythmias. The chief limitation of conventional RFCA continues to be the risk of thromboembolism. Thromboembolic complications of RFCA have an overall incidence of 0.6%. However, the risk is increased when ablation is performed in the left heart (1.8% to 2%) and for ventricular tachycardia (2.8%) [1–6].

Embolization from venous sheaths or right-sided RF lesions causes deep vein thrombosis, free-floating right atrial thrombosis, and pulmonary embolism, all of which may be clinically silent [7].

Multiple intracardiac catheters are often necessary for electrophysiological study (EPS) and RFCA. Therefore, the placement of multiple venous sheaths through one femoral vein is always required for multiple intracardiac catheter insertion. Severe clinical problems such as pulmonary emboli following local venous thrombosis are rare, but lethal and devastating. Nevertheless, these complications are worth taking into account. Thrombogenicity of multiple catheters were documented by previous studies [8, 9]. The safety of placing multiple separate venous sheaths has been studied previously in a non-randomized study [10], but the placement of multiple sheaths via just one line has not been fully studied.

We studied the safety of placing multiple sheaths via one line, and the effect of heparin on the incidence of vascular complications and on the risk of *in situ* and deep vein thrombosis (DVT). This is the first randomized study regarding the local venous complications resulting from EPS procedures.

## Methods

### Study population

A prospective randomized clinical trial was conducted, with 200 patients undergoing right heart EPS/RFCA for the diagnosis and/or treatment of right-sided supraventricular and ventricular tachyarrhythmias. All patients gave informed consent before inclusion in the study. Patients were eligible if they were at least 15 years old and weighed at least 45 kg.

### Study design

EPS and RFCA procedures were performed according to established practices. All RFCA procedures were performed in the temperature-controlled mode to keep the patients in a lower coagulability

state (60°C) [11]. The percutaneous Seldinger technique was used to access the lower extremity.

Then, two or three sheaths (6 to 7 F) were inserted into one or both femoral veins through a single venous puncture or using separate cannulation according to the study protocol. The number of indwelling sheaths or catheters was determined by the operator, based on the clinical requirements. Heparin was administered with a loading dose of 5,000 U to one group but was not given to the control group. The activated clotting time (ACT) was monitored to assess the level of anticoagulation achieved. After the procedure, all sheaths were removed in the electrophysiology laboratory. All patients rested in bed for six hours.

For all patients, a data sheet was filled in by the operator. This data sheet included the number of catheters used on the right (and left, if present), the number of needle insertions in both sides, the presence of *in situ* thrombosis during catheter removal as a strand of thrombus connected to the tip of the catheter, and the duration of the procedure. *In situ* thrombosis was detected and documented by the first procedure operator.

### Duplex ultrasonography evaluation

Duplex ultrasonography evaluation of the bilateral or unilateral lower leg veins, including the proximal femoral vein, was done to evaluate the venous flow pattern, thrombus formation, hematoma, thrombophlebitis, and DVT 24 hours after the procedure. Duplex ultrasound images were taken in the supine position with a 10 MHz linear probe. Duplex criteria for complete venous thrombosis with occlusion were defined as the absence of flow and an incompressible venous segment. A patent femoral vein was defined as a completely compressible vein with spontaneous phasic flow. The operator was unaware of which group a patient belonged to. All patients were asked about pain at the catheter site, dyspnea, pleuritic chest pain, and were examined for evidence of hematoma at the catheterization site.

### Statistical methods

Continuous variables were presented as the mean  $\pm$  standard deviation and were compared using paired and unpaired Student's *t* test where appropriate. Differences in mean values between groups were assessed using the Student *t* test. Categorical data were compared using Fisher's exact test. Statistical analysis was subsequently carried out with univariate and multivariate analysis using logistic regression analysis. All above analyses were considered significant at  $p < 0.05$  (two tailed). We

**Table 1.** Patients' clinical characteristics.

	Frequency	Percentage
Diabetes mellitus	19	9.5
Cigarette smoking	16	8.0
Obesity	19	9.5
DVT risk factors (N)		
0	153	
1	44	22.0
2	3	1.5
Total	200	100.0
Hemoglobin [mg/dL]		
≥ 12	122	61.0
≤ 10 but < 12	66	33.0
Total	200	100.0
LV systolic function		
Normal	170	85.0
Mildly reduced	6	3.0
Moderately reduced	14	7.0
Severely reduced	10	5.0
Total	200	100.0

DVT — deep vein thrombosis; LV — left ventricle

used SPSS 15.0 (SPSS Inc., Chicago, USA) for data storage and analysis.

## Results

### Patient characteristics and periprocedural outcomes

In the 200 patients enrolled, there were 333 femoral veins approaches (200 right femoral vein approaches and 133 left femoral vein approaches). All veins contained two or more catheters that were inserted either through a single or multiple separate venous punctures.

Of the 200 patients, 111 were women, 89 were men; background heart disease of the patients included cardiomyopathy in 22, coronary heart disease in 19, and valvular heart disease in seven; 151 patients had no underlying heart disease (Table 1).

*In situ* thrombosis was detected and documented by the first procedure operator. The rate of *in situ* thrombosis was not different in smokers vs non-smokers ( $p = \text{NS}$ ), in patients with obesity ( $p = 0.7$ ), and in whom the hemoglobin was less than 12 ( $p = 0.55$ ). There was a trend of more *in situ* thrombosis in patients with severe left ventricular systolic dysfunction ( $\text{EF} < 20\%$ ,  $p = 0.23$ ) and in diabetics vs non-diabetics patients ( $26.3\%$  vs  $18.9\%$ ,  $p = 0.5$ ). Aspirin administration before the procedure had no effect on the rate of thrombosis ( $p = \text{NS}$ ).

We found a significant difference between the rate of thrombosis in patients in whom the sheaths were inserted through a single venous puncture and those in whom the sheaths were inserted through multiple venous punctures (Table 2).

A significant decrease in the rate of *in situ* thrombosis was observed in patients who received heparin during the procedure ( $28\%$  vs  $11\%$ ,  $p = 0.04$ ). The study also showed that the type of venous cannulation significantly affected the *in situ* thrombosis rate independently of the heparinization protocol. The rate of *in situ* thrombosis was higher in the single venous puncture group, regardless of the heparinization protocol ( $16\%$  vs  $6\%$ ,  $p = 0.1$  in the group on heparin and  $38\%$  vs  $18\%$ ,  $p = 0.04$  in the other group). In the single venous puncture group ( $n = 100$ ), heparinization significantly decreased the rate of *in situ* thrombosis ( $16\%$  vs  $38\%$ ,  $p = 0.023$ ) compared to that of the other study group ( $6\%$  vs  $18\%$ ,  $p = 0.12$ ; Table 3). Advanced age had no effect on the rate of *in situ* thrombosis. Surprisingly, there was a significantly higher rate of thrombosis among women than men ( $26\%$  vs  $11\%$ ,  $p = 0.01$ ), regardless of the heparinization protocol or the type of cannulation.

There was an insignificant increase in the rate of *in situ* thrombosis with an increasing number of DVT risk factors (0RF:  $18\%$ , 1RF:  $22\%$ , 2RF:  $33\%$ ,  $p = 0.6$ ). The number of catheters had no effect on thrombosis, independent of the cannulation type ( $p = 0.29$ ), and the same result was found for the number of needle insertions ( $p = 0.28$ ). The duration of the procedure was significantly longer in patients with *in situ* thrombosis (mean  $96 \pm 110$  min,  $p = 0.019$ ) independent of the type of cannulation ( $p = 0.7$ ), the heparinization protocol ( $p = 0.7$ ), or gender ( $p = 0.14$ ).

**Ultrasound results after 24 hours.** There was one case of superficial thrombophlebitis, four cases of hematoma, and no DVT. There was an insignificant increase in the hematoma rate for the single puncture approach relative to separate cannulation ( $3\%$  vs  $1\%$ ,  $p = 0.3$ ). The rate of hematoma was similar in the heparin group and the control group.

## Discussion

### Main findings

This study demonstrated a clear difference between various methods of cannulation in the femoral area. There were several main findings from this study. Firstly, DVT is a very rare complication and independent of the type of cannulation or heparin injection. Therefore, heparinization was not necessary to reduce DVT after right-sided procedures.

**Table 2.** The rate of thrombosis considering the probable risk factors.

		<i>In situ</i> thrombosis				P
		YES number	Percentage	NO number	Percentage	
Hemoglobin	≥ 12	21	17.2%	101	82.8%	0.5
	10–12	15	23.1%	50	76.9%	
	< 10	3	25%	9	75%	
Left ventricular function	Normal	35	20.7%	134	79.3%	0.2
	Mild	1	16.7%	5	83.3%	
	Moderate	0	0	14	100%	
	Severe	3	30%	7	70%	
Diabetes mellitus	No	34	18.9%	146	81.1%	0.5
	Yes	5	26.3%	14	73.7%	
Smoking	No	36	19.7%	147	80.3%	1
	Yes	3	18.8%	13	81.3%	
Acetylsalicylic acid	No	27	19.7%	110	80.3%	1
	Yes	12	19.4%	50	80.6%	
Deep vein thrombosis risk factor (N)	0	28	18.4%	124	81.6%	0.6
	1	10	22.7%	34	77.3%	
	2	1	33.3%	2	66.7%	
Obesity	No	35	19.4%	145	80.6%	0.7
	Yes	4	21.1%	15	78.9%	
		<b>Mean</b>		<b>Mean</b>		
Number of needle insertions		2.94		3.76		0.28
Number of catheters		2.3		2.4		0.29
Age		42.5		47.3		0.12

**Table 3.** The rate of thrombosis according to type of cannulation/heparin protocol/sex.

		<i>In situ</i> thrombosis				P
		YES number	Percentage	NO number	Percentage	
Sex	Male*	10	11.4%	78	88.6%	0.011
	Female	29	26.1%	82	73.9%	
Heparin protocol	Was done	49	55.1%	51	45.9%	0.25
	Not done	40	44.9%	60	54.1%	
Type of cannulation	One-line	45	50.6%	55	49.5%	1
	Separate	44	49.4%	56	50.6%	

\*One male patient had missing data for *in situ* thrombosis

Secondly, *in situ* thrombosis depends on the cannulation type and heparinization during a procedure.

Thrombus formation in iliofemoral veins, and local complications such as hematoma formation and long-lasting pain in the femoral area, are well-known complications after EPS procedures. Risk factors for these complications and prophylactic modalities are less defined. Chen et al. [10] reported the results of multiple sheath placements related to DVT and the complications encountered when using duplex ultra-

sonography. They observed a significant incidence (17.6%) of non-occlusive DVT after multiple sheath placements for EPS or RFCA therapy. Nonetheless, most thrombi regressed after one week of follow-up. Furthermore, there was no significant difference in the incidence of major complications when multiple sheaths placement was compared to single sheath placement. In their study, all of the venous thrombi were non-occlusive and asymptomatic. None of the femoral veins developed occlusive DVT.

### Correlation between different types of cannulation and local venous complication

We compared the incidence of complications between patients with two different types of cannulation. The rate of *in situ* thrombosis was significantly higher in the single venous puncture group vs the separate cannulation group (27% vs 12%,  $p = 0.012$ ). This was independent of the heparinization protocol, the duration of the procedure, or gender. This can be explained by the presence of more local pressure and stasis in the one-line cannulation group. We used ultrasound to analyze the catheterization site 24 hours after the procedure to look for superficial thrombophlebitis, hematoma, and DVT. There was no significant difference between the two groups. The rarity of DVT in the absence of a history of previous thromboemboli shows that venous catheters are safe, even in those with long procedures.

### Relationship between the *in situ* thrombosis and heparinization

Heparinization with a 5,000-U loading dose followed by ACT monitoring was associated with a significantly lower rate of *in situ* thrombosis independent of other determinants, without increasing the rate of other complications (such as hematoma formation).

This effect was more prominent and significant in the one-line cannulation group.

These results suggest that heparinization may be useful in reducing this minor complication in all RFCA or EPS procedures, but the clinical and paraclinical benefits were more promising in patients undergoing one-line cannulation.

In women, or during procedures that last a long time (mean 110 min), heparinization may be useful.

Other conventional or possible risk factors for hypercoagulability such as underlying heart disease, left ventricular systolic function, anemia (hemoglobin < 12), smoking, obesity, the number of DVT risk factors, the number of catheters required, and diabetes were not significantly correlated with the incidence of *in situ* thrombosis.

**Ultrasound results after 24 hours.** We attempted to assess venous insufficiency and thrombophlebitis as predictors of DVT and hypercoagulability, but in this study, the incidences of these factors were insignificant. This can be explained by the exclusion of very high risk patients.

### Limitations of the study

The data presented was collected in a single-center feasibility study. The results may be limit-

ed by the relatively small sample size. A much larger prospective randomized study is warranted. High risk patients for thromboemboli were excluded from the study.

### Clinical implications

Given the local venous complications and DVT after EPS procedures, heparinization was not necessary for right-sided EPS procedures. *In situ* thrombosis is a minor complication that can be reduced by heparinization in patients undergoing one-line cannulation.

**Conflict of interest:** none declared

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