#### The Need for Anticoagulation Therapy during the Transseptal Approach of Left Sided Accessory Pathway Ablation and at What Stage of Procedure Anticoagulants Should Be Administered

Ayman Abd El-Aziz Fattoh, Moamed Bader, Mohamed Nab

Cardiology Department, National Heart Institute, Giza, Egypt Ama fattoh@hotmail.com

Abstract: Radiofrequency ablation (RFA) is currently the treatment of choice for most patients with accessory pathway-mediated tachycardia. Left accessory pathways (AP) are the most commonly found in clinical practice and account for 40%-70% of all AP cases referred for catheter ablation. Because of the inherent risks of the approach of the heart's left chambers special technical skills are required for their [of the APs] mapping and ablation. Two major methods have been described for the approach of APs in the mitral ring: the retrograde arterial approach (RAA) which involves a peripheral arterial access, with the manipulation of the catheter in the left ventricle to map the atrioventricular ring (in this approach the atrial connection may also be mapped using retrograde catheterization of the LA) and the transeptal approach (TSA) which consists in trespassing the interatrial septum with a special catheter introducer and place the ablation catheter directly in the LA to map preferably the atrial insertion of these APs **Objective:** The aim of this study is to detect the need for anticoagulation therapy during the transseptal left sided Accessory Pathway (AP) ablation, and to determine at which stage of RF procedure antithrombotic drugs should be administered. The biochemical markers used in this study is direct measures of fibrinolysis (d-dimer, DD). Patients and Methods: This study is a clinical trial that was conducted in EP laboratory of National Heart Institute. This study included twenty patients referred for EP laboratory to do radiofrequecy transcatheter ablation in the left side of heart (twenty patients with left accessory pathway). All patients included in the study were subjected to full history taking, thorough clinical examination to determine baseline heart rate and blood pressure, resting 12-lead electrocardiogram, transthoracic echocardiography, CBC, PT, PTT, Routine laboratory investigations including fasting blood sugar, lipid profile, liver and kidney function tests. From each patient undergoing RF ablation, four blood samples were taken for D-dimer measurement. Initially, blood sample is obtained immediately after insertion of the venous sheaths and before introduction of the electrode catheters (baseline measurements). Subsequently, blood sample is taken on completion of EPS and mapping, just before application of the first RF ablation (post-EPS measurements). The third sample is taken after completion of the RF procedure (post-RF measurements) and before sheath removal. At 36 to 40 hours later and before discharge from the hospital, a fourth blood sample was obtained. Exclusion criteria: Patients with history of recent undergoing electrophysiological study (EPS), Patient with malignant disease, Patient with history of embolic events, recent surgery or trauma, Patients with a history of atrial fibrillation, Patients with an active thrombotic process, renal failure, cerebrovascular stroke or previously identified coagulopathy or thrombocytopenia. Results: The D-dimer level in all the studied patients increased significantly (P < 0.001) from 406.5 ± 254.1 at baseline to 934.8  $\pm$  656.5 after EPS and rose higher to 2406.5  $\pm$  1765.3 after ablation and in spite of that it decrease to 1900.4  $\pm$  1514.3 before discharge but it is still significantly higher than that of the baseline level (P < 0.001). Conclusion: The present study shows there is significant thrombogenic activity during RF catheter ablation of left accessory pathway cases, as it is evidenced by the D-dimer elevation in patients undergoing these procedures. Regarding our results, it is essential to give anticoagulation for all cases of AP during RF catheter ablation. Early heparin administration is a favorable protocol; since it seems evident that in all patients there is an incremental rise in the level of the D-dimer level after a guide wire is inserted, reaching its peak after ablation. Furthermore, it is prefereable to consider a post procedure continuation of administration of heparin, as there is persistent elevation of D-dimer level 48 hours after the procedure. Administration of anticoagulation therapy after ablation may be of possible advantage to protect patients against the risk of thromboembolic events. However, Continued and systematic evaluation of procedural anticoagulation protocols in larger and randomized studies is necessary in order to enrich the evidence platform of the ablative management of cardiac arrhythmias.

[Ayman Abd El-Aziz Fattoh, Moamed Bader, Mohamed Nab. **The Need for Anticoagulation Therapy during the Transseptal Approach of Left Sided Accessory Pathway Ablation and at What Stage of Procedure Anticoagulants Should Be Administered.** *Rep Opinion* 2017;9(7):44-53]. ISSN 1553-9873 (print); ISSN 2375-7205 (online). <u>http://www.sciencepub.net/report.</u> 8. doi:10.7537/marsroj090717.08.

Keywords: Need; Anticoagulation; Therapy; Transseptal; Approach; Ablation; Stage; Procedure; Anticoagulant

#### 1. Introduction:

Radiofrequency ablation (RFA) is currently the treatment of choice for most patients with accessory pathway-mediated tachycardia. Left accessory pathways are the most commonly found in clinical practice and account for 40%-70% of all AP cases referred for catheter ablation (1-4). Because of the inherent risks of the approach of the heart's left chambers special technical skills are required for their [of the APs] mapping and ablation.

Two major methods have been described for the approach of APs in the mitral ring: the retrograde arterial approach (RAA) which involves a peripheral arterial access, with the manipulation of the catheter in the left ventricle to map the atrioventricular ring (in this approach the atrial connection may also be mapped using retrograde catheterization of the LA) and the transeptal approach (TSA) which consists in trespassing the interatrial septum with a special catheter introducer and place the ablation catheter directly in the LA to map preferably the atrial insertion of these APs.

The RA approach is the most widely used in most laboratories. However, with the advancements in ablation procedures for atrial arrhythmias, markedly for atrial fibrillation, the transseptal puncture has been incorporated to the routine of electrophysiologists. Retrospective studies have compared these two techniques and reported controversial results, usually related to the experience of each group (5-13).



**Figure 1.** Septal anatomy with typical variations. (A) Schematic illustration of a bicaval TEE view. Middle inset: Septum primum (black) and septum secundum (red) show complete adhesion. Left inset: Adhesion of the 2 septa only in the cranial part, creating an RSP. Right inset: Missing adhesion between the 2 septa, resulting in a PFO. Note the muscular double layer of the septum secundum with epicardial fat in between (for details see text). (B) Bicaval TEE view depicting an RSP. LA = left atrium; PFO = patent foramen ovale; RA = right atrium; RSP = right-sided pouch; SVC = superior vena cava. For a high quality, full color version of this figure, please see Journal of Cardiovascular Electrophysiology's website: www.wileyonlinelibrary.com/journal/jce

The safety of ablation procedures has improved in the last several years through a better understanding of the procedural risks and advancements in technique and technology (14). However, thrombus formation and embolism during and shortly after the procedure remains a major concern with catheter ablation of the left-sided cardiac chambers. This can be manifested as symptomatic or asymptomatic cerebral embolism (15). In a large inpatient sample in the United States undergoing catheter ablation for AF, the overall incidence of stroke or transient ischemic attack was 1.02% (16).

The incidence of thromboembolic complications of RF-A is between 0.6% to 1.3%. Thrombogenesis provoked by RF-A has been considered to be caused by hemostasis from the placement of the intravascular catheters, and that it disappears immediately after removal of the catheters and introducer sheaths. However, the thrombogenesis has 2 phases: an acute phase during the procedure, and a delayed phase that peaked at 3 days after the procedure. The delayed phase of thrombogenesis is provoked by endothelial damage caused by application of the RF current (17).

## Aim of the Work:

The aim of this study is to detect the need for anticoagulation therapy during the transseptal left sided Accessory Pathway (AP) ablation, and to determine at which stage of RF procedure antithrombotic drugs should be administered. This is done through indirect assessment of thrombogenic effect of radiofrequency catheter ablation RF ablation by using a biochemical marker of thrombogenicity (d-dimer, DD), which is the direct measure of fibrinolysis.

#### 2. Patients and Methods

This study is a clinical trial that was conducted in EP laboratory of National Heart Institute.

This study included twenty patients referred for EP laboratory to do radiofrequncy transcatheter ablation in the left side of heart (twenty patients with left accessory pathway).

#### **Exclusion criteria:**

- Patients with history of recent undergoing electrophysiological study (EPS).

- Patient with malignant disease.

- Patient with history of embolic events, recent surgery or trauma.

- Patients with a history of atrial fibrillation.

- Patients with history of renal failure, cerebrovascular stroke or previously identified coagulopathy or thrombocytopenia.

All patients included in the study were subjected to the following:

1. Full history taking.

2. Thorough clinical examination to determine baseline heart rate and blood pressure.

- 3. Resting 12-lead electrocardiogram.
- 4. Transthoracic echocardiography.
- 5. CBC, PT, PTT.

6. Routine laboratory investigations including fasting blood sugar, lipid profile, liver and kidney function tests.

No medications affecting the function of the platelets was administered in any of the study subjects. Any antiarrhythmic drugs were withdrawn prior to study.

From each patient undergoing RF ablation, four blood samples were taken for D-dimer measurement. Initially, blood sample is obtained immediately after insertion of the venous sheaths and before introduction of the electrode catheters (baseline measurements). Subsequently, blood sample is taken on completion of EPS and mapping, just before application of the first RF ablation (post-EPSmeasurements). The third sample is taken after completion of the RF procedure (post-RF measurements) and before sheath removal. At 36 to 40 hours later and before discharge from the hospital, a fourth blood sample was obtained.

### **EP laboratory procedure:**

• Central venous access was obtained at the femoral vein and the internal jugular vein if necessary.

• Indwelling 7 Fr or 8 Fr vascular catheter were employed, through which 7 Fr electrode catheters were positioned in the right ventricular apex, His position, high right atrium and coronary sinus as deemed clinically necessary.

• Procedures involving catheter manipulation and ablation in the left atrium and ventricle were performed by transseptal approach.

• Patients received an unfractionated heparin bolus of 1000 units typically after entry into the systemic cardiac chambers.

• Stimulation protocols varied depending on the primary electrophysiological diagnosis.

• Upon completion of the diagnostic portion of the procedure, all patients underwent standard temperature-guided radiofrequency ablation with a quadripolar ablation catheter.

• Radiofrequency energy was delivered via a standard commercial cardiac radiofrequency lesion generator (EP Technologies, Menlo Park, CA, U.S.A.) to a maximum power of about 50 W to maintain a tissue temperature between 50 - 75 °C.

• Serial blood samples were drawn at four time points:

• Pre-procedure.

• Upon completion of the diagnostic portion of the study but before any radiofrequency energy application.

• A the end of the procedure (approximately 15 min after the last radiofrequency application).

• 36-48 h post-procedure.

• Procedure duration was defined as the time from initial vascular access to the time of completion of the entire procedure and collection of blood sample.

• Blood samples 1 and 4 were drawn without a tourniquet and with minimal vessel trauma. Samples 2, 3 were drawn through the femoral venous sheath. The first 5 ml of blood was discarded from all samples. Blood samples were immediately centrifuged to separate plasma from whole blood and were stored until assays were conducted.

#### **D-Dimer quantitation:**

D-dimer quantitation was performed by a commercial ELISA technique (Asserachrom\_D-Di, Diagnostica Stago, Asnieres-Sur-Seine, France) with a normal value of less than 400 ng / ml and a lower limit of detection of 5 ng/ml.

## Statistical analysis:

• Statistical analysis were performed using SPSS version 10.05 software.

• Descriptive analysis are expressed as mean and standard deviation and percentage.

• To determine differences in D-deimer at the different stages of the procedure was done using paired student's t-test.

• P values < 0.05 were considered statistically significant.

#### 3. Results

This study included twenty patients referred to the EP laboratory of National Heart Institute. The twenty patients were referred for radiofrequency transcatheter ablation for left lateral accessory pathway in the left side of the heart via transeptal approach. They were 12 males (55%) and 8 females (45%). Their mean age was  $36.7 \pm 8.5$  years.

There was no significant difference regarding their sex distribution, mean age, pulse, systolic and diastolic blood pressure as well as associated co-morbid conditions as hypertension, diabetes, rheumatic heart disease and ischemic heart disease (P > 0.05). (table 1).

Table (1): Baseline general characteristics of the two groups

Variable	Left side AP cases	P value
Mean $\pm$ S.D. or <i>n</i> (%)	N = 20	
Age (years)	$39.5 \pm 9.4$	> 0.05
Male/female	12/8	> 0.05
Hypertension	7 (35%)	> 0.05
Hyperlipidemia	5 (20%)	> 0.05
Diabetes	4 (20%)	> 0.05
Current smoker	9 (45%)	> 0.05
RHD	6 (30%)	> 0.05
IHD	1 (5%)	> 0.05
Pulse (B/min.)	$85 \pm 10.4$	> 0.05
SBP (mm Hg)	$120 \pm 5$	> 0.05
DBP (mm Hg)	$80 \pm 7.5$	> 0.05

Results of the current study regarding the different laboratory investigations showed that there was no significant difference regarding the fasting blood sugar, lipid profile, kidney and liver function tests (P > 0.05) (table 2).

Table (2): Results of laboratory investigations among the cases

	Left side Mean ± SD	P value
Fasting blood sugar (mg/dl)	$105 \pm 8.6$	> 0.05
Total cholesterol (mg/dl)	$189.7 \pm 37.5$	> 0.05
HDL (mg/dl)	$39.2 \pm 6.3$	> 0.05
LDL (mg/dl)	$109.7\pm44.3$	> 0.05
TG (mg/dl)	$106.9 \pm 21.9$	> 0.05
Uric acid (mg/dl)	$4.7 \pm 2.0$	> 0.05
GPT (Unit)	$31.3 \pm 10.8$	> 0.05
GOT (Unit)	$29.4 \pm 7.7$	> 0.05
Urea (mg/dl)	$36.4 \pm 10.2$	> 0.05
Creatinine (mg/dl)	$0.98\pm0.016$	> 0.05
APTT	$30.9 \pm 3.7$	> 0.05
РТ	$10.3 \pm 0.7$	> 0.05

Results of the current study regarding the different echocardiographic parameters showed that there was no significant difference (P > 0.05) (table 3).

Table (3): Echocardiographic study results

Echocardiographic finding		Left side Mean ± SD	P Value
Systoli	c indexes		
-	EDD (cm)	$4.7\pm0.6$	> 0.05
-	ESD (cm)	$2.9\pm0.4$	> 0.05
-	EF (%)	$63.9 \pm 6.3$	> 0.05
-	FS (%)	$33.0 \pm 3.1$	> 0.05
-	LA	$3.4 \pm 3.1$	> 0.05
-	Ao	$3.1 \pm 0.9$	> 0.05
-	RV	$1.6 \pm 0.4$	> 0.05

Results of the current study regarding the characteristics of radiofrequency ablation procedure accessory pathway (left sided) showed it was  $73.4 \pm 36.5$  minutes for patients with AP and this difference was not significant (P > 0.05). The RF delivery duration was it was  $7.5 \pm 8.6$  seconds for patients with AP, the mean ablation temprature was  $65.7 \pm 5.6$  seconds for the patients with AP. There was significant difference regarding the different characteristics of RF ablation procedure (P < 0.05) (table 4).

Table (4): Characteristics of radiofrequency ablation of accessory pathway (left sided)

Daramatar	Left side	Р	
raianicici	$Mean \pm SD$	Value	
EPS duration (min.)	$73.4 \pm 36.5$	> 0.05	
RF delivery duration (seconds)	$17\overline{5.5 \pm}$	< 0.05	
Ki derivery duration (seconds)	75.7	< 0.05	
Total procedure time (min)	110.5 ±	< 0.05	
rotar procedure time (initi.)	31.2	< 0.05	
Number of RF application	$7.5 \pm 8.6$	< 0.05	
Tissue temperature during	657+56	< 0.05	
ablation	$03.7 \pm 3.0$	< 0.03	
EDC. El. duralter interiore de la			

EPS: Electrophysiologic study

RF: radiofrequency ablation.

The D-dimer level in all the studied patients increased significantly (P < 0.001) from 406.5  $\pm$  254.1 at baseline to 934.8  $\pm$  656.5 after EPS and rose higher to 2406.5  $\pm$  1765.3 after ablation and in spite of that it decrease to 1900.4  $\pm$  1514.3 before discharge it is still significantly higher than that of the baseline level (P < 0.001) (table 5 and figure 2).



Fig. (7): Characteristics of radiofrequency ablation procedure between AVNRT (right sided) and accessory pathway (left sided)



Fig. (8): D-dimer level of all patients at the different stages of the procedure

stuges of the procedure		
	D-dimer level	
Stage	N = 40 patients	
	Mean $\pm$ SD	
Baseline	$406.5 \pm 254.1$	
After EPS	934.8 ± 656.5*	
After ablation	2406.5 ± 1765.3*	
Before discharge	$1900.4 \pm 1514.3^*$	

Table (5): D-dimer level in all patients at the different stages of the procedure

\* P < 0.001 (highly significant difference) in relation to the baseline D-dimer value.

#### 4. Discussion

Ablationists rightfully try to avoid any RF ablation procedure-related complication. However, stroke as a periprocedural complication evokes particular dread because the event and its sequelae are so devastating, and we lack a clear understanding of how to prevent it (18, 20). While advances in remote/ robotic catheter navigation along with better online imaging techniques, experience with safe catheter manipulation, and knowledge and ability to recognize appropriate RF ablation targets may decrease other complications, they do not necessarily affect the risk of thrombus formation. The pathogenesis of thrombus and subsequent embolization during left atrial ablation is multifactorial (21). During transseptal puncture, the endothelial denudation that occurs may be thrombogenic. Simply placing sheaths or catheters in the circulation may be sufficient to give rise to soft thrombus. Most importantly, however, during RF energy delivery, the associated local temperature rise can result in coagulum formation that in turn can be a nidus for propagating soft thrombus (19, 22). Periprocedural heparinization has been the mainstay for interventionalists to decrease this complication. We review approaches that involve increased intensity, duration, or location for heparinization and describe the limitations of this pharmacological agent in influencing the occurrence of coagulum during ablation. These limitations are responsible for the unfortunate statistic that despite adequate heparinization, about 2% of complex left-sided ablation procedures continue to be associated with thromboembolism (23, 24). Bleeding and vascular complications during AF ablation can occur with the multiple catheters and sheaths frequently required for complex procedures. Access site bleeding and various vascular complications including pseudoaneurysm formation and retroperitoneal bleeding are more common with these procedures. Further, cardiac perforation is a potentially fatal occurrence and occurs in about 2.4% of patients undergoing left sided ablation (25). While pericardiocentesis and possible placement of indwelling drains or open-chest surgical closure of the perforation may prevent catastrophe, these bleeding risks significantly impact outcomes (25). While

anticoagulation at least in part mitigates against major thromboembolism, there is an inherent increase in the risk for bleeding and vascular complications. Each approach to minimize thromboembolic risk must be evaluated not only in terms of its own efficacy but also against the extent of the propensity to increase bleeding.

In cases of ablation of left-sided accessory pathways and focal left atrial tachycardia, it is essentially mentioned that Accessory pathways (APs) are located on the left side in more than 50% of cases and their ablation carries a higher acute success and a lower recurrence rate than septal or right-sided accessory pathways (26). Over the past years, the preferred access route for ablation changed from the retrograde aortic access, targeting the ventricular insertion site of the AP, to the antegrade transseptal approach targeting the atrial insertion of the AP. In elderly patients, the antegrade approach also avoids the crossing of potentially calcified aortic valves and the associated embolic risk. Historical rates of cardiac tamponade range from 0.13 to 1.1% and cerebrovascular accidents from 0.15 to 0.49% (27,28). The access route is the same utilized for ablation of AF and left sided atrial tachycardia (AT). Although there are only limited data concerning the real thromboembolic risk with contemporary ablation equipment, it can be assumed that the actual risk is lower than the rates reported from the 1990s and in the AF/AT population. Patients undergoing AP ablation are also younger and have usually no or few risk factors for thrombembolic events. Furthermore, there is only a single catheter with or without one long sheath in the left atrium or the left ventricle, and the ablation is usually focal resulting in much shorter total ablation times and time spent in the left atrium.

Since there is no scientific evidence supporting peri-interventional anticoagulation of AP cases, the potential risks of bleeding have to be taken into account. Some centers may consider prior anticoagulant therapy is not warranted. After arterial access, 5000–15 000 units (or 90–200 U/kg) of intravenous sodium heparin is recommended followed by 1000 U/h during the procedure (29). Long sheaths should be continuously flushed to avoid thrombus formation. There is no evidence, supporting the post-interventional use of oral anticoagulation or aspirin.

This study aimed at confirming the indication of anticoagulant therapy during transseptal left accessory pathway ablation. It is done by assessing the biochemical marker of thrombogenicity. The biochemical markers used in this study is direct measures of fibrinolysis (d-dimer, DD). Twenty patients referred to the EP laboratory of National Heart Institute were included in the study.

The included twenty patients referred for radiofrequency transcatheter ablation for accessory

pathway in the left side of the heart. They were 12 males (55%) and 8 females (45%). Their mean age was  $36.7 \pm 8.5$  years.

Our results showed that there was no significant difference regarding the fasting blood sugar, lipid profile, kidney and liver function tests (P > 0.05). Also, there was no significant difference regarding the different echocardiographic parameters (P > 0.05). These results rejected the possibility of any difference in D-Dimer in any of the studied groups due to systemic or cardiac disease.

Results of the current study regarding the characteristics of radiofrequency ablation procedure accessory pathway (left sided) showed that in patients with AP patients, the EPS duration was  $73.4 \pm 36.5$  minutes. and this difference was not significant (P > 0.05). The RF delivery duration was  $175.5 \pm 75.7$  seconds, the Pulse count was  $7.5 \pm 8.6$  for the patients with AP and the mean ablation temprature was  $65.7 \pm 5.6$  seconds.

The D-dimer level in all the studied patients increased significantly (P < 0.001) from 406.5  $\pm$  254.1 at baseline to 934.8  $\pm$  656.5 after electrophysiology study EPS and rose to substantially higher level to 2406.5  $\pm$  1765.3. After ablation and despite reasonable drop of D-dimer level to 1900.4  $\pm$  1514.3 before discharge it is still significantly higher than that of the baseline level (P < 0.001).

D-dimer assay is recognized as highly sensitive (> 90%) with high negative predictive value, making it very useful clinical tool for detecting vascular thrombosis (30). Although the elevation in D-dimer may be resulted from the peripheral effects induced by sheath insertion and catheter manipulation (31), the marked elevation of D-dimer in this study mainly resulted from the central effects of RF ablation application, which is caused mainly by endomyocardial injury and higher temperature.

# Is there a need for anticoagulation in cases of left sided RF catheter ablation?:

According to our study, there is a marked and statistically significant rise of D-dimer level by the end of procedure and sustained high even before discharge. This means significant development of thrombogenic activity during RF catheter ablation.

Our results are integrated with Micheucci's study (32) which evaluated several parameters of the hemostatic system in relation to the electrophysiologic procedure. They found that at the end of the procedure, spontaneous platelet aggregation in whole blood, prothrombin fragment 1+2, thrombin-antithrombin complex, and D-dimer levels increased significantly in all patients. The hemostatic changes were more marked after RFA thon after electrophysiology. Spontaneous aggregation in whole blood, prothrombin fragment 1+2 and thrombin-antithrombin complex levels at 24 hours

after the procedure were similar to those observed before the procedure in both groups; D-dimer levels were still elevated with respect to preprocedure levels, with a trend toward higher levels in patients undergoing RFA rather than electrophysiology. A significantly more marked activation of coagulation (prothrombin fragment 1+2, P <.005) was found in patients in whom the mean duration of energy application was higher than 23.5 seconds. They suggested that antithrombotic prevention with a prolonged administration of heparin and/or the association of antiplatelet agents should be considered in patients undergoing RFA.

Therefor now, Anticoagulation with UFH represents one of the cornerstone strategies to reduce thromboembolic complications during left-sided ablation procedures (33). The use of effective anticoagulation is out of question during left atrial

ablation procedures in order to minimize the risk of thrombus formation and embolism (34).

Now, thrombogenicity of RF ablation can be detected by using intracardiac echocardiography (ICE). A Linear phased-array intracardiac ultrasound imaging has been extensively used during AF ablation procedure (35-41) (Figure 1). Although not directly a measure to prevent thromboembolism or bleeding, this imaging modality strongly impacts various other techniques that aim to minimize complications. ICE (Acuson, Siemens Medical Solutions, Malvern, PA) visualization is performed from the right atrium with an 8-10 Fr probe placed via the femoral veins. Imaging of the left atrium and pulmonary veins during ablation is used to recognize thrombus formation and possibly allow extraction of the thrombus when it occurs (39).



**Figure 2:** Intracardiac ultrasound using a linear phased-array probe placed in the right atrium visualizing the intraatrial septum and the left atrium. Note a strand-like structure consistent with thrombus noted in the left atrium despite adequate heparinization

## What is the best timing for anticoagulation during the whole RF catheter ablation procedure?

According to our results, it is preferably to adopt early heparinisation approach (after insertion of sheath and before transeptal puncture), this is because marked elevation of D-dimer level after insertion of femoral sheath. Some reports are supporting our conclusion, as intracardiac thrombus formation is frequent when heparin is administered after transseptal access and not associated with previously described risk factors for clinical and subclinical embolism. Early administration of heparin (i.e., before transseptal access) diminishes this risk but did not affect the rate of CVAs (42).

Another study supported early administration of heparin also in cases of AF ablation. Bruce and coworkers reported their findings in 508 patients who underwent AF ablation with ICE guidance (43). All patients received unfractionated heparin during the procedure, but the timing varied. In the first group of 31 patients, heparin was given immediately after vascular access was obtained and well prior to the first transseptal puncture. In the second group of 257 patients, heparinization was done after the first but before the second transseptal puncture. Finally, in the third group of 220 patients, heparinization was initiated only after the second transseptal puncture. ICE-detected thrombus was significantly lower in the group where the earliest heparinization occurred (0% group 1, 3.1% group 2, and 9% group 3 where anticoagulation was done only after the second transseptal puncture).

However, Because of the risk of cardiac perforation occurring specifically during transseptal puncture, heparin administration was routinely delayed until after the last (usually second) transseptal puncture was performed (44).

It is worth mention that there is noticeable elevation of the D-dimer immediately and 48 hours after the procedure indicated a potential subclinical thrombosis immediately after the RF ablation and a continuing risk that may persist up to 48 hours thereafter. It means it is essential to continue anticoagulation postprocedure. This why many reports suggest that Oral anticoagulation should be continued for at least 2 months after ablation, since there is evidence that the vast majority of thromboembolic events occurs in the first 4 weeks after ablation (45).

### Recommendation

The present study shows there is significant thrombogenic activity during RF catheter ablation of left accessory pathway cases, as it is evidenced by the D-dimer elevation in patients undergoing these procedures.

Regarding our results, it is essential to give anticoagulation for all cases of AP during RF catheter ablation. Early heparin administration is a favorable protocol; since it seems evident that in all patients there is, an incremental rise in the level of the D-dimer level after a guide wire is inserted, reaching its peak after ablation.

Furthermore, it is preferable to consider a post procedure continuation of administration of heparin, as there is persistent elevation of D-dimer level 48 hours after the procedure. Administration of anticoagulation therapy after ablation may be of possible advantage to protect patients against the risk of thromboembolic events.

However, Continued and systematic evaluation of procedural anticoagulation protocols in larger and

randomized studies is necessary in order to enrich the evidence platform of the ablative management of cardiac arrhythmias.

## References

- Jackman WM, Xunzhang W, Friday KJ, Roman CR, Moulton KP, Beckman KJ, et al. Catheter ablation of accessory atrioventricular pathways (Wolff-Parkinson-White syndrome) by radiofrequency current. N Eng J Med.1991; 324: 1605-11.
- 2. Lesh MD, Van Hare GF, Schamp DJ, Chien W, Lee MA, Griffin JC, et al. Curative percutaneous catheter ablation using radiofrequency energy for accessory pathways in all locations: results in 100 consecutive patients. J Am Coll Cardiol. 1992; 19: 1303-9.
- Calkins H, Langberg J, Sousa J, el-Atassi R, Leon A, Kou W, et al. Radiofrequency catheter ablation of accessory atrioventricular connections in 250 patients: abbreviated therapeutic approach to Wollf-Parkinson-White Syndrome. Circulation. 1992; 85: 1337-49.
- Calkins H, Kim Y-N, Schmaltz S, Sousa J, el –Atassi R, Leon A, et al. Eletrogram criteria for identification of appropriated target sites for radiofrequency catheter ablation of accessory atrioventricular connections. Circulation. 1992; 85: 565-73.
- Natale A, Wathen M, Yee R, Wolfe K, Klein G. Atrial and ventricular approaches for radiofrequency catheter ablation of left-sided accessory pathways. Am J Cardiol 1992; 70: 114-6.
- 6. Lesh MD, Van Hare GF, Scheinman MM, Ports TA, Epstein LA. Comparison of the retrograde and transseptal methods for ablation of left free wall accessory pathways. J Am Coll Cardiol. 1993; 22: 542-9.
- Swartz JF, Tracy CM, Fletcher RD. Radiofrequency endocardial catheter ablation of accessory atrioventricular pathway atrial insertion sites. Circulation. 1993; 87: 487-99.
- 8. Saul JP, Hulse E, De W, Weber AT, Rhodes LA, Lock JE, et al. Catheter ablation of accessory atrioventricular pathway in young patients: use of long vascular sheats, the transseptal approach and a retrograde left posterior parallel approach. J Am Coll Cardiol. 1993; 21: 571-83.
- 9. Manolis AS, Wang PJ, Mark Estes 3<sup>rd</sup> NA, Dhala AA, Blanck Z, Bajwa TK, et al. Radiofrequency ablation of left-sided accessory pathways: transaortic versus transseptal approach. Am Heart J. 1994; 128: 896-902.
- 10. Deshpande SS, Bremner S, Sra JS. Ablation of left free-wall accessory pathways using

radiofrequency energy at the atrial insertion site: Transseptal versus transaortic approach. J Cardiovasc Electrophysiol. 1994; 5: 219-31.

- 11. Sternick EB, Gerken LM, Barbosa MR. Ablação por cateter com radiofrequência em vias acessórias esquerdas: Abordagem transaórtica versus transseptal. Reblampa. 1997; 10: 177-85.
- 12. Vora AM, McMahon S, Jazayeri MR, Dhala AA. Ablation of atrial insertion sites of left-sided accessory pathways in children: efficacy and safety of transseptal versus transaortic approach. Pediatr Cardiol. 1997; 18: 332-8.
- 13. Law IH, Fischbach PS, Leroy S, Lloyd TR, Rocchini AP, Dick M. Access to left atrium for delivery of radiofrequency ablation in young patients: retrograde aortic vs transseptal approach. Pediatr Cardiol. 2001; 22: 204-9.
- 14. Siontis K.C., Oral H. Novel interventional strategies for the treatment of atrial fibrillation. Arrhythm. Electrophysiol Rev. 2016;5:50–56.
- 15. Gaita F., Caponi D., Pianelli M. Radiofrequency catheter ablation of atrial fibrillation: a cause of silent thromboembolism? Magnetic resonance imaging assessment of cerebral thromboembolism in patients undergoing ablation of atrial fibrillation. Circulation. 2010;122:1667–1673.
- Deshmukh A., Patel N.J., Pant S. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: analysis of 93 801 procedures. Circulation. 2013;128:2104–2112.
- Tetsuo S, Kenzo H, Kei Y, Mihoko Kawabata, Kauru O: Delayed thrombogenesis following radiofrequency catheter ablation. Circulation J 2002;66:671-676.
- 18. Asirvatham SJ, Friedman PA. Silent cerebral thromboembolism with left atrial ablation: A lurking danger. J Cardiovasc Electrophysiol 2006;17:8-10.
- Lim B, Venkatachalam KL, Jahangir A, Johnson SB, Asirvatham SJ. Concurrent application of charge using a novel circuit prevents heat-related coagulum formation during radiofrequency ablation. J Cardiovasc Electrophysiol 2008;19:843-850.
- Epstein MR, Knapp LD, Martindill M, Lulu JA, Triedman JK, Calkins H, Huang SK, Walsh EP, Saul JP. Embolic complications associated with radiofrequency catheter ablation. Atakr investigator group. Am J Cardiol 1996;77:655-658.
- 21. Demolin JM, Eick OJ, Munch K, Koullick E, Nakagawa H, Wittkampf FH. Soft thrombus formation in radiofrequency catheter ablation. Pacing Clin Electrophysiol 2002;25:1219-1222.

- 22. Haines D. Biophysics of ablation: Application to technology. J Cardiovasc Electrophysiol 2004;15:S2-S11.
- 23. Zhou L, Keane D, Reed G, Ruskin J. Thromboembolic complications of cardiac radiofrequency catheter ablation: A review of the reported incidence, pathogenesis and current research directions. J Cardiovasc Electrophysiol 1999;10:611-620.
- 24. Thakur RK, Klein GJ, Yee R, Zardini M. Embolic complications after radiofrequency catheter ablation. Am J Cardiol 1994;74:278-279.
- 25. Bunch TJ, Asirvatham SJ, Friedman PA, Monahan KH, Munger TM, Rea RF, Sinak LJ, Packer DL. Outcomes after cardiac perforation during radiofrequency ablation of the atrium. J Cardiovasc Electrophysiol 2005;16:1172-1179.
- 26. Calkins H, Yong P, Miller JM, Olshansky B, Carlson M, Saul JP et al. Catheter ablation of accessory pathways, atrioventricular nodal re-entrant tachycardia, and the atrioventricular junction: final results of a prospective, multicenter clinical trial. The Atakr Multicenter Investigators Group. Circulation 1999;99:262–70.
- 27. Scheinman MM, Huang S. The 1998 NASPE prospective catheter ablation registry. Pacing Clin Electrophysiol 2000;23:1020 –8.
- 28. Blomstrom-Lundqvist C. Scheinman MM. Aliot EM, Alpert JS, Calkins H, Camm AJ et al. Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular A. ACC/AHA/ESC guidelines for the management of supraventricular patients with arrhythmias—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Arrhythmias). Circulation 2003;108:1871 -909.
- 29. Blanc JJ, Almendral J, Brignole M, Fatemi M, Gjesdal K, Gonzalez-Torrecilla E et al. Consensus document on antithrombotic therapy in the setting of electrophysiological procedures. Europace 2008;10:513 –27.
- 30. Hains DE, Verow AF: Observations on electrode-tissue interface temperature and effect on electrical impedance during radiofrequency catheter ablation of ventricular myocardium. Circulation 1990;82:1034-1038.
- Le Groupe de Rythmologie de la Societe Francaise de Cardiologie. Complications of radiofrequency ablation: A French experience. Arch Mal Coeur Vaiss 1996; 89: 1599–605.

- 32. Michelucci A, Antonucci E, Conti AA, *et al.* Electrophysiologic procedures and activation of the hemostatic system. Am Heart J 1999; 138: 128–32.
- 33. Charles Dussault, Santiago Rivera, Mariano Badra-Verdu, *et al.* life experience with a new anticoagulation regimen for patients undergoing left-sided ablation procedures. Indian Pacing and Electrophysiology Journal 2016 Nov-Dec; 16(6): 181–184.
- 34. H. Calkins, J. Brugada, D. L. Packer et al., "HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation," Europace, vol. 9, no. 6, pp. 335–379, 2007.
- 35. Asirvatham SJ, Bruce CJ, Friedman PA. Advances in imaging for cardiac electrophysiology. Coron Artery Dis 2003;14:3-13.
- 36. Callans DJ, Wood MA. How to use intracardiac echocardiography for atrial fibrillation ablation procedures. Heart Rhythm 2007;4:242-245.
- 37. Corrado Klein AL, Santarone G, M. Echocardiography atrial fibrillation. in I Cardiovasc Med (Hagerstown) 2006;7:498-504. 26. Ren JF. Marchlinski FE. Utility of intracardiac echocardiography in left heart ablation for tachvarrhythmias. Echocardiography 2007:24:533-540.
- Ren JF, Marchlinski FE. Utility of intracardiac echocardiography in left heart ablation for tachyarrhythmias. Echocardiography 2007;24:533-540.
- Ren JF, Marchlinski FE, Callans DJ, Herrmann HC. Clinical use of acunav diagnostic ultrasound catheter imaging during left heart radiofrequency ablation and transcatheter closure procedures. J Am Soc Echocardiogr 2002;15:1301-1308.
- 40. Chu E, Kalman JM, Kwasman MA, Jue JC, Fitzgerald PJ, Epstein LM, Schiller NB, Yock PG,

7/18/2017

Lesh MD. Intracardiac echocardiography during radiofrequency catheter ablation of cardiac arrhythmias in humans. J Am Coll Cardiol 1994;24:1351-1357.

- 41. Chu E, Fitzpatrick AP, Chin MC, Sudhir K, Yock PG, Lesh MD. Radiofrequency catheter ablation guided by intracardiac echocardiography. Circulation 1994;89:1301-1305.
- 42. Stefan Asbach, Jurgen Biermann, Christoph Bode and Thomas S. Faber. Early Heparin Administration Reduces Risk for Left Atrial Thrombus Formation during Atrial Fibrillation Ablation Procedures. Cardiology Research and Practice Volume 2011 (2011), Article ID 615087, 5 pages.
- 43. Bruce CJ, Friedman PA, Narayan O, Munger TM, Hammill SC, Packer DL, Asirvatham SJ. Early heparinization decreases the incidence of left atrial thrombi detected by intracardiac echocardiography during radiofrequency ablation for atrial fibrillation. J Interv Card Electrophysiol 2008;22:211-219.
- 44. Di Biase L, Burkhardt JD, Santangeli P, Mohanty P, Sanchez JE, Horton R et al. Periprocedural stroke and bleeding complications in patients undergoing catheter ablation of atrial fibrillation with different anticoagulation management: results from the role of coumadin in preventing thromboembolism in atrial fibrillation (AF) undergoing patients catheter ablation (COMPARE) randomized trial. Circulation 2014;129:2638 - 44.
- 45. Karasoy D, Gislason GH, Hansen J, Johannessen A, Kober L, Hvidtfeldt M et al. Oral anticoagulation therapy after radiofrequency ablation of atrial fibrillation and the risk of thromboembolism and serious bleeding: long-term follow-up in nationwide cohort of Denmark. Eur Heart J 2015;36:307 –14a.