Detection of Thrombogenicity Induced by Radiofrequency Catheter Ablation

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Abstract: Background: The incidence of thromboembolic complications of Radiofrequency Catheter Ablation (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 potential mechanisms of thrombogenesis during ablation procedures are multiple and include endothelial disruption, coagulation necrosis, electrical injury, mechanical damage in the vessel wall, and heating of circulating blood elements by radiofrequency energy. The above mechanisms can cause activation of the cascade of events that ultimately results in thrombin generation and platelet activation. **Objective:** The aim of this study is to determine the independent and incremental procoagulant effect of RF ablation by assessing biochemical marker of thrombogenicity. The biochemical markers used in this study are direct measures of fibrinolysis (d-dimer, DD). **Methods:** This study is a comparative clinical trial that was conducted in EP laboratory of National Heart Institute. It has been started since 7/11/2006. To 1/09/2007 This study included forty patients are divided into twenty patients referred for EP laboratory to do radiofrequency transcatheter ablation in right side of the heart (twenty patients with AVNRT) and in the left side of heart(twenty patients with left accessory pathway). 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. **Results:** Comparison between the two groups regarding the D-dimer level at the different stages of the procedure showed that there was no significant difference between the two groups ($P > 0.05$) which means that both right sided and left sided ablation procedure is associated with significant elevation of the D-dimer. **Conclusion:** The D-dimer level in all the studied patients increased significantly after ablation and decreased before discharge but is still significantly higher than that of the baseline level. (1) In both right sided ablation and left sided ablation, the D-dimer level in patients with VNRT increased significantly ($P < 0.001$) after EPS and rose higher after ablation and in spite of that it decreased significantly before discharge it is still significantly higher than that of the baseline level. (2) There was no significant difference between the right sided and left sided procedure ($P > 0.05$) which means that both right sided and left sided ablation procedure is associated with significant elevation of the D-dimer.
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Key words: D-dimer; thrombogenicity; radiofrequncy transcatheter ablation; AVNRT.

1. Introduction:

The use of radiofrequency (RF) ablation has rapidly expanded over the past few years, and the method has become standard therapy for certain arrhythmias, mostly supraventricular tachyarrhythmias. Potential thrombogenicity of RF lesions has remained an issue over the years because of echocardiographic observations of endocardiac thrombi and reports of clinical thromboembolic events complicating the procedure (*Manolis et al., 1996*). However, there have been no systematic efforts to study the thrombogenic potential of these endocardial lesions, and recommendations are lacking regarding antithrombotic or anticoagulant therapy during or after the procedure. Information regarding activation of the coagulation and fibrinolytic systems can be obtained by measurement of a biochemical marker such as D-dimer, a product of fibrin degradation that is mediated by plasmin, which provides an index of thrombus formation and reactive fibrinolysis (*Manolis et al., 1996*).

A number of thromboembolic complications has been reported in association with radiofrequency ablation (RF-A). Whereas systemic thromboembolic complications such as stroke have been of concern, there are increasing numbers of recent reports of both fatal and non-fatal pulmonary embolism. The factors that predispose to these risks have not been elucidated

and thus strategies to administer anticoagulation to the subgroup of patients at greatest risk have not been devised. The empirical strategy that is typically employed to minimize thromboembolic complications may entail heparin and aspirin for left-sided ablations, and aspirin alone for right sided ablations, which may sub-optimally prevent a potential worst-case scenario of fatal massive pulmonary embolism (**Lee et al.,2001**). The potential mechanisms of thrombogenesis during ablation procedures are multiple and include endothelial disruption, coagulation necrosis, electrical injury, mechanical damage in the vessel wall, and heating of circulating blood elements by radiofrequency energy. The above mechanisms can cause activation of the cascade of events that ultimately results in thrombin generation and platelet activation (**Lee et al., 2001**).

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 (**Tetsue et al., 2002**).

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 (**Tetsue et al., 2002**).

Ten percent incidence of left atrial (LA) thrombus formation has been detected using intracardiac echocardiography (ICE) imaging monitoring during LA ablation (**Jian-Fang et al., 2005**)

ICE–diagnosed spontaneous echo contrast (SEC) before transseptal catheterization identifies an increased risk of LA thrombus. Increased intensity of heparin anticoagulation (activated clotting time > 300 second) during LA ablation for AF may prevent LA thrombus formation especially in patient with SEC (**Jian-Fang et al., 2005**)

Aim of the Work:

The aim of this study is to determine the independent and incremental procoagulant effect of RF ablation by assessing biochemical marker of thrombogenicity. The biochemical markers used in this study are direct measures of fibrinolysis (d-dimer, DD).

2. Patients and Methods

This study is a comparative clinical trial that was conducted in EP laboratory of National Heart Institute. It has been started since 7/11/2006 to 1/09/2007.

This study included forty patients are divided into twenty patients referred for EP laboratory to do radiofrequncy transcatheter ablation in right side of the heart (twenty patients with AVNRT) and 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-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.

EP laboratory procedure:

- Central venous access was obtained at the femoral vein and the internal jugular vein if necessary.
- Arterial access was obtained at the femoral artery. Standard aseptic techniques were employed using the Seldinger technique for vascular access.
- 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 a retrograde aortic or 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 ^{o}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.

This study included 40 patients referred to the EP laboratory of National Heart Institute. Patients were divided into two groups according to the site of radiofrequency current application:

Group I (right sided ablation): Included twenty patients referred for radiofrequency transcatheter ablation for atrioventricular nodal reentrant tachycardia (right side of the heart). They were 11 males (55%) and 9 females (45%). Their mean age was 36.7 ± 8.5 years.

Group II(left sided ablation): Included twenty patients referred for radiofrequency transcatheter ablation for left lateral accessory pathway in the left side of the heart. They were 12 males (55%) and 8 females (45%). Their mean age was 36.7 ± 8.5 years.

There was no significant difference between the two groups 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	Right side	Left side	P value
Mean±S.D. or n (%)	N = 20	N = 20	
Age (years)	36.7 ± 8.5	39.5± 9.4	> 0.05
Male/female	11/9	12/8	> 0.05
Hypertension	4 (20%)	7 (35%)	> 0.05
Hyperlipidemia	6 (30%)	5 (20%)	> 0.05
Diabetes	5 (25%)	4 (20%)	> 0.05
Current smoker	8 (40%)	9 (45%)	> 0.05
RHD	4 (20%)	6 (30%)	> 0.05
IHD	2 (10%)	1 (5%)	> 0.05
Pulse (B/min.)	87.9 ± 15.6	85 ± 10.4	> 0.05
SBP (mm Hg)	125 ± 10.5	120 ± 5	> 0.05
DBP (mm Hg)	84 ± 7.3	80 ± 7.5	> 0.05

Results of the current study regarding the different laboratory investigations of the two groups showed that there was no significant difference between the two groups 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 two groups

	Right side Mean ± SD	Left side Mean ± SD	P value
Fasting blood sugar (mg/dl)	103 ± 7.9	105 ± 8.6	> 0.05
Total cholesterol (mg/dl)	207.9 ± 49.8	189.7 ± 37.5	> 0.05
HDL (mg/dl)	34.6 ± 4.1	39.2 ± 6.3	> 0.05
LDL (mg/dl)	115.4 ± 41.3	109.7 ± 44.3	> 0.05
TG (mg/dl)	174.6 ± 22.4	106.9 ± 21.9	> 0.05
Uric acid (mg/dl)	5.3 ± 1.9	4.7 ± 2.0	> 0.05
GPT (Unit)	27.3 ± 9.6	31.3 ± 10.8	> 0.05
GOT (Unit)	25.6 ± 1b0.3	29.4 ± 7.7	> 0.05
Urea (mg/dl)	33.6 ± 7.6	36.4 ± 10.2	> 0.05
Creatinine (mg/dl)	0.92 ± 0.02	0.98 ± 0.016	> 0.05
APTT	31.8 ± 4.1	30.9 ± 3.7	> 0.05
PT	10.6 ± 0.9	10.3 ± 0.7	> 0.05

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

Table (3): Echocardiographic study of the two groups

Echocardiographic finding	Right side Mean ± SD	Left side Mean ± SD	P Value
Systolic indexes			
- EDD (cm)	4.9 ± 0.7	4.7 ± 0.6	> 0.05
- ESD (cm)	3.1 ± 0.3	2.9 ± 0.4	> 0.05
- EF (%)	64.5 ± 5.9	63.9 ± 6.3	> 0.05
- FS (%)	32.1 ± 2.4	33.0 ± 3.1	> 0.05
- LA	3.7 ± 2.5	3.4 ± 3.1	> 0.05
- Ao	3.3 ± 1.1	3.1 ± 0.9	> 0.05
- RV	1.9 ± 0.5	1.6 ± 0.4	> 0.05

Results of the current study regarding the characteristics of radiofrequency ablation procedure between AVNRT (right sided) and accessory pathway (left sided) showed that in patients with AVNRT the EPS duration was 79.8 ± 31.5 minutes while it was 73.4 ± 36.5 minutes for patients with AP and this difference was not significant ($P > 0.05$). The RF dekivery duration was 125.9 ± 65.3 seconds for patients with AVNRT while it was 175.5 ± 75.7 seconds, the number of RF application was 10.5 ± 5.0 for patients with AVNRT while it was 7.5 ± 8.6 seconds for patients with AP, the mean ablation temprature was 53.5 ± 5.0 for patients with AVNRT while it was 65.7 ± 5.6 seconds for patients with AP. There was significant difference between the two groups regarding the different characteristics of RF ablation procedure ($P < 0.05$) (Table 4).

Table (4): Characteristics of radiofrequency ablation procedure between AVNRT (right sided) and accessory pathway (left sided)

Parameter	Right side Mean ± SD	Left side Mean ± SD	P Value
EPS duration (min.)	79.8 ± 31.5	73.4 ± 36.5	> 0.05
RF delivery duration (seconds)	125.9 ± 65.3	175.5 ± 75.7	< 0.05
Total procedure time (min.)	125.6 ± 42	110.5 ± 31.2	< 0.05
Number of RF application	10.5 ± 5.0	7.5 ± 8.6	< 0.05
Tissue temperature during ablation	53.5 ± 5.0	65.7 ± 5.6	< 0.05

EPS: Electrophysiologic study; RF: radiofrequency ablation.

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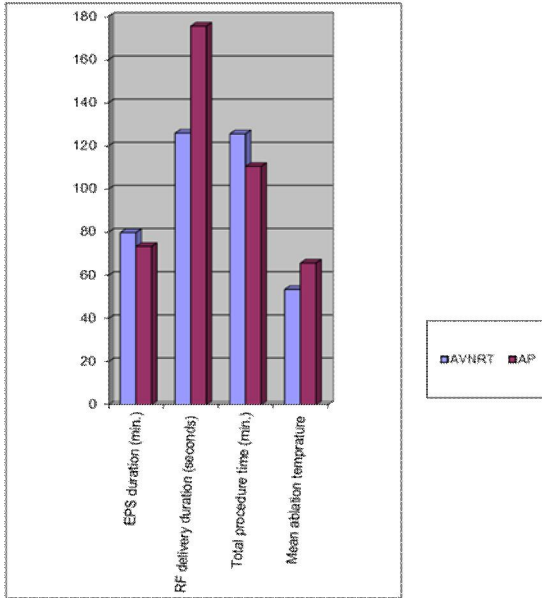

Fig. (1): Characteristics of radiofrequency ablation procedure between AVNRT (right sided) and accessory pathway (left sided)

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

Stage	D-dimer level N = 40 patients Mean ± SD
Baseline	406.5 ± 254.1
After EPS	934.8 ± 656.5*
After ablation	2406.5 ± 1765.3*
Before discharge	1900.4 ± 1514.3*

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

The D-dimer level in patients with AVNRT increased significantly ($P < 0.001$) from 398.7 ± 245.6 at baseline to 946.7 ± 629.9 after EPS and rose

higher to 2510.5 ± 1688.3 after ablation and in spite of that it decrease to 1895.4 ± 1623.7 before discharge it is still significantly higher than that of the baseline level ($P < 0.001$) (Table 6 and Figure 3).

The D-dimer level in patients with AP increased significantly ($P < 0.001$) from 421.6 ± 236.9 at baseline to 919.5 ± 546.7 after EPS and rose higher to 2469.8 ± 17989.4 after ablation and in spite of that it decrease to 1951.3 ± 1723.2 before discharge it is still significantly higher than that of the baseline level ($P < 0.001$) (Table 6 and Figure 3).

Comparison between the two groups regarding the D-dimer level at the different stages of the procedure showed that there was no significant difference between the two groups ($P > 0.05$) which means that both right sided and left sided ablation procedure are associated with significant elevation of the D-dimer (Table 6 and Fig. 3).
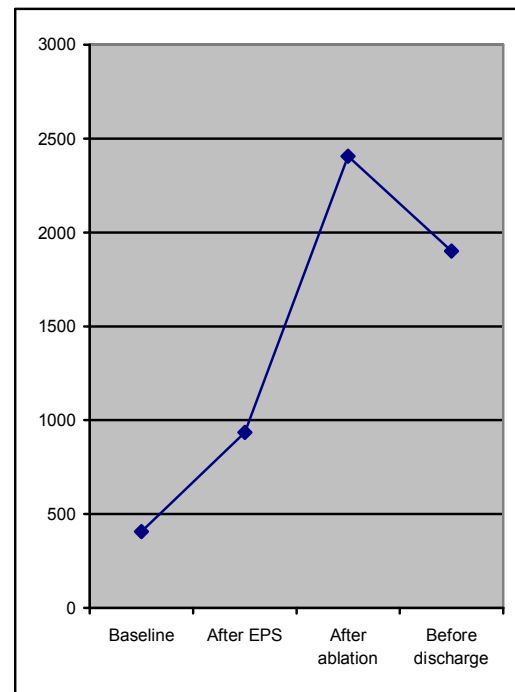

Fig. (2): D-dimer level of all patients at the different stages of the procedure

Table (6): D-dimer level in the two groups at the different stages of the procedure

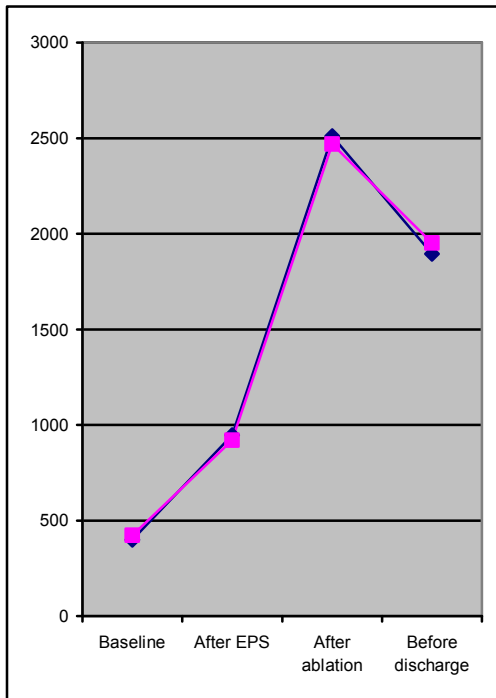| Stage	Right side Mean ± SD	Left side Mean ± SD	P value
Baseline	398.7 ± 245.6	421.6 ± 236.9	> 0.05
After EPS	946.7 ± 629.9	919.5 ± 546.7	> 0.05
After ablation	2510.5 ± 1688.3	2469.8±17989.4	> 0.05
Before discharge	1895.4 ± 1623.7	1951.3 ± 1723.2	> 0.05

Fig. (3): D-dimer level of the two groups at the different stages of the procedure

Discussion

Since its first clinical use in 1986, RF ablation has evolved as an effective nonpharmacological therapy for a wide array of tachyarrhythmias. Although the procedure carries a low risk of cardiovascular complications, thromboembolism is of concern. Although rare in otherwise healthy patients, thromboemboli may have devastating long-term consequences. Radiofrequency ablation procedures are used widely for the management of arrhythmias (*Ganz et al., 1995*). It is reported that complications occur infrequently [*Scheinman et al., 1994*] but a number of thromboembolic complications has been reported in association with radiofrequency ablation (*Hindricks et al., 1993, Kugler et al., 1994, Epstein et al., 1996, Zhou et al., 1999*). Whereas systemic thromboembolic complications such as stroke have been of concern, there are increasing numbers of recent reports of both fatal and non-fatal pulmonary embolism (*Greene et al., 1994*).

The factors that predispose to these risks have not been elucidated and thus strategies to administer anticoagulation to the subgroup of patients at greatest risk have not been devised. The empirical strategy that is typically employed to minimize thromboembolic complications may entail heparin and aspirin for left-sided ablations, and aspirin alone for rightsided ablations, which may sub-optimally

prevent a potential worst-case scenario of fatal massive pulmonary embolism (*Jais et al., 1999*).

The potential mechanisms of thrombogenesis during ablation procedures are multiple and include endothelial disruption, coagulation necrosis, electroporation injury, mechanical damage in the vessel wall, and heating of circulating blood elements by radiofrequency energy *(Kunze et al., 1998)*. The above mechanisms can cause activation of the cascade of events that ultimately results in thrombin generation and platelet activation *(Mansourati et al., 1997)*

This study aimed at determining the independent and incremental procoagulant effect of RF ablation by assessing biochemical marker of thrombogenicity. The biochemical markers used in this study is direct measures of fibrinolysis (d-dimer, DD). 40 patients referred to the EP laboratory of National Heart Institute were included in the study. They were divided into two groups:

Group I:

Included twenty patients referred for radiofrequency transcatheter ablation for atriventricular nodal reentrant tachycardia (right side of the heart). They were 11 males (55%) and 9 females (45%). Their mean age was 36.7 ± 8.5 years.

Group II:

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 ± 8.5 years.

Our results showed that there was no significant difference between the two groups regarding the fasting blood sugar, lipid profile, kidney and liver function tests ($P > 0.05$). Also, there was no significant difference between the two groups 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 between AVNRT (right sided) and accessory pathway (left sided) showed that in patients with AVNRT the EPS duration was 79.8 ± 31.5 minutes while it was 73.4 ± 36.5 minutes for patients with AP and this difference was not significant ($P > 0.05$). The RF delivery duration was 125.9 ± 65.3 seconds for patients with AVNRT while it was 175.5 ± 75.7 seconds, the Pulse count was 10.5 ± 5.0 for patients with AVNRT while it was 7.5 ± 8.6 for patients with AP, the mean ablation temprature was 53.5 ± 5.0 for patients with AVNRT while it was 65.7 ± 5.6 seconds for patients with AP. There was significant difference

between the two groups regarding the different characteristics of RF ablation procedure ($P < 0.05$).

Reports from early literatures have indicated that duration and site of ablation procedure, rather than RF energy may play a key role in activating the hemostatic system *(Dubue et al., 1998).*

The D-dimer level in all the studied patients increased significantly ($P < 0.001$) from 406.5 ± 254.1 at baseline to 934.8 ± 656.5 after EPS and rose higher to 2406.5 ± 1765.3 after ablation and in spite of that it decrease to 1900.4 ± 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 (*Heines et al., 1990*). Although the elevation in D-dimer may result from the peripheral effects induced by sheath insertion and catheter manipulation (*Le groube et al., 1996*), the marked elevation of D-dimer in this study mainly resulted from the central effects of RF ablation application, which caused endomyocardial injury and higher temperature.

The mechanism explaining the elevation of D-dimer and the possible occurrence of thromboembolic complications of RF ablation procedure is that:

Some authors believe that thromboembolic complications occur as a result of catheter manipulation and not ablation *(Chang et al., 1990), (Van Oevern et al., 1999).* A study by Manolis AS found that D-dimer levels doubled after catheter manipulation but increased 6-fold after ablation *(Manolis et al., 1996).*

A report described a lobulated 1-cm thrombus identified by transesophageal echocardiography attached to the right atrial septum at the ablation site.*(Ren et al.,2001)*. A study described a spontaneous contrast or thrombus formation detected by TEE and ICE which were performed during RF current application in the end stage of ablation.*(Aleksander et al.,2006).* With RF ablation, events leading to thrombus formation are thought to be initiated by endothelial cell injury.1 Endothelial cells are highly sensitive to injury and are damaged or destroyed by RF energy, despite selective applications.*(Lee et al.,2001*)

When continuity of the endothelium is interrupted, anticoagulant properties are lost. Subendothelial components such as collagen, tissue factor, and von Willebrand's factor become exposed to circulating blood. *(Mester et al., 1995)*Consequently, platelet adhesion and activation and thrombin production ensue. Given this proposed pathophysiological mechanism, it may be expected

that thrombus size would be directly related to extent of RF tissue injury.

The D-dimer level in patients with AVNRT increased significantly ($P < 0.001$) from 398.7 ± 245.6 at baseline to 946.7 ± 629.9 after EPS and rose higher to 2510.5 ± 1688.3 after ablation and in spite of that it decrease to 1895.4 ± 1623.7 before discharge it is still significantly higher than that of the baseline level ($P < 0.001$). The D-dimer level in patients with AP increased significantly ($P < 0.001$) from 421.6 ± 236.9 at baseline to 919.5 ± 546.7 after EPS and rose higher to 2469.8 ± 17989.4 after ablation and in spite of that it decrease to 1951.3 ± 1723.2 before discharge it is still significantly higher than that of the baseline level ($P < 0.001$).

Our results are in agreement with that reported by (*Micheucci et al., 1999)* who 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.

Comparison between the right sided and left sided ablation groups regarding the D-dimer level at the different stages of the procedure showed that there was no significant difference between the two groups ($P > 0.05$) which means that both right sided and left sided ablation procedures are associated with significant elevation of the D-dimer.

Our results agreed with that reported by(*Charng et al., 2004)* who compared the hemostatic activation created by right and left heart RF catheter ablation and found that similar hemostatic activation occurred during and immediately after RF ablation in both groups. On follow-up, they found that sustained elevation in D-dimer after the ablation procedure in the right side was observed as a significant therapeutic and prognostic implication.

Some of the difference was observed in our study between right sided and left sided procedure as lower ablation temperature and more frequent RF current application in the right than in the left side heart procedure. However elevation of the D-dimer immediately and 48 hours after the procedure especially in the right side (but the elevation was not significant), indicated a potential subclinical thrombosis immediately after the RF ablation and a continuing risk that may persist up to 48 hours thereafter.

Recommendation

The present study offers a new approach to studying activation of the coagulation cascade during catheter ablation. It suggests that sub clinical thrombosis may be ubiquitous after catheter ablation, as evidenced by the D-dimer elevation in patients undergoing these procedures.

The continuation of the administration of heparin and/or the association of antiplatelet agents may be of possible advantage, especially for patients of advanced age and in those with a risk of thrombotic events (eg, diabetes, estroprogestin).

It now seems evident that all patients should receive anticoagulation therapy immediately after guide wire is inserted as there is incremental increase in the level of the D-dimer level during the procedure reach its peak after ablation.

Anticoagulation protocols vary widely between different centers. However there is only one study answers the question "when should heparin preferable be administered during radiofrequency catheter ablation?" it shows by administering heparin (100 IU/kg, IV as a bolus then 1000 IU/hour as maintenance dose this regimen was used in study) immediately after introduction of the venous sheaths, haemostatic activation is significantly decreased.*(Anfinsen et al.,2001).*

More recently study has shown that additional use of heparin reduced the incidence of thrombosis by 63% as it has been assessed by transesophageal and intracardiac echocardiography. *(Aleksander et al., 2006).*

Therefore future clinical research should address the evaluation of the effectiveness, tolerability, and safety of both the prophylactic and the postprocedural anticoagulation and antiplatelet therapy. A large trial looking at thrombotic complications and for randomized clinical trials of antithrombotic therapy.

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