

# Plasmatic D-dimers – A test for left auricular thrombosis in the persistent atrial fibrillation

Petrus D. PETCU, MD, PhD<sup>a</sup>; Cristina FLORESCU, MD<sup>a</sup>; Constantin BATAIOSU, MD<sup>a</sup>,  
Laura BOGDAN, MD<sup>a</sup>, Coriolan PETCU MD<sup>b</sup>, Petrica BADEA, MD, PhD<sup>a</sup>

<sup>a</sup>The Cardiology Centre of Craiova, Romania

<sup>b</sup>Institute for Cardiovascular Diseases, Bucharest, Romania

## ABSTRACT

*The study analyzes the relation between the plasmatic concentration of the D-dimers and the thromboembolic accidents in the persistent atrial fibrillation converted electrically to the sinus rhythm.*

*35 patients with the persistent atrial fibrillation were included in the study. The patients were allotted according to the data of the transesophageal echocardiography in two groups: a witness group consisting of 22 patients without thrombosis in the left atrial appendage and the second group consisting of 13 patients with thrombosis or suspicion of thrombosis in the left atrial appendage.*

*The plasmatic D-dimers had a concentration of  $0.358 \pm 0.159$  in patients in the witness group and a concentration of  $0.921 \pm 0.678$  in patients with the thrombosis or suspicion of left auricular thrombosis, with a significant statistical *p* value ( $p=0.000659$ ;  $p<0.001$ ). The interval of confidence for the plasmatic D-dimers was between 0.28-0.42 for 95% of patients without the auricular thrombosis and between 0.51-1.38 for 95% of patients with the left auricular thrombosis.*

**Key words:** D-dimers, left auricular thrombosis, atrial fibrillation, transesophageal echography

## INTRODUCTION

**T**he plasmatic D-dimers are the indirect markers of the fibrin formation or the activation of the coagulation pathway. The role of the plasmatic D-dimers in the diagnosis of the thromboembolic disease was clarified, but the embolic risk for atrial fibrillation (AF) is not elucidated (1). The conversion of the persistent atrial fibrillation to the sinus rhythm (SR) is accompanied by the embolic risk

(2,3). This can be reduced with a 3 weeks' course of anticoagulant treatment and through locating the thrombi in the left atrial appendage or in other cardiac cavities with the aid of the transesophageal echocardiography (TEE) (4-7). □

## AIM

**T**he study proposes to analyze the relationship between the plasmatic concentration of the D-dimers and the risk of

*Address for correspondence:*

Petrus D. Petcu, MD, PhD, The Cardiology Centre of Craiova, 60 Ion Antonescu Blvd, Craiova, Romania  
email address: petrus\_dorel.petcu@yahoo.com

thromboembolic events in patients with persistent AF electrically converted to SR.

### MATERIAL AND METHOD

There were selected for the study 35 patients, presenting the criteria for persistent atrial fibrillation, these patients being hospitalized in the Cardiology Centre of Craiova for the period between 01.09.2007-29.02.2008.

We didn't include in this study the cases with atrial fibrillation and with increased plasmatic D-dimers due to other diseases (profound venous thrombosis (8), non-massive pulmonary thrombo-embolism, surgical interventions, severe infections, neoplasm).

The plasmatic D-dimers were performed using the micro-chromatography technique with a Cardia Reader apparatus. TEE was performed with the standard technique using a SONOS AGILENT 5500 echocardiograph. The echocardiogram was interpreted by 2 doctors through the real time observation of the image and through the reassessment of recorded images. The patients were assigned to 2 groups, according to modifications detected by TEE: a witness group which is formed by 22 patients without thrombus in the left atrial appendage and a group formed by the patients with thrombus image or with suggestive image of thrombus in the left atrial appendage on TEE. TEE was performed the same day with cardio-conversion.

The determination of the plasmatic D-dimers value preceded the TEE, but became operational after performing the TEE. TEE is considered the

“gold” standard in localizing the auricular thromboses (1,9).

The concentration of the plasmatic D-dimers was considered suggestive for the auricular thrombosis if its value was > 0,50 micrograms/ml, consistent with the actual data from the literature (9). All 35 patients received the anticoagulant treatment (acenocumarol 2-4 mg/day) for 7 to 21 days and they had a INR=2-3 before the electrical conversion. The patients without the embolic risk were converted to SR through the application of a synchronic biphasic electrical shock of 100-150 J. The patients were followed-up for at least 3 months after their discharge. The values of the plasmatic D-dimers are presented as an average ± standard deviation of the average and related to TEE. The “t-test” test was used for the comparative analysis. □

### RESULTS

In this study, after the initial evaluation, 35 patients were included, among these 13 being females (37.2%) and 22 males (62.8%), with an average age of 56.2±9.7 (55.4±10.2 for females and 56±9.39 for males) (TABLE 1).

The characteristics of the 2 groups of patients included in this study are showed in TABLE 2.

The left auricular thrombosis was detected through the TEE in 3 patients; in 10 patients, this thrombosis was suspected after the first TEE. In 22 patients, TEE excluded the thrombus in the left atrial appendage (FIGURE 1).

The plasmatic concentration of the D-dimers in the witness of patients (22 patients without signs of thrombosis or suspicion of thrombosis in the left atrial appendage), had an average ± standard deviation interval of 0.921±0.678 with statistically significant p value (p<0.001; p=0.000659) (TABLE 3).

In 13 patients with thrombosis or suspicion of thrombosis in left atrial appendage, the plasmatic D-dimers determinations and the TEE were repeated after 3 to 5 days (all the patients were under anticoagulant treatment with an INR of 2 to 3). TEE was analyzed by 2 cardiologists and the left auricular thrombosis was excluded in 8 patients. The plasmatic D-dimers values in these patients had an average of 0.361 ± 0.121. The suspicion of left auricular thrombosis using the TEE was caused by the structural anomalies of the left atrial appendage and of the pectinated muscles (FIGURE 2).

Sex	Females	Males	Total
Nr. Patients	13	22	35
Percentage	37.2	62.8	100
Average age	55.4±10.2	56±9.31	56.2±9.7

TABLE 1. Age and sex distribution of patients included in the study

Patients characteristics	Nr. patients
Persistent atrial fibrillation	35
Systemic hypertension	18
Coronary disease	13
Diabetes mellitus	3
Mitral valvulopathy	11
Left ventricle ejection fraction <35%	4
Left atrium>45mm	4

TABLE 2. Morbid characteristics of patients included in the study

Investigation	Nr. of patients with thrombosis or with suspicion of left atrial thrombosis	Nr. of patients without left atrial thrombosis	Total
TEE	13	22	35
D-dimers	0.921±0.678	0.358±0.159	
	P = 0.000659 (p < 0.001)		

TABLE 3. Results of both investigations (TEE and D-dimers plasmatic test)

The sensitivity and specificity of the diagnosis of left auricular thrombosis through TEE were 86%, respectively 73%. The plasmatic D-dimers test had average values of  $1.31 \pm 0.51$  for the 5 patients. From these, 3 patients have had thrombosis detected at the first TEE and 2 patients have had thrombosis in the left atrial appendage confirmed at the second TEE examination and through the D-dimers test. An 95% confidence interval for the plasmatic D-dimers tests in the 22 patients without auricular thrombosis (the witness group) was 0.28-0.42, and for the group with the auricular thrombosis it was 0.51-1.38.

In patients with the coronary disease and high blood pressure, the level of the D-dimers was between  $0.71 \pm 0.57$ , respectively between  $0.92 \pm 0.60$ . □

### DISCUSSIONS

The TEE excludes the presence of the thrombus in the left atrial appendage and defines a low risk of thrombo-embolism in patients with persistent FA. The 22 patients without thrombosis and with plasmatic D-dimers values  $< 0.358 \pm 0.159$  micrograms/ml were converted electrically to SR without thrombo-embolic events during the hospitalization and for the first 3 months after discharge.

One patient presented a negative test of D-dimers (and the TEE detected a calcified thrombus in the left atrial appendage).

A particular anatomical structure of the left atrial appendage was interpreted at the first TEE exam as thrombosis in 8 patients, but the plasmatic D-dimers values were  $< 0.358 \pm 0.159$  micrograms/ml. Re-doing a TEE and a plasmatic D-dimers determination excluded the left auricular thrombosis. The cardioversion was achieved also in these patients, without embolic events during hospitalization and for 3 months after discharge. □

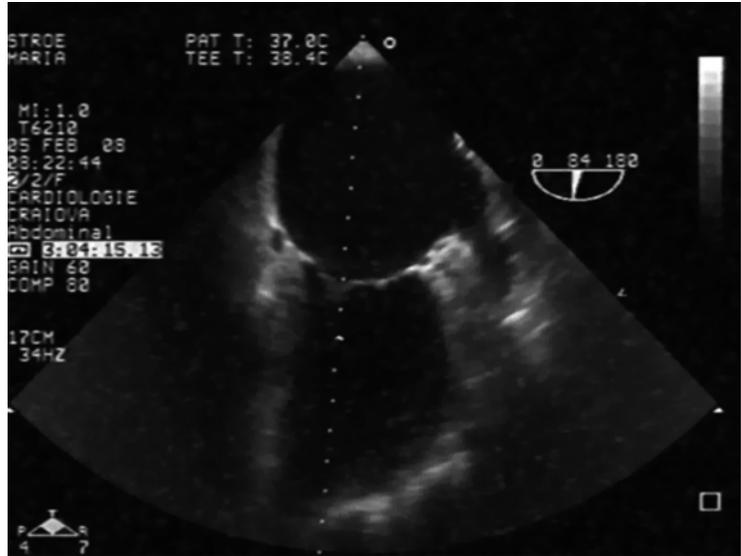


FIGURE 1. TEE left atrium free of thrombus in a 63-year-old female patient

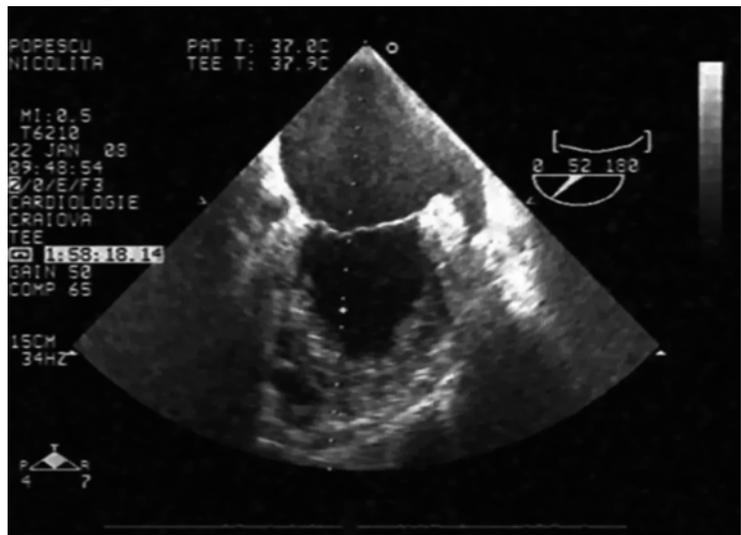


FIGURE 2. TEE left atrium with suspicion of thrombosis in 53-year-old female patient

### Preliminary data

1. The patients with persistent FA have thromboembolic risk at a confidence interval for the plasmatic D-dimers at

0.51-1.32. A confidence interval for the plasmatic D-dimers tests of 0.28-0.48 excludes the thromboembolic risk in patients with persistent FA.

2. The thromboembolic risk in patients with persistent FA increases when there have co-morbidities like high systemic blood pressure, coronary heart disease or mitral valvulopathy.
3. An extended similar study may lead to the introduction of this biochemical marker (plasmatic D-Dimers) in the clinical medical practice along with the transesophageal echocardiography for the assessment of the thromboembolic risk in patients with the atrial fibrillation. ▣

## REFERENCES:

1. Miklos Somloi, Ianos Tomcsanyi, Attila Bezzegh – D-Dimer Determination as a Screening Tool to Exclude Atrial Thrombi in Atrial Fibrillation, *The American Journal of Cardiology*, Vol. 92 July 1, 2003
2. Heppell RM, Berkin KE, McLenachan JM, et al – Haemostatic and haemodynamic abnormalities associated with left atrial thrombosis in non-rheumatic atrial fibrillation. *Heart* 1997; 77:407-411
3. Lip GY – The prothrombotic state in atrial fibrillation: new insights, more questions, and clear answers needed. *Am Heart J* 2000; 140:348-350.
4. Klein AL, Grimm RA, Murray RD, et al – Use of transesophageal echocardiography to guide cardioversion in patients with atrial fibrillation. *N Engl J Med* 2000; 344:1411-1420
5. Yasaka M, Miyatake K, Mitani M, et al – Intracardiac mobile thrombus and D-dimer fragment of fibrin in patients with mitral stenosis. *Br Heart J* 1991; 66:22-25
6. Fatkin D, Scalia G, Jacobs N, et al – Accuracy of biplane transesophageal echocardiography in detecting left atrial thrombus. *Am J Cardiol* 1996; 77:321-323
7. Manning WJ, Weintraub RM, Waksmonski CA, et al – Accuracy of transesophageal echocardiography for identifying left atrial thrombi. A prospective, intraoperative study. *Ann Intern Med* 1995; 123:817-822
8. Van der Graaf F, van den Borne H, van der Kolk M, et al – Exclusion of deep venous thrombosis with D-dimer testing-comparison of 13 D-dimer methods in 99 outpatients suspected of deep venous thrombosis using venography as reference standard. *Thromb Haemost* 2002; 83:191-198
9. Fuster V, Ryden LE, Asinger R\V, et al – ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation. 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 and Policy Conferences (committee to develop guidelines for the management of patients with atrial fibrillation) developed in collaboration with the North American Society of Pacing and Electrophysiology. *Eur Heart J* 2000; 22:1852-1923