

## REVIEW

of the PhD thesis of Dr. Vassil Borislavov Traykov, Head of Dept. of Invasive Electrophysiology, Clinic of Cardiology, Acibadem City Clinic Tokuda Hospital – Sofia

By: Prof. Tosho Balabanski, MD, PhD, cardiologist at the National Heart Hospital – Sofia

**Title:** “Catheter ablation of atrial fibrillation: procedural characteristics and role of triggering structures for arrhythmia perpetuation”.

**Doctoral advisor:** Prof. Tchavdar Shalганov, MD, PhD, National Heart Hospital – Sofia

### RELEVANCE

The topic of the PhD thesis is completely relevant, contemporary and of high scientific and clinical value. Procedural characteristics of atrial fibrillation catheter ablation as well as some aspects of the mechanisms of atrial fibrillation initiation and maintenance have not been studied in a relatively large patient population in Bulgaria up to that point.

**CENTRAL TOPICS** in the PhD thesis of Dr. Vassil Traykov are: 1) to study clinical and procedural characteristics of patients with atrial fibrillation undergoing catheter ablation with and without general anaesthesia; 2) to analyse the triggering structures in patients with paroxysmal atrial fibrillation.

**THE INTRODUCTION** is concise and clearly delineates the significance of the problem.

**LITERATURE REVIEW:** The scientific evidence on the topic have been presented in detail and on a contemporary level, in 37 pages. There are 191 references based on which the review provides a detailed and critical analysis of the available evidence. The majority of publications cited by Dr. Traykov include key papers on the topic published in the last 10-15 years. The references include 28 from the period 1991-2000, 65 from the period 2001-2010 and 92 from the period 2011-2020. The remaining and earlier publications including those from 1959, 1962 and 1964 are a proof for the extensiveness of the literature review.

**THE AIM** of the dissertation logically follows the literature review. **THE TASKS** have been well defined and correspond to the analysis of results, conclusions and contributions in the field of catheter ablation of atrial fibrillation.

**THE WORK INCLUDES THREE GROUPS OF PATIENTS** as follows: 1) Group 1 which includes 108 patients who have undergone catheter ablation of atrial fibrillation under general anaesthesia; 2) Group 2 (59 patients) who have undergone catheter ablation with sedation only; 3) Group 3 which includes 26 patients who have been studied and treated

in Szeged (Hungary) and Philadelphia (USA). The patients from this group have been studied prospectively in a research project with the leadership of Dr. Vassil Traykov. In this group pulmonary vein isolation has been carried out under sedation and has been preceded by induction of atrial fibrillation episodes. The study presented by Dr. Traykov includes diagnostic and therapeutic work of **a considerable volume and complexity.**

## METHODS

All the patients have undergone preprocedural assessment which includes analysis of the clinical findings, routine laboratory tests, conventional echocardiography and contrast enhanced cardiac computed tomography. Catheter ablation in the different groups has been carried out under general anaesthesia or conscious sedation. The electrophysiology procedure includes bilateral femoral venous access with introduction of catheters in the heart under fluoroscopic guidance in the His bundle region, coronary sinus as well as in the pulmonary veins and the left atrium following double transseptal puncture. Intracardiac echocardiography has been used to guide left atrial access and mapping in the patients from group 3. Three-dimensional mapping of the left atrium following computed tomographic image integration is carried out. Radiofrequency energy is used for catheter ablation directed to antral pulmonary vein isolation. Manual tagging of the radiofrequency lesions is used to mark lesions based on subjective assessment of catheter stability. Entrance block to the pulmonary veins has been proved by the lack of high frequency signals during atrial pacing. Exit block is demonstrated by the presence of dissociation of pulmonary vein potentials from the electrical activity of the rest of the atria, recorded by the circular mapping catheter.

Group 3 patients have undergone atrial fibrillation induction and intracardiac echocardiography for exact localization of the catheters in the pulmonary veins. Intracardiac signals have been recorded and processed using LabView software package. The analysis has determined the highest dominant frequency in the spectrograms derived from all bipoles for each structure (pulmonary vein or part of the atria).

During follow up arrhythmia recurrences and procedural complications are evaluated and recorded. Patient follow-up is carried out by: clinical check-up, ECG, Holter ECG or telephone interview.

**The methods applied in the study have been presented very accurately** using 14 figures.

**Statistical methods** used in the study by Dr. Vassil Traykov are contemporary, completely adequate and serve to provide reliable results. The study uses software package SPSS® (version 16.0), which includes a large set of statistical programs. The applied statistical methods include descriptive analysis, tests for normality of distribution of continuous variables, tests for comparison – Student's t-test, ANOVA, Mann-Whitney, Wilcoxon, Kruskal-Wallis,  $\chi^2$  test and Fischer's exact test. Kaplan-Meier analysis is used to study the survival free of arrhythmia. ROC analysis is used to determine the diagnostic value of some of the predictors of arrhythmia recurrence following catheter ablation identified by logistic regression.

## RESULTS

The results are presented in a systematic and well-structured manner. They include demographical and clinical patient characteristics, procedural characteristics (total procedural time, fluoroscopy time, dose-area product, number of radiofrequency lesions, cumulative radiofrequency time), complications, remote procedural results (procedural success following a single or multiple procedures, final clinical success). HAS-BLED value above 1 and the presence of left ventricular hypertrophy have been identified as predictors of lower chances of achieving success of catheter ablation of atrial fibrillation. The statistical analysis of the data also demonstrates that performing the procedure under general anesthesia is associated with shorter procedural duration, lower radiation dose, lower number of lesions and shorter cumulative radiofrequency time. The results reported by Dr. Traykov show that performing the procedure under general anesthesia does not result in better remote procedural results and is associated with a similar rate of vascular and cardiac complications compared to sedation only. Triggering activity initiating atrial fibrillation episodes is reported to originate most commonly from the left superior pulmonary vein and left carina.

The results are presented using 16 tables and 27 figures. **Exceptional advantage of the study by Dr. Traykov is the comprehensive analysis** of the results by presenting them in tables and figures along with immediate statistical results. The author clearly defines not only the conclusions from the study but also scientific hypotheses which might generate future studies.

## DISCUSSION AND EVALUATION

This retrospective study includes 3 groups with a total number of 193 patients at a mean age of 57 years (from 28 to 79 years) with clinical history of paroxysmal atrial fibrillation (in 90% of the patients) and preserved left atrial dimensions and left ventricular systolic function. This is the first larger-scale study in Bulgaria to investigate the procedural characteristics of atrial fibrillation ablation. The study also evaluates the role of structures demonstrating activity as triggering structures initiating atrial fibrillation episodes. Compared to other studies in the field the current study is relatively large based on the number of enrolled patients and conducted tests and evaluations.

The final results of the study have been presented in great detail and clarity in the text as well as schematically in the tables and figures.

## CONCLUSIONS

The conclusions of the PhD thesis of Dr. Vassil Traykov are based entirely on data from his study. They are presented in a concise manner and systematically ordered in eight entries.

## CONTRIBUTIONS OF THE PhD THESIS

The study reports data on procedural characteristics, procedural success and complication rate in a large for Bulgaria patient series with atrial fibrillation undergoing catheter ablation.

Dr. Traykov reports predictors for procedural success for the first time in our country. Among them is the HAS-BLED score which has not been reported in the literature up to now.

The study presents evidence demonstrating the superiority of performing the procedure under general anaesthesia in terms of reduced procedural time, radiation dose, fluoroscopic time, number of radiofrequency lesions and cumulative radiofrequency time.

The current work further confirms the role of catheter ablation in the treatment of atrial fibrillation in our country.

Dr. Vassil Traykov introduces for the first time in Bulgaria the frequency analysis of atrial intracardiac electrograms recorded during induced episodes of arrhythmia in patients with atrial fibrillation.

The study demonstrates the role of pulmonary veins in the maintenance of the fibrillatory process.

Dr. Traykov has altogether 6 publications associated with the PhD thesis which have appeared in international journals. Four of them are in journals with the following impact factors: IF 1.746 (PACE, 2013), IF 1.303 (PACE, 2019), IF 0.51 (Heart Rhythm Case Reports, 2018), IF 0.553 (Current Cardiology Reviews, 2012). There have been two presentations on the topic at high-ranking international scientific forums. The abstract from one of them has been published in a journal with impact factor IF 4.080 (Heart Rhythm, 2010).

## **CRITICAL REMARKS**

All the major critical remarks to the PhD thesis of Dr. Vassil Traykov have been covered by the author himself in chapter 4.10. *Limitations of the study*.

There are a few minor, non-essential critical remarks which do not hinder the reading of the PhD thesis. Among them are for example:

- 1.1. Misprint in the section “Contributions”.
- 1.2. Figure 24 and the text to it represent the percentage distribution of the number of procedures in the study group. The sum of all procedures in percent is not equal to 100%.

## **CONCLUSION**

The PhD thesis of Dr. Vassil Traykov has genuine theoretical and clinical implications.

The role of HAS-BLED score as a predictor of procedural success put forward by the current study requires further investigation in prospective studies.

There is a need for further large prospective and randomised trials to show the advantage of general anaesthesia compared to sedation in terms of procedural characteristics and single procedure success put forward by Dr. Traykov.

Implementation in Bulgaria of the methods used to study the spectral components of variation of intracardial potentials could improve atrial fibrillation diagnostics and treatment by catheter ablation.

**I do, without any doubt, recommend to the esteemed scientific jury to award Dr. Vassil Borislavov Traykov the educational and scientific degree “Doctor” in the program “Cardiology” and professional field “Medicine”.**

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