

# Abstract

*Introduction:* Atrial fibrillation is most common sustained cardiac arrhythmia characterized by rapid, unorganized atrial electrical activation. Its incidence increases with age and comorbidities. The presence of AF has been demonstrated to be independently associated with increased morbidity and mortality. The treatment of AF remains challenging. The aim of the present work is to use the analysis of heart rate variability in prediction of AF occurrence, and during treatment procedures of AF for better understanding of physiology of AF. Results of time-, frequency- and non-linear analyses were used in two present studies.

The first study was study of patients undergoing hybrid ablation of atrial fibrillation. Hybrid ablation consists of surgical epicardial thoracoscopic procedure, followed by electrophysiological catheter ablation. The second part is done 1-3 months after the surgical part. The aim was to establish the coincidental damage of ganglionated plex during the first, surgical procedure, using the analysis of heart rate variability during the electrophysiological procedure.

The aim of the second study was the prediction of post-operative AF in patients undergoing open-chest cardiac surgery, using the pre-operative heart rate variability analysis.

*Methods:* Study 1: Patients with paroxysmal, persistent or long-standing persistent AF were enrolled. Three groups of patients were studied. 1) HYBRID group: patients (persistent or LSPe AF) referred to hybrid ablation. The patients underwent thoracoscopic epicardial AF ablation as the first step of the hybrid procedure, followed by percutaneous, endocardial EP procedure and catheter ablation 1-3 months later on. As part of the second procedure, ablation of ganglionated plexi was done. 2) GP group: patients (paroxysmal or persistent AF), referred for percutaneous catheter ablation. The procedure consisted of pulmonary vein isolation and the ablation of ganglionated plexi. The ablation of ganglionated plexi was done in similar manner as in the hybrid Group. 3) PVI group. Patients (paroxysmal or persistent AF), referred for catheter ablation. During the procedure, only pulmonary vein isolation was done, without ablation of gan-

gionated plexi. In all three groups, 5 min ECG was recorded before and at the end of EP study. HR variability, and frequency analysis (high frequency band, low frequency band) were done.

Study 2: Study 2: Patients indicated for planned cardiac surgery due to coronary artery disease, or valve disease, without a history of atrial fibrillation were enrolled in the study. Two hours long ECG recordings were performed in all of them one day before the surgery. Based on the occurrence of postoperative AF, patients were divided in two groups: patients with postoperative AF (AF group) and without postoperative AF (NoAF group). The goal was to find preoperative measure in heart rate variability associated with postoperative AF occurrence, i.e. a parameter that could predict postoperative AF.

*Results:* Study 1: Sixty-seven patients were enrolled, 19 in the Hybrid group, 27 in the PVI group and 21 in the GP group. Ganglionated plex were ablated in the Hybrid and GP group. A positive vagal response was not present in any patient in the Hybrid group. However, it was present in 15(56%) patients in the PVI group, and 13(62%) patients in the GP group. Heart rate after the procedure increased significantly (as compared to the heart rate before the procedure) only in the PVI group (before  $68.1 \pm 10.8$  beats/min and after  $79.7 \pm 14.2$  beats/min,  $p = 0.002$ ). The increase in heart rate was in GP group but it was non-significant. In Hybrid group was the smallest increase and non-significant. Regarding frequency analysis, significant decrease in LF/HF ratio was present in the PVI and in the GP group (PVI group before  $1.7 \pm 1.5$  and  $0.7 \pm 0.6$ ,  $p < 0.001$ , GP group before  $2.5 \pm 2.3$  and after  $1.5 \pm 1.8$ ,  $p = 0.024$ ). In contrast, no change in LF/HF ratio was present in the Hybrid group.

Study 2: Two hundred and fifty-five patients were enrolled; the analysis was available in 220 of them (the remaining 35 were not analyzed because of insufficient quality of ECG recordings). Postoperative AF occurred in 83(37,5%) patients (AF group). Regarding clinical parameters, variables that were demonstrated to be associated with increased risk of post-operative AF were increasing age (odds ratio 1,051), and the history of myocardial infarction (odds ratio 2,093). With regard to the heart rate variability analysis, parameters that were found to be

associated with increased risk of AF were the absolute power in the low frequency band, and with less extend, some of the non-linear parameters (Slope index, SD2 or D2).

*Conclusion:* Study 1: Since vagal response were observed in the Hybrid and PVI groups, the antral isolation of the pulmonary veins (even without targeted ablation of the ganglionated plexi) is associated with at least partial damage of the ganglionated plexi. Then, the targeted ablation of the ganglionated plexi had no effect on HRV parameters. It might be present by previous damage of the ganglionated plexi during the epicardial surgical procedure.

Study 2: In accordance with previous studies, older age and history of myocardial infarction is associated with higher risk of postoperative AF. However, selected parameters of heart rate variability were useful in the prediction of postoperative AF, and should be validated in further studies.