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ScienceDirect

Journal of Electrocardiology 49 (2016) 423 – 428

JOURNAL OF Electrocardiology

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The relation between oxidative stress biomarkers and atrial fibrillation after pulmonary veins isolation

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Abstract

Introduction: The current paradigm claims a link between oxidative stress and atrial fibrillation. The aim of our research was to study a relation between the percentage of time spent in atrial fibrillation (AF burden) and concentrations of oxidative stress biomarkers, before and after pulmonary veins isolation (PVI).
Methodology: We included 19 patients (mean age 55 ± 10 years, 4 females and 15 males) with implanted loop recorders undergoing PVI. Plasmatic concentrations of advanced glycation end-products (AGEs), fructosamine, advanced oxidation protein products and thiobarbituric-acid reacting substances (TBARS) were measured and AF burden was recorded immediately before and 3 months after the PVI. AF burden was also recorded 9 months after the PVI.
Results: Post procedural AGEs concentration significantly negatively correlated with AF burden after 3 months ($\rho = -0.63$; $p < 0.01$) and 9 months ($\rho = -0.5$; $p = 0.04$), respectively as well as TBARS concentration significantly negatively correlated with AF burden after 9 months ($\rho = -0.61$; $p = 0.01$).
Conclusion: Our study showed AGEs and TBARS to be potential predictors for AF burden after the PVI. We suppose that the more oxidative stress after the PVI is provoked, the more fibrotic tissue is produced. That means a better electrical isolation of pulmonary veins and consequently a lower AF burden.

Keywords: Atrial fibrillation; Oxidative stress biomarkers; Implantable loop recorder; Radiofrequency catheter ablation

Introduction

The current paradigm claims a strong link between inflammation and atrial fibrillation (AF). Several studies showed that prevalence and prognosis of AF are both associated with serum levels of inflammatory biomarkers such as C-reactive protein, tumor necrosis factor-α, interleukin-2, interleukin-6, and interleukin-8 [1,2] The consequence of the inflammatory process is a production of free radicals, which in turn leads to increased oxidative stress which seems to be an important pathophysiological mechanism in the etiology and sustainability of AF. [3] Several studies showed a significant increase in oxidative damage in AF compared to sinus rhythm. Furthermore, gene expression associated with the production of reactive oxygen species was increased in AF. [4,5,6].

Radiofrequency catheter ablation is an effective treatment strategy for AF. [7,8] However, it is thought that this procedure also induces inflammation with oxidative stress and potential arrhythmogenic substrates that may lead to an early or a late recurrence of arrhythmia. [9,10].

The aim of our research was to study a relation between the oxidative stress (OS) biomarkers and AF burden, detected by an implantable loop recorder (ILR), before and after radiofrequency catheter ablation with pulmonary veins isolation (PVI).

Material and methods

Study population, inclusion and exclusion criteria

The study was designed as a prospective monocentric study. Total 19 consecutive patients (15 males and 4 females)

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http://dx.doi.org/10.1016/j.jelectrocard.2016.03.007
0022-0736/

with symptomatic AF undergoing PVI in the Slovak National Institute of Cardiovascular Diseases were included.

The inclusion criteria were: Age 18 or greater; planned PVI; implanted ILR at least 2 months before the PVI; symptomatic and drug refractory, paroxysmal AF characterized by spontaneous termination within 7 days of onset or persistent AF lasting more than 7 days (but not more than 40 days) with either spontaneous or pharmacological or electrical cardioversion to sinus rhythm documented prior to the ILR implantation; continuous, effective oral anticoagulation with warfarin (INR 2–3) at least one month prior to the PVI; ability and willingness of the patients to provide written informed consent with the study; antiarrhythmic therapy with beta blocker and amiodarone started at least 3 months before ILR implantation and continued at least 3 months after the PVI. Characteristics of the study population is presented in Table 1.

Patients with previous catheter ablation; implanted pacemaker or ICD; anticipating major cardiac surgery within the course of this study; stable coronary artery disease functional class (CCS: 3–4) or recent acute coronary syndrome; myocardial infarction within three months prior to the ILR implantation; heart failure (NYHA: III-IV); history of acute or chronic inflammatory disease; chronic kidney disease; left atrial thrombus detected by transesophageal echocardiography prior to the PVI and uncontrolled hyperthyroidism were excluded.

The study was approved by the ethical committee of the Slovak National Institute of Cardiovascular Diseases and a written informed consent was obtained from all patients before the study inclusion.

Radiofrequency catheter ablation with pulmonary veins isolation (PVI)

Patients remained on their original antiarrhythmic therapy treatment before the study. Effective oral anticoagulation (INR 2–3) was administered to all patients. Transesophageal echocardiography for exclusion of left atrium (LA) thrombus was performed immediately prior to the ablation (ABL). All patients underwent a contrast CT scan for documentation of individual LA anatomy.

Complete electrophysiological study was performed before entire AF ABL to exclude any other arrhythmia than AF. During the AF ABL procedure one 6Fr quadripolar diagnostic catheter (Supreme™, SJM, USA) was inserted via the right femoral vein to the His bundle area. A 6Fr decapolar diagnostic catheter (Response™, SJM, USA) was positioned in the coronary sinus via the right jugular vein. Fluoroscopically guided double transseptal puncture was performed by the Brockenbrough needle (BK1) inserted via the right femoral vein through an 8.5 Fr long sheath (SL1, SJM, USA) continuously flushed with heparinized normal saline. Two fixed curve sheaths or deflectable transseptal sheaths (AGILIS, SJM, USA) were used for entering LA and for stabilizing the circumferential mapping catheter (Lasso, Biosence-Webster, USA), and irrigated-tip ablation catheter (NaviStar Thermocool, Biosence-Webster, USA or Therapy Cool Path, SJM, USA) in the LA. In cases with difficult LA anatomy, intracardiac echocardiography was performed to guide the procedure. During the entire procedure, the activated clotting time (ACT) was measured each 20 min and maintained between 250 and 300 s.

Table 1
Descriptive statistics of the study population.

Baseline characteristics	Total (n = 19)
Age, (years)	55 ± 10
Female gender, no. (%)	4 (21%)
BMI, (kg/m^2)	28.5 ± 4.2
AF history before PVI, (years)	6.2 ± 4.5
LA size at PVI, (mm)	44 ± 4
Arterial hypertension, no. (%)	16 (84%)
Stable coronary artery disease, no. (%)	3 (16%)
Stroke, no. (%)	1 (5%)
Diabetes mellitus, no. (%)	0 (0%)
Heart failure, no. (%)	0 (0%)
Smoking, no. (%)	0 (0%)

Surface ECGs and bipolar endocardial electrograms were monitored continuously and stored in a computer-based digital amplifier/recording system (PRUCKA, GE, USA or AXIOM Sensis, Siemens, Germany). The procedure was performed in an analgo-sedated conscious state, with addition of midazolam, propofol or fentanyl in the case of an intolerable pain during the ABL.

An electroanatomic mapping system (CARTO, Biosense-Webster or NavX, SJM) generated a three-dimensional map to support the creation and validation of radio – frequency (RF) lesions during ABL. In patients with exclusively AF episodes, ABL consisted of pulmonary veins (PV) disconnection only, creating circular lines of conduction block around each PV ostium. Radiofrequency pulses were delivered through a Stockert (Biosense-Webster, USA) or IBI Therapy (Irvine Biomedical, Inc.) generator using irrigated-tip catheter in a temperature-controlled mode limited to 43 °C using a maximal power of 40 W and an irrigation rate up to 20 ml/min. in LA or 30 ml/min. in RA. PV disconnection was confirmed by the abolition or dissociation of the local PV potentials on the circumferential mapping catheter placed in an ostial position of each PV. PV disconnection that persisted during AF more than 30 min after the last RF application had to be confirmed in sinus rhythm, too. Additional LA linear lesions (LA roof line, mitral isthmus line – between mitral annulus and left inferior pulmonary vein) as well as cavotricuspid isthmus ABL were performed in patients with history of persistent AF, as well as in patients with regular atrial tachyarrhythmias that were documented prior to the ABL on standard ECG, by ICM or during entire ABL procedure. Linear lines were performed anatomically, and no electrical block was assessed.

Implantable loop recorder (ILR)

For the purpose of the study, the intra – cardiac monitor (ICM) Reveal® XT (Model 9529, Medtronic Inc., Minneapolis, MN) was used to perform continuous ECG monitoring. Each patient was implanted with the ICM several months before the procedure in order to characterize the baseline status of AF. All devices were inserted under