International Journal of Cardiology 174 (2014) 276–281

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Cerebral microembolization during atrial fibrillation ablation: Comparison of different single-shot ablation techniques

Alexandra Kiss *[,1], Edina Nagy-Baló [1], Gábor Sándorfi [1], István Édes [1], Zoltán Csanádi [1]

Institute of Cardiology, University of Debrecen, Debrecen, Hungary

ARTICLE INFO

Article history:
Received 14 January 2014
Received in revised form 10 March 2014
Accepted 29 March 2014
Available online 12 April 2014

Keywords:
Atrial fibrillation
Pulmonary vein isolation
Transcranial Doppler
Cerebral microemboli

ABSTRACT

Background: Clinically silent cerebral ischemia (SCI) detected by diffusion-weighted MRI has been reported in 5–40% of patients undergoing pulmonary vein isolation (PVI). Although initial reports suggested a high rate of SCI with phased radiofrequency (RF) ablation on use of the pulmonary vein ablation catheter (PVAC), the incidence was subsequently markedly reduced in consequence of procedural modifications in recent studies.
We analyzed cerebral microembolization as assessed with transcranial Doppler during phased RF ablation and with two other single-shot AF ablation technologies: the cryoballoon (CB) and the nMARQ™ multipolar irrigated RF ablation system.
Methods and results: A total of 89 patients (mean age: 57, SD: 12 years; 62 males) with paroxysmal or persistent AF underwent PVI. Phased RF was used according to the initial protocol in 7 patients (PVAC Group I), with procedural modifications and a newer (14.4) version of the RF generator in 37 patients (PVAC Group II) and with the most recent (version 15.1) generator in 18 patients (PVAC Group III). Ablation was performed with the CB in 13 and with the nMARQ system in 14 patients.
The number of microemboli (mean + (SD)) detected in the middle cerebral arteries was 2703 (918) in PVAC Group I, 1087 (542) in PVAC Group II, 719 (469) in PVAC Group III, 1057 (784) with CB and 2166 (1047) with nMARQ ($p < 0.01$).
Conclusion: Significant decreases in MES counts were observed thanks to the procedural modifications and newer RF generator with phased RF. High MES counts comparable to those with the initial phased RF resulted from the use of nMARQ.

1. Introduction

Pulmonary vein (PV) isolation (PVI) is an established method for the treatment of atrial fibrillation (AF), with a relatively low risk (<1%) of major periprocedural complications, including clinical stroke or transient ischemic attack (TIA) [1]. However, significant concern has been raised regarding the long-term safety of PVI as clinically silent cerebral ischemia (SCI) detected by diffusion-weighted (DW) MRI has been reported in 5–40% of the patients, depending on the ablation technology used [2–8]. Further, the limited data available suggest that a cognitive decline potentially related to SCI can be demonstrated several months after these ablations in some patients. In some studies, a markedly higher incidence of SCI was reported after PVI performed with phased radiofrequency (RF) and the PV ablation catheter (PVAC), as compared with the cryoballoon (CB) or focal irrigated RF ablation [2,3]. More recent reports with phased RF ablation, however, demonstrated a significant decrease in the incidence of SCI, these favorable results were attributed to the use of more rigorous periprocedural anticoagulation protocols and some specific modifications in the procedural technique [9–11]. These procedural changes were based on the results of animal studies [12,13] and included the avoidance of overlap between 2 electrodes during RF applications and careful sheath management to prevent air embolization. Software modifications refining the power handling of the GENius RF generator have also been implemented.

The recording of microembolic signals (MESs) in the middle cerebral arteries (MCAs) by transcranial Doppler (TCD) has been used to assess microembolization during different cardiovascular procedures [14–16]. Although DW MRI is regarded as the gold standard for the demonstration of cerebral lesions post-ablation, recording of the MESs provides a unique opportunity through which to monitor the intensity of microembolus generation during different phases of the procedure. In line with the initial DW MRI results, when we used the earlier version of the GENius generator we detected a significantly higher number of MESs during ablation with the PVAC as compared with the CB [17]. Further, we demonstrated that the majority of the microemboli were

* Corresponding author at: Institute of Cardiology, University of Debrecen, 22 Móricz Zs. Krt., Debrecen H-4032, Hungary. Tel.: +36 304152604; fax: +36 52414928.
E-mail address: kiss.alexandra@hotmail.com (A. Kiss).
[1] All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijcard.2014.03.175
0167-5273/

generated during the energy delivery (ED) with phased RF ablations, while the rate of microembolization was relatively uniform throughout the procedure with the CB. Whether the procedural and technical modifications which decreased lesion formation on DW MRI with the phased RF technology would also reduce the microembolization detected by TCD is unknown.

Phased RF ablations with the PVAC have been performed for 5 years in our center, using subsequent versions of the GENius RF generator together with specific procedural modifications to improve safety as suggested by the literature data. MESs are detected with TCD routinely during all AF procedures in our laboratory. In this study, we analyzed our TCD data obtained with phased RF ablations in relation to the procedural changes implemented in recent years. In order to view these results in context with other single-shot AF ablation technologies designed for fast and simplified PVI, we have compared the MES data with those obtained by using the CB and the novel nMARQ™ (Biosense Webster, Inc., Diamond Bar, CA, USA) multipolar irrigated RF ablation system.

2. Methods

2.1. Patients

Consecutive patients undergoing PVI for symptomatic paroxysmal or persistent AF not adequately controlled by at least one antiarrhythmic drug were considered for inclusion in the study. Exclusion criteria included long-standing persistent AF, hyper- and hypothyroidism, significant valvular heart disease, heart failure of NYHA class III or IV, a left ventricular (LV) ejection fraction ≤40%, a left atrial (LA) diameter exceeding 50 mm, a LA thrombus, unstable angina or myocardial infarction within the last 3 months, severe chronic obstructive pulmonary disease, known bleeding disorders, a contraindication to oral anticoagulation and pregnancy. All participating patients provided their signed informed consent prior to the procedure.

Further prerequisites for inclusion in this study were as follows:

1. Pre-ablation treatment with a vitamin K antagonist (VKA) for a minimum of 3 weeks and a therapeutic (above 2.0) international normalized ratio (INR) confirmed on the day of the procedure, and activated clotting time (ACT) levels above 300 s during ablations.
2. Bi- or unilateral TCD recordings of sufficient quality of the middle cerebral artery (MCA) throughout the LA access period.
3. Ablation performed with one of 3 single-shot technologies designed for PVI: phased RF, CB or nMARQ. As PVI with phased RF and the PVAC was performed with the use of 3 different versions of the GENius generator, and this was also accompanied by significant procedural modifications, the MES data acquired with this technology were analyzed separately in 3 treatment groups (PVAC Groups I, II and III).

2.2. Pre-ablation evaluation and LA catheterization

Patients were admitted to the hospital 1 or 2 days prior to the procedure. Transesophageal echocardiography was performed to exclude the presence of an intracardiac thrombus within 24 h before the ablation. All patients received oral anticoagulation before the PVI, with a target INR of 2.0 to 3.0.

All procedures were performed under conscious sedation with midazolam and fentanyl. Decapolar (BARD Electrophysiology Inc., Lowell, MA, USA) and quadripolar (Woxx 4 J, 6 F, Biotronik, SE & Co. KG, Berlin, Germany) catheters were advanced from the femoral vein and positioned into the coronary sinus and the right ventricle. Surface electrocardiograms and bipolar intracardiac electrograms were registered with a Prucka, GE Medical digital recording system. A single transseptal puncture was performed under fluoroscopic, or in some cases under intracardiac echocardiographic (ICE) guidance, using a Brockenbrough needle (St. Jude, Inc., Zaventem, Belgium) and a Swartz sheath (St. Jude, Zaventem, Belgium). This sheath was exchanged for the deflectable 12 Fr FlexCath sheath (Medtronic CryoCath LP, Kirkland, Quebec, Canada), which was flushed continuously with heparinized saline, and which was used with any of the ablation catheters utilized in this study. Immediately after the transseptal puncture, a 150 IU/kg body weight intravenous (iv) heparin bolus was administered, followed by a continuous infusion to maintain a minimum ACT target level of 300 s during ablations. Additional 2000–5000 IU iv boluses of heparin were administered as needed to attain the minimum target ACT level.

2.3. Ablation techniques

2.3.1. Phased RF ablation

The technical specifications of the PVAC and the GENius RF generator (Medtronic Inc., Minneapolis, MN, USA) have been described in detail [17–20]. The catheter was advanced through the FlexCath sheath over a 0.032-inch guidewire (BARD Electrophysiology Inc., Lowell, MA, USA), which was positioned selectively in each PV. The electrical conduction properties of the PV were assessed on the basis of the signals recorded by the PVAC electrodes after placement inside the ostium. Before the first RF application at each PV, the positions of the electrodes relative to the PV ostium were always confirmed by means of contrast injection through the FlexCath sheath. Care was always taken to apply the RF outside the PV in the antral region, targeting potentials of high amplitude on as many electrodes as possible for each application. RF energy was applied for 60 s, usually 3–4 times per PV, until PVI was achieved. The target temperature was 60 °C, measured separately for all bipoles. Any electrode pair that failed to reach at least 50 °C during RF delivery was switched off to avoid ineffective ED due to improper contact at the electrode–tissue interface. Common ostia were isolated by inserting the guidewire into the different side branches and ablating subsequent segments of the targeted veins. The PV conduction was reassessed after each RF application, the electrodes being advanced inside the ostium. The endpoint of the procedure was the electrical isolation of all PVs, as confirmed by an entrance block.

The GENius RF generator is capable of delivering RF in a duty-cycled mode with different bipolar/unipolar ratios to any or all of the electrodes on the PVAC. Three consecutive versions of the GENius RF generator (Medtronic Inc., Minneapolis, MN, USA) were used in the course of recent years, also coupled with some procedural modifications as follows:

1. *PVAC Group I.* Initial series of ablations were performed with the use of software version 14.3 for the GENius generator. Bipolar/unipolar RF application was started at a ratio of 4:1 for each PV and changed to a bipolar/unipolar ratio of 2:1 for a deeper lesion when a sufficient reduction in local electrogram amplitude could not be achieved after multiple RF deliveries. No attempts were made to avoid the potential interaction between the first and the last electrode (E1–E10) in the PVAC.
2. *PVAC Group II.* Ablations were performed with software version 14.4 for the GENius generator. Modifications in the procedural technique were implemented in this group of patients as follows. Potential interaction between the most distal (E1) and the most proximal (E10) electrodes was considered and simultaneous EDs on these poles were attempted only after fluoroscopic assessment of the interelectrode distance, which was considered adequate if the space between E1 and E10 was at least double the fixed 3-mm interelectrode distance as assessed from multiple projections. Furthermore, ablations were started in the 2:1 mode and changed to 1:1 in those rare instances when adequate amplitude change and PVI could not be achieved after multiple RF applications. In addition, the distal circular segment of the PVAC catheter was submerged and captured by the introduction device in a saline bath prior to insertion into the FlexCath sheath. This maneuver was used to prevent air entrapment around the array and the introduction of air into the LA through the transseptal sheath.
3. *PVAC Group III.* Ablations were performed using the most recent software version (15.1) for the GENius generator. RF delivery to E10 is not supported by this software thereby excluding the possibility of E1–E10 interaction. No procedural modifications as compared to those in PVAC Group II were implemented during these ablations.

2.3.2. CB ablation

The technology of CB ablation has been described in detail [17]. In brief, a 28-mm CB was used in all cases. The CB was introduced into the PV ostium over an inner lumen mapping catheter (Achieve, Medtronic Ablation Frontiers LCC, Carlsbad, CA, USA) which is capable of mapping PV potentials before, during and after cryo applications. The best possible occlusion of the PVs was facilitated by the steerable sheath and by positioning the guidewire in a PV branch to provide maximal support. Furthermore, all special maneuvers described previously, such as the “pull-down” or the “hockey stick” techniques, were used as needed [21].

PV occlusion was assessed by means of a hand-held injection of contrast medium (Optiray Covidien Deutschland GmbH, Neustadt/Donau, Germany) through the injection side-port of the Arctic Front catheter. A minimum of two 5-min freezing cycles were applied per PV. The balloon was repositioned for each application, preferably with the guidewire situated in a different branch of the PV in order to maximize the effect of freezing at different aspects of the ostium. Before the start of ablation of the septal veins, a quadripolar catheter was placed in the superior caval vein, where constant capture of the right phrenic nerve could be achieved. One stimulus at maximal output was delivered every 5 s, with manual assessment of the diaphragmatic movement. The freezing cycle was terminated immediately if loss or weakening of the diaphragm response occurred. PVI was assessed on the basis of the signals recorded by the Achieve wire.

2.3.3. nMARQ ablation

The nMARQ™ (Biosense Webster, Inc., Diamond Bar, CA, USA) is a multi-electrode, irrigated RF ablation catheter with a uni-directional deflectable tip. The distal tip section is circular or semilunar and contains 10 platinum ring electrodes with irrigation holes at both ends for stimulation, recording and ablation. The diameter of the circular or semilunar loop is variable to accommodate the LA anatomy. The catheter is integrated with the CARTO 3 electroanatomical mapping system, which provides mapping and real-time navigation capabilities. For ablation, the catheter is used in conjunction with the nMARQ ™ Multi-Channel RF Generator, which is able to deliver RF simultaneously to multiple electrodes in unipolar or bipolar mode.

The circular-tip catheter was used exclusively in this study. The catheter was advanced to the LA through the FlexCath guiding sheath. The 3-dimensional map of the LA was constructed by using the CARTO™ electroanatomical mapping system (Biosense Webster, Inc., Diamond Bar, CA, USA) equipped with Cartomerge™ software (Biosense Webster, Inc., Diamond Bar, CA, USA). The pre-ablation cardiac CT image of the LA with the proximal portions of the PVs was imported and registered for real-time mapping, focusing on the PVs and the PV antra of the LA. In addition, the positions of the electrodes relative to the PV ostium were always confirmed before the first RF application at each PV, by means of contrast injection through the FlexCath sheath. Care was taken to apply