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Original Article

The feasibility of a Box isolation strategy for non-paroxysmal atrial fibrillation in elderly patients

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ABSTRACT

Background: Catheter ablation of non-paroxysmal atrial fibrillation (non-PAF) is a therapeutic challenge especially in elderly patients. This study describes the feasibility of a posterior left atrium isolation as a substrate modification in addition to pulmonary vein isolation, the so-called Box isolation, for elderly patients with non-PAF.

Methods: Two hundred twenty-nine consecutive patients who underwent Box isolations for drug-refractory non-PAF were divided into two groups according to their age; younger group comprising 175 patients aged <75 years and elderly group comprising 54 patients aged ≥ 75 years.

Results: During 23.7 ± 12.0 months of follow-up, the arrhythmia-free rates after one procedure were 53.1% in younger group versus 48.1% in elderly group ($p=0.50$). Following the second procedure, all patients had electrical conduction recoveries along the initial Box lesion. However, a complete Box re-isolation was highly established in both age groups (87.1% vs. 92.9%, respectively; $p=1.00$). Recurrence of macro-reentrant atrial tachycardia was mainly associated with the gaps through the initial Box lesion in both age groups (25.8% vs. 21.4%, p=1.00), but typical cavo-tricuspid isthmus (CTI) dependent atrial flutter was significantly observed in the elderly patients' group only (all events were observed within 6 months after the initial procedure; 3.2% vs. 28.6%, $p=0.009$). After two procedures, the arrhythmia-free rates increased to 73.1% in younger group versus 66.7% in elderly group ($p=0.38$). The occurrence rate of procedural-related complications did not differ between the two age groups, and there were no life-threatening complications even in elderly patients.

Conclusions: Box isolation of non-PAF is effective and safe even in elderly patients. A prophylactic CTI ablation combined with Box isolation might be feasible to improve the long-term outcome.

1. Introduction

The prevalence of atrial fibrillation (AF) increases steadily with age [1]. Since elderly patients have age-related degenerative changes that result in high rates of medical comorbidities, hepatic and kidney dysfunction, and physiologic changes of the atrial substrate, these factors can render the catheter ablation of AF a therapeutic challenge [2–4]. Nonetheless, because of the remarkable progress of catheter ablation of AF over the last decade, the effectiveness and safety of catheter ablation in elderly patients have been reported [4–7]. Moreover, the indications of AF ablation have been broadened in clinical practice. However, catheter ablation of non-paroxysmal AF (PAF) for elderly patients remains a therapeutic challenge since it has a less favorable outcome than that of PAF, and frequently requires additional ablation strategies for substrate modification, in addition to pulmonary vein isolation (PVI) [8,9]. There is still a paucity of data regarding catheter ablation as a therapeutic choice for non-PAF in elderly patients.

Referring to the ablation strategies for substrate modification of non-PAF, there are two most widely used additional ablation strategies that target the roof and mitral isthmus linear lesions [8–10] or complex fractionated electrograms [8,9,11]. However, in the Substrate and Trigger Ablation for Reduction (STAR) of AF II trial, those ablation strategies could not improve the cure rate as compared to PVI alone [8]. There is another method for an extensive substrate modification ablation targeting the isolation of the posterior left atrium (PLA), the so-called Box isolation [12,13]. This strategy arose from the concept that the PLA would play an

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important role in the maintenance of AF [14–16]. In the latest study, the PLA isolation with a PVI demonstrated a significantly high rate of sinus maintenance compared to PVI alone in patients with persistent AF [17]. However, to the best of our knowledge, there have been no reports on the feasibility of the Box isolation strategy regarding the impact of aging. Therefore, the aim of this study was to evaluate the long-term efficacy and safety of this Box isolation strategy for elderly patients with non-PAF.

2. Materials and methods

2.1. Study population

This retrospective study included all the patients who underwent catheter ablation with the Box isolation strategy for drug-refractory non-PAF, at Hayama Heart Center between January 2012 and December 2014. All patients underwent computed tomography (CT) before each procedure for exclusion of any left atrial thrombi and assessment of the morphology of the PVs and left atrium (LA). In the case of an uncertain thrombus, an additional trans-esophageal echocardiogram was performed to confirm it. The exclusion criteria in this study were patients with prior AF ablation attempts (radiofrequency hot balloon-based, surgical-based, or catheter-based), under dialysis, or those who had failed to be followed up for no less than 6 months. The enrolled patients were divided into two groups according to age <75 years and ≥ 75 years. Persistent AF was defined as AF episodes lasting >7 days and/or requiring intervention for termination, and long-standing persistent AF was defined as continuous AF uninterrupted for >1 year [18]. All the patients gave their written informed consent before the procedure.

2.2. Electrophysiological study

All the procedures were performed under intravenous sedation. A probe (Esophastar, Japan Lifeline) that during the procedure was inserted through a nasogastric tube monitored the intraluminal esophageal temperature (LET) [19]. After the transseptal access, an initial intravenous heparin bolus (100–200 IU/kg) was administered, with an additional bolus to maintain the activated clotting time between 300 and 400 s. Two decapolar circular mapping catheters (Libero, Japan Lifeline, Japan) through two long sheaths (SL-0, St Jude Medical, St. Paul, MN) and a quadripolar open 3.5-mm tip irrigated radiofrequency ablation catheter (Thermocool Navistar, Biosense Webster or CoolPath Duo Sofiable, St. Jude Medical, St. Paul, MN) through a deflectable sheath (Ultimum Agilis, St. Jude Medical, St. Paul, MN) were introduced into the LA by one transseptal puncture. A steerable quadripolar electrode catheter (Inter NOVA, Chiba, Japan) was positioned in the right ventricular apex; a duo-decapolar electrode catheter (Inter NOVA, Chiba, Japan) was positioned within the right atrium; and a duo-decapolar electrode catheter (Inquiry catheter, St. Jude Medical, St Paul, MN) was positioned within the coronary sinus (CS). The mapping and ablation were guided by a 3 dimensional electroanatomic mapping system integrated with multislice CT imaging (CARTO Merge, Biosense Webster, Diamond Bar, CA, or NavX, St. Jude Medical, St. Paul, MN).

2.3. Ablation protocol for the Box isolation in the initial procedure

At the beginning, a contiguous line was created at the roof of the LA between the superior PVs with a radiofrequency (RF) power of 25–30 W. The energy was delivered at each site until local electrograms were no longer obtained (or reduced to <0.05 mV) or the impedance dropped by 20 Ω. In creating a contiguous line, the formation of double potentials was also defined as the local endpoint of the ablation. After completion of the roof line, a left ipsilateral PV isolation was performed by first creating a contiguous line at the anterior portion, while the posterior portion of the ipsilateral PVs was electrically ablated, targeting only the sites of the earliest activation. Thereafter, a contiguous line was created at the floor line connecting both the inferior PVs. The RF energy was reduced to 20 W near the esophageal region. When the LET exceeded 39 °C during the RF delivery, the energy was terminated immediately, and 10–20 mL of cooling solution was repeatedly injected through the gastric tube to prevent the incidence of esophageal thermal injury [19]. Finally, the right antra of the ipsilateral PVs were ablated with the same technique as that for the left PVs. By moving up the anterior-superior contiguous line to join the previous roof line, the Box lesion was created. Further, a mapping catheter was placed on the posterior wall to confirm whether the PLA potentials still existed. If any potential remained within the Box lesion, detailed point-by-point mapping along the roof and floor lines was performed to identify any gaps. If needed, a decapolar ring catheter was placed on the posterior wall in order to determine the activation sequence or identify the earliest breakthrough, and another repetitive mapping and ablation was performed. Thereafter, if AF did not convert to sinus rhythm, electrical cardioversion was administered aiming to restore the sinus rhythm. The endpoint of the Box isolation was (1) all electrical activity dissociated or absent within the Box area during sinus rhythm or under CS pacing, and (2) pacing from the PLA and all four PVs during sinus rhythm was unable to capture the myocardium outside the Box area.

Finally, 20 mg of ATP was rapidly injected to evaluate the dormant conduction. If any sustained typical cavo-tricuspid isthmus (CTI) dependent atrial flutter (AFL) was documented before or during the procedure, a CTI ablation was performed. No aggressive attempt was made to create a mitral isthmus line unless any sustained perimitral AFL appeared during the procedure.

2.4. Study endpoints and follow-up

Follow-up visits were scheduled every 1–3 months after the procedure, including a physical examination and 12-lead electrocardiogram. Twenty-four-hour Holter monitoring was performed every 6 months, and before the discontinuation of anti-arrhythmic drugs (AADs) or when the patients felt an irregular pulse or any symptoms of recurrence. The patients were recommended to have an event recorder and were instructed not only to record all symptomatic events, but also to record at fixed intervals to detect any asymptomatic events. In patients with implanted devices such as a pacemaker, ICD, or CRT, interrogation of the devices was also used to confirm any arrhythmia recurrence. Oral anticoagulation therapy (OAT) was generally discontinued after 3–6 months in patients without AF recurrences, according to the $CHADS_2$ score. The AADs were gradually decreased after 3 months, depending on any AF/atrial tachycardia (AT) recurrence or the referring physician's decision. Recurrence was defined as episodes of AF or AT lasting >30 s that were documented by any monitoring modality. A second procedure was strongly recommended after the 3-month blanking period.

2.5. The second procedure

The electrophysiological study was the same as that in the initial procedure. First, if the patients were in macro-reentrant AT when the procedure was initiated, they underwent activation and entrainment mapping using electroanatomical mapping and ablation. Thereafter, mapping along the entire previous ablation line was systematically performed to identify the gaps under sinus