Pulmonary vein isolation with "ablation index" via single trans-septal crossing: Critical role of carina isolation.

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Abstract

Background. Pulmonary veins (PV) reconnection is the most common reason for atrial fibrillation (AF) recurrence. The ablation-index is a marker of ablation lesion quality which use achieves high percentages of first pass isolation and improved results of AF ablation. Most operators use a double trans-septal approach with confirmation of PV isolation with a circular mapping catheter. In the present study we aimed to show that an ablation-index guided procedure using a single trans-septal approach and ablation catheter only would achieve adequate PV isolation while demonstrating the critical role of the carina in PV isolation. Methods. 76 consecutive patients with paroxysmal AF: 34 patients underwent WACA, 32 patients underwent WACA+ (including empiric carina isolation) and 10 patients underwent a staged procedure of WACA followed by WACA+ in case of lack of first pass isolation. All procedures were performed via single trans-septal. Results. Compared to WACA-only, WACA+ increased the odds of PV isolation from 65% to 91%, p=0.012. In WACA-only, ablation of the carina was needed to achieve PV isolation. The role of the carina was confirmed in 10 patients with sequential ablation. PV isolation was confirmed by inserting a circular mapping catheter through the single trans-septal sheath. At 18 months of follow-up [IQR 15.2-20.8 months], freedom from AF was 84% for the entire cohort. Conclusion. Our study confirms the high success rate of PV isolation using ablation index and shows that this can be achieved via single trans-septal crossing. Our study confirms the role of the carina in PV isolation.

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Methods. 76 consecutive patients with paroxysmal AF: 34 patients underwent WACA, 32 patients underwent WACA+ (including empiric carina isolation) and 10 patients underwent a staged procedure of WACA followed by WACA+ in case of lack of first pass isolation. All procedures were performed via single trans-septal.

Results. Compared to WACA-only, WACA+ increased the odds of PV isolation from 65% to 91%, p=0.012. In WACA-only, ablation of the carina was needed to achieve PV isolation. The role of the carina was confirmed in 10 patients with sequential ablation. PV isolation was confirmed by inserting a circular mapping catheter through the single trans-septal sheath. At 18 months of follow-up [IQR 15.2-20.8 months], freedom from AF was 84% for the entire cohort.

Conclusion. Our study confirms the high success rate of PV isolation using ablation index and shows that this can be achieved via single trans-septal crossing. Our study confirms the role of the carina in PV isolation.

Introduction :

Radiofrequency (RF) catheter ablation is an accepted therapy for patients with symptomatic, drug-refractory, paroxysmal atrial fibrillation (AF). A fundamental step during this ablation procedure, involves performing electrical isolation of the pulmonary veins (PVs) by creation of a set of circular lesions around the pulmonary veins antrum (WACA).[1-10] However, permanent and complete isolation of all pulmonary veins is challenging. In fact, electrical reconnection of the pulmonary veins is the most frequent finding when a second ablation procedure is performed following recurrence of atrial fibrillation.[11-16] Therefore, technological innovations that will improve the thoroughness of ablation during WACA are continuously developed.

The Visitag module with ablation-index was recently integrated in the Carto 3V4 mapping system (Biosense Webster, Inc, Diamond Bar, CA,USA) as an indicator of ablation lesion quality. The ablation-index formula incorporates contact force (CF), power and ablation-delivery time into a single value that also takes into account catheter stability at the time of RF delivery. In a prospective study, Das et. al showed that lack of achievement of minimum values of ablation-index, at any given pulmonary vein segments, was predictive of pulmonary vein reconnection at a repeated electrophysiology study performed two months later.[17] More recently, Hussein et al. reported a 97% isolation of the pulmonary veins following a first pass of WACA when an ablation index of 500 and 400 were used at the roof-ridge and the posterior-inferior quadrants, respectively.[18] In the remaining 3% of WACA with lack of first pass isolation, additional RF delivery was needed and this was invariably at the carina level.[18] In these studies, a double trans-septal technique was performed to allow for the introduction of a circular mapping catheter along the ablation catheter in the left atrium, to monitor and confirm PV isolation during WACA. Continuous recording of the PV electrograms during WACA may represent a potential bias since the operator could instinctively ablate longer of more diffusely in area of WACA associated with changes in activation on the circular mapping catheter or leading to PV isolation.

Limiting the number of trans-septal crossings during an ablation procedure is important, particularly for safety reasons but also for an economic perspective. We therefore performed the present study to show that: 1) An ablation-index guided procedure *using a single trans-septal approach* would succeed in achieving complete acute PV isolation while obviating the need for a double transeptal. 2) RF ablation of the carina area is crucial for achieving complete PV isolation. Accordingly, we tested the following new strategy: 1) WACA based on the new ablatio-index was performed with a single trans-septal puncture. 2) The completeness of pulmonary vein isolation was confirmed with the ablation catheter. As part of the study protocol, at the end of the procedure the ablation catheter was replaced by a standard circular mapping catheter to confirm that the assessment of PV isolation made with the ablation catheter is indeed correct. 3) We tested the contribution of carina ablation to achieve acute complete PV isolation by comparing the acute success rate (defined as first pass complete PV isolation) among patients undergoing a standard WACA vs. patients undergoing WACA plus carina isolation (WACA+).

Methods .

Study patients. The study included consecutive patients with symptomatic, drug-refractory paroxysmal AF, referred for a first ablation. All the procedures were performed by a single operator (R.R.) experienced with atrial fibrillation ablation procedure, including the use of contact-force sensing ablation-catheters and the use of Visitag and ablation-index. The AF ablations were performed between December 2017 and April 2019. Outcome data were extracted from an institutional review board-approved registry.

Atrial fibrillation ablation technique. The procedure was performed under uninterrupted warfarin therapy (aiming for an INR of 2 on the day of the procedure) or after skipping a single dose of new oral anticoagulants (NOAC). All antiarrhythmic agents, except amiodarone, were discontinued before the procedure. A computerized tomography angiogram (CTA) of the left atrium was performed before the ablation to assess the left atrial size, PV anatomy and to exclude the presence of left atrial appendage thrombi. Patients in whom the CTA could not definitively exclude the presence of left atrial appendage thrombi underwent a trans-esophageal echocardiogram (TEE) before or during the procedure. The ablation procedure was conducted under general anesthesia.

One decapolar and 1 quadripolar catheter were positioned in the coronary sinus and the His bundle position through the right femoral vein. One 8.5F long sheath (SL1, St. Jude Medical, Minneapolis, USA) was introduced into the left atrium with a single trans-septal puncture. Intravenous bolus of heparin was injected intravenously just prior to the trans-septal puncture and repeated as needed to maintain an activated clotting time (ACT) of >350 seconds throughout the procedure. All PVs were visualized by selective angiography. The PV antrum was defined with angiography and the segmented left atrial CTA imported in the Carto 3 mapping system (Biosense Webster). A Lasso circular mapping catheter (Biosense Webster) was introduced through the SL1 sheath into the left atrium for electrical mapping of the PVs and then retrieved. At this point, an irrigated ablation catheter3.5-mm D-F curve ablation catheter with smart-touch technology (Navistar Thermocool, Biosense Webster) was introduced through the original SL1 sheath into the left atrium for ablation. In case of difficulties in positioning the ablation catheter in the left atrium, the SL-1 sheath was replaced with a steerable sheath (Agilis 8.5F, t. Jude Medical, Minneapolis, USA). The ablation catheter was used to create a fast-anatomic map (FAM) of the left atrium, to set landmarks (PV drop-off points into the left atrium) necessary to merge the CTA scan of the left atrium to the FAM (Carto Merge, Biosense Webster, Inc). Ablation was performed with a "point by point" technique. Settings were: catheter irrigation-flow rate of 18 mL/min, target temperature 45° and maximal energy of 25 W for the posterior atrial wall and 30 W for the ridge and carina areas. During the ablation we aimed to achieve a contact force of 10 to 50 grams at all times. RF energy was applied at each ablation site using the automated lesion tagging ablation-index to mark the location and efficacy of each lesion. The ablation-index settings were: catheter stability position minimum-time of 5 seconds, and maximum range 3-4 mm, minimum force 3 g, (the blue and yellow marks give two different contact force values) and lesion tag of 2 mm. The maximal RF time at each ablation site was 60 seconds. We aimed for a minimum ablation-index value of 415 for the back wall and posterior half of the carinas, 515 for the anterior ridge, roof, inferior quadrants and anterior half of the carinas. We aimed for ablation dots that overlap each other along the WACA. The exclusion of gaps in between the dots was also evaluated with the use of the grid function on the mapping system. The grid function identifies all areas where radiofrequency energy was delivered including those were Visitag did not tag the ablation due to poor catheter stability. This feature allows for better identification of potential gaps hiding in between the Visitag dots.

Ablation groups. The first 34 patients underwent two WACA ablation lesions, each one encircling the antrum of two ipsilateral pulmonary veins (WACA group). A second group of 32 patients underwent, in addition to the WACA ablation, also ablation along the carinas (WACA+ group) (fig.1). After realizing that the WACA+ plus had better results in terms of PV isolation, we added a small third group of 10 patients who underwent a staged procedure. For these 10 patients, we first performed a standard WACA step. Upon completion of the WACA, the presence of PV isolation was evaluated by placing the ablation catheter at the carina, proximal to the WACA line. Isolation was assumed to be present if pulmonary vein potentials were not recorded distal to the WACA and exit block was demonstrated. In case of residual electrograms recorded with the ablation catheter distal to the WACA, the location of earliest activation was tagged on the mapping system. As for the original 2 groups (WACA and WACA+ groups), the isolation was then confirmed with the circular mapping catheter.

Ablation endpoint. Upon completion of the ablation set, the ablation catheter was withdrawn from the left atrium and replaced by a lasso circular mapping catheter. The acute end-point of the procedure was first pass electrical isolation of the PVs demonstrated by disappearance of local PV electrograms and confirmed by standard pacing maneuvers, to confirm entrance and exit block, with a lasso circular mapping catheter. In case of lack of isolation, the conduction gaps were tagged on the mapping system and additional RF ablation with the same ablation index targets was delivered in the identified gap areas. At this point the ablation catheter was once again exchanged for the circular mapping catheter and PV isolation was checked again. In case of lack of isolation, the same maneuver was repeated until the vein was isolated. After a waiting period of 20 minutes from the last ablation, each pulmonary vein was assessed for entrance and exit block. Each vein was also assessed for the presence of dormant pulmonary vein-left atrium connection with intravenous adenosine 18 mg injection. Patients with evidence of dormant connections revealed by adenosine challenge, received additional ablations according to the mapping catheter until the connections were completely abolished.

Post-procedure Care. After the ablation procedure, patients on warfarin received low molecular weight heparin until an INR of 2.0–3.0 was achieved. Warfarin was administered for at least 3 months in patients with CHA2DS2VASc 0–1 score or indefinitely in patients with CHA2DS2VASc of 2 or more. Patients previously treated with NOACs, underwent the ablation after skipping one dose. The NOAC therapy was restarted between 3-5 hours post procedure and continued for at least 3 months in patients with CHA2DS2VASc 0–1 score or indefinitely in patients with CHA2DS2VASc of 2 or more. Antiarrhythmic therapy was restarted immediately after the procedure and continued for 1 month.

Follow-Up. Clinical and electrocardiographic follow-up was performed at 3, 6, 9, and 12 months, respectively, and every 6 months thereafter. Holter monitoring was performed at 2- and 3-months post procedure and then twice every 6 months. Holter recordings and trans-telephonic monitoring were also performed when symptoms suggested recurrence. Episodes of atrial tachycardia on Holter (number of episodes, number of beats and heart rate) lasting less then 30 seconds were analyzed for the prediction of atrial fibrillation recurrence. AF recurrence was defined by the presence of symptoms suggestive of AF and/or electrocardiographic documentation of> 30 seconds of AF/atrial flutter/atrial tachycardia beyond the first 3 months after the procedure off antiarrhythmic drugs AADs.

Statistical methods.

Continuous variables are shown as Mean ± SD or as Median [IQR] as appropriate, while discrete variable as n(%). Comparison of continuous variables was preformed using Mann-Whitney U test, while comparison of discrete variables using Fisher's exact test. Event free survival was assed using Kaplan-Mayer curves, statistical significance of the difference between curves was assessed using a log-rank test. Results were considered significant when $p<0.05$. All calculations were done using R version 3.5.0, R Foundation for Statistical Computing, Vienna, Austria.

Results.

A total of 76 consecutive patients with symptomatic, drug refractory paroxysmal AF were enrolled. The study group included 34 patients undergoing WACA and 32 patients undergoing WACA+. Finally, 10 patients underwent a staged procedure of WACA that was followed by WACA+ in case of lack of first pass isolation with WACA only (Table 1). Procedural time, dwell time, fluoroscopy time and radiofrequency time were not different between the study (WACA and WACA+) groups (Table 2).

In contrast to a WACA only approach, the WACA+ approach (of systematically performing ablation of the carina in addition to WACA) increased the odds of achieving PV isolation from 65% (22 of 34 in the WACA group) to 91% (29 of 32 in the WACA+ group, p=0.012). Analysis of patients not achieving first pass PV isolation further demonstrated the crucial role of the carina. In the WACA-only group, first pass isolation was not achieved in 12 patients: in 7 patients (representing 20% of the WACA group and 58% of the WACA not achieving first pass PV isolation), the right carina had to be ablated to achieve right sided veins isolation; in 3 patients, the left carina had to be ablated to achieve left sided veins isolation; finally, in 2 (6.7 %) patients both carinas had to be ablated to achieve pulmonary veins isolation.

In the WACA+ group, first pass isolation confirmed with circular mapping catheter was achieved in 29 (91%) of patients. Two patients (9%) required additional ablations to achieve isolation. In the first, this was delivered at the anterior ridge where the previous ablation reached an ablation index value of 480, while in the second additional ablation was required at the anterior carina.

Based on the results of the study group (WACA and WACA+ groups) pointing out at the carina as a critical site that needs to be ablated to achieve complete PV isolation, we added a small third group of 10 patients who underwent a step-by-step ablation of WACA and carina. In group 3, before the carina was ablated, first pass isolation was achieved in 2 patients (20%) patients only. In all patients the lack of isolation and its location demonstrated with the ablation catheter was confirmed with the circular mapping catheter. In the remaining 8 patients, the left carina, the right carina and both carina areas, had to be ablated to achieve PV isolation in 4 (40%), 2 (20%) and 2 (20%) patients, respectively.

Adenosine challenge revealed dormant PV-LA connections in 5/34 (14.7%) in the WACA group, 4/32 (12.5%) in the WACA+ patients and 1/10 (10%) in group 3 (p=NS). In 4 of 5 patients with dormant PV-LA connection revealed by adenosine in group 1, the dormant connection was detected in the 3 at the left carina, in 1 in the right carina and in 1 at the anterior ridge. In group 2, the dormant connections were detected at the left carina and the right carina in 2 patients each. In group 3 dormant connection was detected at the left carina.

At the procedure termination, acute pulmonary vein isolation was achieved in 100% of pulmonary veins ablated in the three groups.

No major complications occurred in any of the patients enrolled.

At a mean follow up of 18 months [IQR 15.2-20.8], freedom from atrial fibrillation was 84% for the entire cohort. In group 1 the success rate was 76.5% (26/34). In group 2 the success rate was 87.5% (28/32), (p=0.342). In group 3 the success rate was 90% (9/10). In view of the small number of patients, the success rate of group 3 was not compared to that of group 1 and 2.

Discussion.

The present study confirms the high success rate of pulmonary vein isolation using ablation index: Our long-term results, with freedom from atrial fibrillation in 84% of patients, are similar to those achieved by other groups using ablation index.[18-21]

Previous studies have shown a higher rate of first pass isolation using ablation index compared to conventional ablation settings and force time integral (FTI) and the need for ablation of the carina in case of lack of first pass isolation.[18 20 22] In all these studies, the ablation was conducted with a circular mapping catheter positioned at the pulmonary vein to confirm isolation during the ablation through as double trans-septal approach. In contrast, in the present study we demonstrate that a strategy of ablation solely based on the use of the ablation catheter through *a single trans-septal puncture*consisting of *WACA plus empiric carina ablation guided by ablation index* , can reliably achieve high percentages of first pass isolation. Moreover, the confirmation of pulmonary vein isolation can be effectively performed with the use of the ablation catheter only by the identification of residual electrograms distal to the WACA and by pacing maneuvers demonstrating exit block. A strategy solely based on the use of the ablation catheter via single trans-septal crossing, has several potential advantages. Every trans-septal puncture potentially involves important risk of complications in particular pericardial effusion and tamponade, inadvertent puncture of the aorta or air embolism.[23-25] A single trans-septal puncture would intuitively results in a lower incidence of complications. Also, use of only an ablation catheter would results in reduction in procedural costs. Finally, having only one (as opposed to two catheters) in the left atrium, simplifies catheter manipulation during the ablation procedure, particularly in small atria.

The role of carina ablation to achieve pulmonary vein isolation has been previously reported[26-29] and is here confirmed. In our study first pass isolation was significantly higher in patients when the strategy of WACA was complemented by carina ablation. This is probably due to the presence of pulmonary vein muscular fibers connecting ipsilateral veins at the carina.[30 31] Indeed first pass isolation was achieved in all but two patients in whom empiric carina ablation was added to the WACA and in one of the two patients with residual PV electrograms the residual connection was located at a site on the anterior ridge where the AI didn't reach the target value of 515. Moreover, dormant PV-LA connections, revealed by adenosine challenge, were mapped at the carina in all but one case. The presence of dormant PV-LA connections at the carinas despite RF ablation this area an ablation index between 415 and 515, and the need for additional RF applications at this area, might be related to the epicardial nature of the muscular sleeves connecting the ipsilateral PVs at the carina[30 31].

Limitations:

Our study has potential limitations. The study is single center and was non-randomized and therefore bias related to the strategy of ablation applied for each patient cannot be excluded. Nevertheless, the findings of the present study are important. A strategy of ablation based solely on the use of ablation catheter with single trans-septal, ablation guided by AI based on WACA and additional carina ablation can achieve high rate of first pass isolation safely and with high long-term success rate. Randomized, larger studies are needed to confirm the feasibility of this approach.

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`Table 2.Procedural data.docx` available at https://authorea.com/users/357822/articles/480221-pulmonary-vein-isolation-with-ablation-index-via-single-trans-septal-crossing-critical-role-of-carina-isolation

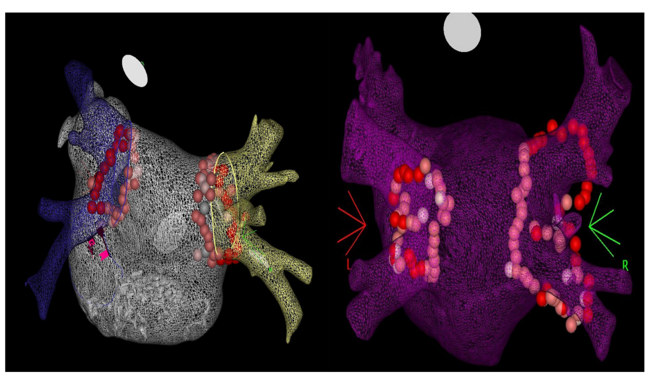

Fig1.: Posterior-anterior view of the ablation set in WACA only in A and WACA+ in B