Coronary Sinus Electrograms May Predict New-onset Atrial Fibrillation After Typical Atrial Flutter Radiofrequency Ablation (CSE-AF)
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Introduction
Cavo–tricuspid (CTI) radiofrequency ablation (RFA) is a standard treatment for common atrial flutter (AFL). Due to high safety profile and success rate, this procedure is appreciated as a first line of management[1]. Nevertheless, atrial fibrillation (AF) is commonly associated and documented after CTI ablations[2–5].

The coronary sinus is electrically connected to the right and left atrium and hence its signal obtained from this position reflect right and left atrial activities[6]. Fractionated atrial electrograms suggest inhomogeneous intra atrial conduction with great predisposition to develop AF[7]. Patients who develop AF post ablation have higher prevalence of proximal CS complex fractionation that, in turn, is associated with slowed electrical conduction[8].

The aim of our study was to assess whether the presence of fractionated CSE and delayed electrical conduction at coronary sinus os region are associated with a risk of developing AF after CTI ablation in patients undergoing typical flutter ablation and no prior history of AF. These parameters signify the role of Atrial scar burden in development of AF[6],[8],[9].

Methods
Patient Characteristics
The study was approved by Queen’s University research and ethics board, Kingston, Canada. The retrospective cohort was selected from consecutive patients admitted to Kingston General Hospital for catheter ablation of common typical AFL from January 2008 to December 2011 were followed up over a time period of 55.1± 15.8 months. Most of the patients were at sinus rhythm (30/40, 75 %) with clearly documented typical AFL before admission to the cath lab.

Patients were excluded if they had: (i) redo-ablations, or history of any previous ablation (ii) non CTI-dependent circuits, (iii) use of antiarrhythmic drugs after the ablation, (iv) Patient underwent pacemaker implant and/or developed another atrial arrhythmias or (v) lost to follow-up records. Demographics, co-morbidities, history of cardiac disease, CHADS2 score and echocardiographic parameters

Key Words
Atrial Fibrillation, CSEs Represent Left Atrium, Radiofrequency Ablation (RFA), Cavo-tricuspid (CTI)
prior to ablation, including LA diameter and left ventricular ejection fraction (LVEF) were also collected during follow up. We have no patients with history of cardiomyopathy at the time of ablation.

**Electrophysiology Study and Catheter Ablation**

The coronary sinus was cannulated in all cases using a decapolar coronary sinus catheter (Abbott, St. Paul, MN, USA) with 2 mm interelectrode distance and 5 mm space between two electrode pairs. The proximal pair of electrodes was positioned at the coronary sinus ostium and the distal pair of electrodes was located at the lateral aspect of the great cardiac vein. Stability of the electrode catheters within the coronary sinus was maintained by fluoroscopic monitoring. A 20-poles (i.e. Halo) catheter (2-4-2 mm spacing) was positioned close to the anterior/superior tricuspid annulus (St. Jude Medical, St. Paul, MN, USA)

Ablation was performed using a 4-mm irrigated FlexAbility catheter (St. Jude Medical, St. Paul, MN, USA) positioned along the CTI until termination of atrial flutter and/or the development of bidirectional block (in SR group). CTI block was accepted when (1) complete reversal of the right atrial depolarization on the 24-pole catheter when pacing in the coronary sinus, (2) conduction delays from proximal (i.e. CS 9-10 poles) to lateral CTI at distal Halo pole 1-2 (i.e. lower lateral right atrium) greater than any other intervals between those two points and the same apply other direction (i.e. lateral to medial).

**Study Protocol and Signal Recording**

CS electrograms were analysed electronically off line using computerized recording system (Cardiolab System by Prucka Engineering Inc., Houston, Texas). Bipolar electrograms were filtered at a frequency of 30–500 Hz.

The total duration of the CS electrogram was measured from initial activation to electrogram termination. Total signal durations of proximal (C 9-10), mid (C 5-6) and distal (C 1-2) coronary sinus electrograms were recorded. CS electrograms within these locations with more than two deflections were considered fractionated signals [Figure 1 & 2]. Initial CS potential duration was defined as the interval from initial deflection to the peak or nadir of the initial wave [Figure 3]. An initial delay of potential propagation was defined as a wave with duration exceeding 10 ms. Continuous signal recordings were performed with atrial pacing of a 600-ms drive train from lateral CTI electrode (lower lateral poles “poles 1–2”) and also during sinus rhythm. For each patient a random window of 5 consecutive EGMs was examined during SR and pacing and median figure was documented for further statistical analysis. The fractionated signals were reported if there were more than 2 deflections.

**Post-ablation Follow-up**

We recorded a follow up period of 55.1± 15.8 months. Episodes of new-onset of AF occurrence with or without sustained fast atrial arrhythmia more than 30 seconds were identified from 12-lead ECGs, Holter monitoring and device interrogations. All patients (100% of patients) underwent a 12-lead ECG and 71% had a 24- or 48-hour Holter monitoring within 3 months of catheter ablation and then further follow up was arranged as routine (with ECG and Halters). Any documented symptoms of AF were also recognised.

**Statistical Analysis**

Data were analysed using SPSS software version 21.0 (SPSS, Chicago, IL, USA) and presented as mean ± standard deviation and median (interquartile range (IQR)). The distribution of the variables was analysed with the Kolmogorov–Smirnov test. Differences between two groups were tested using independent Student’s t-tests for normally distributed variables, and the Mann Whitney U test was used for non-parametrically distributed variables. Differences between the categorical variables were analysed using the χ²-test. A p-value of less than 0.05 was considered statistically significant.

**Results**

During the study period, a total of 40 patients fulfilled the inclusion
Coronary Sinus Electrograms During Sinus Rhythm

During sinus rhythm, proximal coronary sinus electrograms (PCS) were significantly fractionated in AF group (30% vs. 65%; P = 0.03). The same observation was recorded in middle CS poles (30% vs. 60%, P = 0.03). However, the initial conduction time of the electrograms, total electrogram duration and velocity from proximal to distal CS electrograms were comparable between both groups (P < 0.05)[Table 2].

Description of Coronary Sinus Electrograms during Atrial Pacing

Pacing at cycle train of 600 ms from distal poles[1,2] from 20 poles duo-decapolar catheter has shown a significant delay in electrogram conduction at CS os (7.1 ± 3.6 Vs. 12.3 ± 9.2, P = 0.03), which was not associated with the same pattern in the distal CS electrograms (P = 0.52). Interestingly, distal CS electrograms were more fractionated in AF group when compared with control group (p < 0.05) during pacing.

Follow Up

Follow up period up to average of 56 month was recorded in both groups of patients. The period of follow up was comparable between AF group and controls (54.3 ± 15.8 months vs. 56 ± 16.1 months, p = 0.73).

Discussion

AF is commonly documented in isolated AFL and may occur in 50% post AFL ablation[12]. This is extremely important as it impacts on the potential long-term outcome from AFL ablation and may influence the long-term oral anticoagulation management.

In this study, we carefully examined the standard coronary sinus electrograms - at the beginning of AFL ablation procedure - to predict AF occurrence. In our study, we examined the relationship between CS fractionation and CSEs potential delays in AF occurrences. This relationship highlight the role of high scar (i.e. as seen in fractionated CSEs) burden in AF development[6,8,9].

Major findings

In our study, half of the patients (50%) developed AF during follow up period of 55.1 ± 15.8 months. This observation is previously well documented in isolated AFL underwent RF ablation treatment[4,11,14]. Chronologically, the highest occurrence rate of AF was documented in the first year of follow up (12/40 patients, 30%). Then by the end of the second year we documented 16 patients that developed AF (40%). In AF group, we found proximal and mid CS electrograms fractionated at SR and they developed easily greater potential delay during activation from lower lateral RA region. Moreover, distal CS (i.e. reflecting LA fractionation) electrograms were remarkably fractionated with Rt lower atrial pacing.

Anatomical correlations of coronary sinus electrograms

Anatomic structure of the proximal CS is unique and quite complex. The CS os and proximal CS are surrounded by a cuff of a striated muscle which extends to the distal CS. The proximal CS OS is connected with the RA and similarly the mid to distal CS are well connected to the left atrium (LA)[15] as proved by the work of Antz et al.[6,15]. In proximal CS electrograms, the right atrial components are depicted as initial sharp potentials and shorter duration while far field potentials of LA are at lower amplitude and longer duration. The opposite occurs in distal CS electrograms where LA EGMs are sharp[11]. More than 2 deflections in proximal and distal CS electro grams are considered pathological[12] and they may reflect scar volume.
Fractionated coronary sinus electrograms

Fractionated PCS electrograms represents RA source rather than LA only[10]. Yokoyama E et al. found similar findings of fractionated EGMs and highest ratio of dominant frequency (DF) electrograms in proximal CS region in a non PV source of paroxysmal AF[17]. Moreover, another study documented higher prevalence of PCS fractionation and AF occurrence when seen in sinus rhythm CSE due to wave collusions at coronary sinus os due to slow propagation in presumably associated scar tissue[8,18]. This may support the importance of the results of our study of fractionated EGMs around PCS in SR within the group that developed AF. The mid CSE are also fractionated, and although the nature of CS musculature signals is quite complex, this still may emphasis the contribution of both the RA and CS future development of AF. Again, these findings were documented during SR. However, during lower right atrial pacing, distal CS electrograms became clearly fractionated, suggesting a possible intra left atrial inhomogeneous substrate (i.e. scar) for AF[7-19]. Various mechanisms may explain these findings. First, waveform frequencies increase, either by pacing or during AF fibrillation, will increase EGMs fractionation, duration and lead to re-entry in relation with the conduction disturbance. That mechanism of dynamics underlying conduction distortions was called percolation and was confirmed as a driver for AF initiation by Vignmond E et al[20]. Another theory is explained by tissue related anisotropy resulting in a ramble path of the propagating waveform. This occurs as a consequence to electrical uncoupling of the side-to-side connections between small groups of scars and fibrous tissue[21]. These explain the significance of complex fractionated CS electrograms in predicting AF[22]. This theory applied on distal CS signals which probably represents the scar burden in the LA.

Delayed atrial electrical potentials

Delayed electrical conduction is commonly seen in AF patients indicating intra-atrial conduction delay[9]. The existence of site-dependent intra-atrial conduction delays advocates non-uniform anisotropic characteristics of the posterior triangle of Koch may be critical for AF routers and induction. A possible explanation in the slow conduction in the post Kogh triangle may be required for reentry and may initiate AF[23]. In our study, we observed the same finding in the group who developed AF with delayed electrical propagation of proximal CS EGMs. This finding gives further insight into the potential pathophysiology underlying atrial fibrillation and the importance of the CS os region in AF development in our study. Although the exact underlying pathophysiology undermining both AF & AFL is unclear, there are some electrophysiological properties similar to both[21]. Re-entrant mechanisms appear to be necessary for the development of AF along with abnormal intra-atrial conduction particularly in the posterior triangle of Koch[20]. As a result, it is not surprising that AF often develops in large proportion of patients post isolated AFL ablation that may result in a requirement for further RFA & reintroduction of medication. Predicting patients who may be at risk of developing AF post AFL ablation is not only provides useful insight into the pathophysiology underlying the development of AF but it may also influence treatment therapy post CTI including oral anticoagulation for high risk cohort for cerebrovascular events.

Study limitations

The limitations in the paper include the fact the sample size was quite small, retrospective study of 40 patients but it has a quite prolonged follow up period for 5 years. We believe this study may serve as a platform to continue investigating the low right atrium and its role in the development of AF post AFL ablation.

Moreover, while paced electrograms are expected to be more fractionated at the CS os and mid CS, the opposite was documented in our study. The explanation is that we kept pacing at slow rate at CL of 600 ms without added extrastimuli (i.e. which probably mimic most of the cathlab cases flow and protocols). Also, when Ching Tui et al. reported increased fractionation, that was in the context of increasing stimulus prematurity at faster CL than what we used in our paper. However, delayed potentials in CS os was clear in both paced and during intrinsic SR. Another limitation is the fractionated signals were documented in SR, and we had no AF patients to study the correlations of these signal during AF. However, these fractionations were not rate related as the velocity was comparable in both groups during SR and paced rhythm to suggest a scar related fractionations. Despite of a lower EF noted in AF occurrence group, the LA size over not different in both groups. On the other hand, previous studies demonstrated that patients with and without LVSD had similar risk for recurrent AF or AT after catheter ablation[24]. Moreover, none of the study cohort has underlying cardiomyopathy process in the history. We believe further investigation needs to be performed questioning whether the extent of fibrotic remodeling within the RA/ LA from a reduction in EF may contribute directly to these electrophysiological findings in this study.

Conclusion

Atrial fibrillation incidence is associated with fractionated proximal and mid CSE in sinus rhythm and distal CSE in paced rhythm. Delays of proximal CSE potentials during sinus and paced rhythm are correlated with AF occurrence. Further studies to validate these findings are recommended.

Conflict of Interest

None.

References

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