Pulmonary Vein Isolation and QT prolongation in Paroxysmal Atrial fibrillation : What Have We Learned?

Farah Abdulhai[1] and Marwan Refaat[2]

[1]American University of Beirut Faculty of Medicine
[2]American University of Beirut Medical Center

June 15, 2020

Atrial fibrillation (AF) is the most common sustained arrhythmia and is a significant public health burden.[1,2] Many mutations in ion-channel and non ion-channel structural genes are linked to AF especially in patients with family history and no risk factors.[3] The pulmonary vein muscle sleeves are the main trigger for AF. [4] Many studies showed that pulmonary vein isolation (PVI) via catheter ablation is superior to medical therapy in decreasing all-cause mortality, hospitalizations and recurrence [5-7]. Though it is still controversial, vagal denervation and targeting the major atrial ganglionated plexi (GP) have been reported by Pappone et al. to improve the outcome after PVI.[8] GP ablation has been associated with QT prolongation and ventricular arrhythmias[9]. PVI affects the atrial GP, modifies the intrinsic cardiac autonomic nervous system and could lead to QT prolongation and lethal ventricular arrhythmias such as torsade de pointe and ventricular tachycardia.[10]

In their study published in this issue of the Journal of Cardiovascular Electrophysiology, Chikata et. al investigated the effect of PVI on the QT interval in patients with paroxysmal AF, and identified associated predisposing factors . [11] This was a retrospective observational study of 117 patients (out of 280 patients who were screened) with paroxysmal AF who underwent PVI via cryoballoon, hotballoon and radiofrequency at Toyama Prefectural Center in Japan between January 2016 and June 2019. The authors assessed 12 lead electrocardiograms (ECGs) at baseline and after four hours, one day, one month and three months. At each evalulaion point, they included only patients with sinus rhythm and excluded those taking antiarrhythmic drugs, drugs known to prolong QT intervals, patients undergoing renal transplant or having electrolyte imbalances in order to eliminate possible confounding factors. They measured the QRS, heart rate, QT interval and calculated QTc using the Bazett, Fridericia, Framingham and Hodges formulas at each evaluation point. All patients underwent PVI under conscious sedation with the same anesthesia regimen. They performed Cavotricuspid isthmus line ablation only if the Cavotricuspid isthmus dependent atrial flutter was noted, and they did not perform any intentional GP ablation. The study showed that QTc interval calculated by Bazett formula and the Fridericia formula was significantly prolonged at each time point ,whereas that of the Framingham formula and the Hodges formula was significantly prolonged only in the acute phase. The authors attributed this discrepancy to how each formula correlates with heart rate (HR). Since PVI could lead to autonomic denervation, a reflex increase in heart rate can be expected especially during the acute phase following the procedure. Furthermore, the study showed that in the acute phase post PVI, women had significantly prolonged QTc interval as compared to their baseline and to men ($P < 0.05$).

The authors explained that QTc calculated by the Bazzet formula is more prone to error especially at elevated heart rates seen post PVI. In the setting of tachycardia, the QTc can be expected to prolong since the R-R interval shortens to a greater extent than the QT. Hence, the Bazzet's QTc formula will overcorrect and overestimate the prevalence of the QT interval at heart rate greater than 100 bpm, and

linear regression methods to correct the QT interval (such as Hodges) are better for clinical use. Women are known to have a longer baseline QT interval and are more prone to develop torsade de pointe than men[12]. That could be explained by the hormonal effect on the expression of ion channels and by the difference in autonomic regulation between genders.[13,14] Chikata at al show a possible association between gender and QT prolongation post PVI that might be explained by a difference in inflammatory response or a distinguished genetic predisposition found more frequently in women. Further investigation is warranted via prospective studies with larger sample size in the future to corroborate the findings especially with the relatively small sample size and the fact that it was a single center study.

References:

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* . Aug 1991;22(8):983-8. doi:10.1161/01.str.22.8.983

2. Chung MK, Refaat M, Shen WK, et al. Atrial Fibrillation: JACC Council Perspectives. J Am Coll Cardiol. Apr 2020; 75 (14): 1689-1713.

3. Feghaly J, Zakka P, London B, MacRae CA, Refaat MM. Genetics of Atrial Fibrillation. *Journal of the American Heart Association* . Oct 16 2018;7(20):e009884. doi:10.1161/jaha.118.009884

4. Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. The New England journal of medicine. Sep 3 1998;339(10):659-66. doi:10.1056/nejm199809033391003

5. Asad ZUA, Yousif A, Khan MS, Al-Khatib SM, Stavrakis S. Catheter Ablation Versus Medical Therapy for Atrial Fibrillation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Circulation Arrhythmia and electrophysiology* . Sep 2019;12(9):e007414. doi:10.1161/circep.119.007414

6. Refaat MM, Ballout J, Mansour M. Ablation of Atrial Fibrillation in Congenital Heart Disease. Arrhythm Electrophysiol Rev. Dec 2017; 6 (4): 191-4.

7. Oral H, Knight BP, Tada H, et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation* . Mar 5 2002;105(9):1077-81. doi:10.1161/hc0902.104712

8. Pappone C, Santinelli V, Manguso F, et al. Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. *Circulation* . Jan 27 2004;109(3):327-34. doi:10.1161/01.cir.0000112641.16340.c7

9. He B, Lu Z, He W, et al. Effects of ganglionated plexi ablation on ventricular electrophysiological properties in normal hearts and after acute myocardial ischemia. *International journal of cardiology* . Sep 20 2013;168(1):86-93. doi:10.1016/j.ijcard.2012.09.067

10. Münkler P, Wutzler A, Attanasio P, et al. Ventricular Tachycardia (VT) Storm After Cryoballoon-Based Pulmonary Vein Isolation. *The American journal of case reports* . Sep 11 2018;19:1078-1082. doi:10.12659/ajcr.908999

11. Chikata A. Prolongation of QT interval after pulmonary vein isolation for paroxysmal atrial fibrillation *Journal of Cardiovascular Electrophysiology* . 2020;

12. Drici MD, Burklow TR, Haridasse V, Glazer RI, Woosley RL. Sex hormones prolong the QT interval and downregulate potassium channel expression in the rabbit heart. *Circulation* . Sep 15 1996;94(6):1471-4. doi:10.1161/01.cir.94.6.1471

13. Chen YJ, Lee SH, Hsieh MH, et al. Effects of 17beta-estradiol on tachycardia-induced changes of atrial refractoriness and cisapride-induced ventricular arrhythmia. *J Cardiovasc Electrophysiol* . Apr 1999;10(4):587-98. doi:10.1111/j.1540-8167.1999.tb00716.x

14. Huikuri HV, Pikkujämsä SM, Airaksinen KE, et al. Sex-related differences in autonomic modulation of heart rate in middle-aged subjects. *Circulation* . Jul 15 1996;94(2):122-5. doi:10.1161/01.cir.94.2.122