Journal of Integrative Cardiology

Mini Review ISSN: 2058-3702

Pulmonary vein isolation and renal sympathetic denervation in CKD patients with refractory AF

Márcio Galindo Kiuchi*

*Division of Cardiac Surgery and Artificial Cardiac Stimulation, Department of Medicine, Hospital e Clínica São Gonçalo, Brazil

Mini review

Atrial fibrillation (AF) affects approximately 2% of the population worldwide, and this percentage will increase in the next 50 years [1,2]. The prevalence of AF is higher in older people, reaching up to 0.5% at 40 to 50 years of age and ranging from 5% to 15% at 80 years of age [1-5]. Men generally develop AF more frequently than do women. By 40 years of age, the lifetime risk of developing AF is almost 25% [6]. AF frequently complicates Chronic Kidney Disease (CKD) and is associated with adverse outcomes. Progression of end-stage renal disease is a major complication of CKD, and the incidence of AF is associated with a higher risk of developing the end-stage renal disease in patients with CKD [7]. The ideal approach for the treatment of AF is rhythm control, but this is sometimes very hard to accomplish [8]. Pokushalov and colleagues [9] recently reported that renal sympathetic denervation (RSD) diminishes systolic and diastolic blood pressure in drug-resistant hypertensive patients and reduces AF recurrences when combined with pulmonary vein isolation (PVI). Targeting of the pulmonary veins (PVs) and/or the PV antrum is the cornerstone for most AF ablation procedures. If the PVs are targeted, complete electrical PVI should be the goal of the procedure. For such procedures, complete isolation of all PVs is currently widely accepted as the best endpoint. A strategy using percutaneous catheter-based delivery of Radiofrequency (RF) energy was recently settled to interject the sympathetic innervation of the kidneys. This new procedure exposed no severe vascular or renal complications in the long term (up to 36 months). Our group believes that RSD can reduce AF recurrence in patients with CKD by modulation of the sympathetic hyperactivity present in this disease. As reported in the SYMPLICITY HTN-3 trial [10], no significant differences in the 24-h ABPM were observed between 6 and 12 months in the denervation and crossover subjects. Ambulatory data were available for only 20 of 70 (29%) non-crossover subjects at 12 months, given that ABPM was not protocol-mandated for these subjects at this time point. However, in these 20 subjects, a pattern similar to that of office readings was observed, showing a larger 24-h ABPM reduction at 6 than 12 months (−11.0 ± 19.5 *vs.* −6.1 ± 14.4 mmHg at 6 and 12 months, respectively; P=0.272) [10].

Recent data suggesting that the combined number of complete and incomplete ablation runs (*i.e.,* the overall number of ablation attempts) is related to greater blood pressure reductions [11]. Sympathetic activation is a hallmark of the essential hypertensive state occurring early in the clinical course of the disease [12-14]. In CKD, the sympathetic overactivity looks to be expressed at the earliest clinical phase of this condition, being directly related to the severity of the renal failure [15-18]. In both hypertension and renal failure, the mechanisms of the hyper adrenergic state are manifold and include reflex and neurohumoral pathways [12,13,17]. The adrenergic activation has an adverse impact on cardiovascular morbidity and, in the case of renal failure, also on cardiovascular mortality [12,13,18,19]. We believe that this over activity from the essential hypertensive state is in part controlled by anti-hypertensive drugs because patients maintain a normotensive state, leaving only sympathetic hyperactivity due to CKD.

The association of RSD with PVI may be a positive impact on AF recurrence. Once PVI was achieved, the dominant initiating source was eliminated. However, in patients with substantial pathology in the atrial substrate, additional intervention might be required to maximize the antiarrhythmic response. Additionally, ablation of afferent renal nervous input decreases central sympathetic output [15], which might attenuate autonomic triggers of AF and offer the potential for an antiarrhythmic effect superior to medications.

References

1. Stewart S, Hart CL, Hole DJ, McMurray JJ (2001) Population prevalence, incidence, and predictors of atrial fibrillation in the Renfrew/Paisley study. *Heart* 86: 516-521. [Crossref]

2. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, et al. (2001) Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA* 285: 2370-2375. [Crossref]

3. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, et al. (2006) Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence.*Circulation* 114: 119-125. [Crossref]

4. Heeringa J, van der Kuip DA, Hofman A, Kors JA, van Herpen G, et al. (2006) Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J* 27: 949-953. [Crossref]

5. Naccarelli GV, Varker H, Lin J, Schulman KL (2009) Increasing prevalence of atrial fibrillation and flutter in the United States. *Am J Cardiol* 104: 1534-1539. [Crossref]

6. Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, et al. (2004) Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation* 110: 1042-1046. [Crossref]

7. Bansal N, Xie D2, Tao K2, Chen J2, Deo R2, et al. (2016) Atrial Fibrillation and Risk of ESRD in Adults with CKD. *Clin J Am Soc Nephrol* 11: 1189-1196. [Crossref]

8. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, et al. (2010) European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery, Guidelines for the management of atrial fibrillation: the Task Force for the Management

Correspondence to: Márcio Galindo Kiuchi, MD, MSc, PhDDivision of Cardiac Surgery and Artificial Cardiac Stimulation, Department of Medicine, Hospital e Clínica São Gonçalo Rua Cel. Moreira César, São Gonçalo,Rio de Janeiro 24440-400, Brazil; Tel/Fax: +55 (21) 26047744; E-mail: marciokiuchi@gmail.com

Received: August 01, 2016; **Accepted:** August 22, 2016; **Published:** August 24, 2016

of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 31: 2369-429.

9. Pokushalov E, Romanov A, Corbucci G, Artyomenko S, Baranova V, et al. (2012) A randomized comparison of pulmonary vein isolation with versus without concomitant renal artery denervation in patients with refractory symptomatic atrial fibrillation and resistant hypertension. *J Am Coll Cardiol* 60: 1163-70

10. Bakris GL, Townsend RR, Flack JM, Brar S, Cohen SA, et al. (2015) SYMPLICITY HTN-3 Investigators: 12-month blood pressure results of catheter-based renal artery denervation for resistant hypertension: the SYMPLICITY HTN-3 trial. *J Am Coll Cardiol* 65: 1314-2.

11. Kandzari DE, Bhatt DL2, Brar S3, Devireddy CM4, Esler M5, et al. (2015) Predictors of blood pressure response in the SYMPLICITY HTN-3 trial. *Eur Heart J* 36: 219-227. [Crossref]

12. Grassi G1 (2010) Sympathetic neural activity in hypertension and related diseases. *Am J Hypertens* 23: 1052-1060. [Crossref]

13. Grassi G (2009) Assessment of sympathetic cardiovascular drive in human hypertension: achievements and perspectives. *Hypertension* 54: 690-697

14. Paton JF, Raizada MK (2010) Neurogenic hypertension. *Exp Physiol* 95: 569-571. [Crossref]

15. Schlaich MP, Socratous F, Hennebry S, Eikelis N, Lambert EA, et al. (2009) Sympathetic activation in chronic renal failure. *J Am Soc Nephrol* 20: 933-939. [Crossref]

16. Neumann J, Ligtenberg G, Klein II, Koomans HA, Blankestijn PJ: Sympathetic hyperactivity in chronic kidney disease: pathogenesis, clinical relevance, and treatment. Kidney Int 65: 1568–1576, 2004.

17. McGrath BP, Ledingham JG, Benedict CR (1978) Catecholamines in peripheral venous plasma in patients on chronic haemodialysis. *Clin Sci Mol Med* 55: 89-96. [Crossref]

18. Grassi G, Bertoli S, Seravalle G (2012) Sympathetic nervous system: role in hypertension and in chronic kidney disease. *Curr Opin Nephrol Hypertens* 21: 46-51. [Crossref]

19. Zoccali C, Mallamaci F, Parlongo S, Cutrupi S, Benedetto FA, et al. (2002) Plasma norepinephrine predicts survival and incident cardiovascular events in patients with end stage renal disease. *Circulation* 105: 1354-1359.