

Epicardial Thoracoscopic Ablation

Subjects: **Pathology**

Contributor: Celestino Sardu

In this study we evaluated atrial fibrillation (AF) recurrence and Sarcoplasmic Endoplasmic Reticulum Calcium ATPase (SERCA) levels in patients treated by epicardial thoracoscopic ablation for persistent AF. This was a prospective, multicenter, observational study to recruit patients with persistent AF receiving an epicardial thoracoscopic pulmonary vein isolation. About 27 patients, responders ($n = 15$) did not present AF recurrence after epicardial ablation at one-year follow-up; these patients displayed a marked remodeling of the left atrium, with a significant reduction of inflammatory cytokines, B type natriuretic peptide (BNP), and increased levels of SERCA compared to baseline and to non responders ($p < 0.05$). Furthermore, mean AF duration (Heart rate (HR) 1.235 (1.037-1.471), $p < 0.05$), Left atrium volume (LAV) (HR 1.755 (1.126-2.738), $p < 0.05$), BNP (HR 1.945 (1.895-1.999), $p < 0.05$), and SERCA (HR 1.763 (1.167-2.663), $p < 0.05$) were predictive of AF recurrence. Therefore, our data indicate for the first time that baseline values of SERCA in patients with persistent AF might be predictive of failure to epicardial ablative approach. Intriguingly, epicardial ablation was associated with increased levels of SERCA in responders. Thus, SERCA might be an innovative therapeutic target to improve the response to epicardial ablative treatments.

atrial fibrillation

ablation

SERCA

calcium handling

1. Atrial Fibrillation (AF)

Atrial fibrillation (AF) is the most common arrhythmia worldwide [1]. Based on the duration of episodes and the date of onset, AF is defined as paroxysmal, persistent, or permanent [1]. In patients with persistent AF there is an increased risk of thromboembolic stroke, heart failure, and overall worse prognosis [2]. Therefore, in these patients catheter ablation is a valid therapeutic option to ameliorate clinical outcomes via restoration of sinus rhythm [2][3][4]. On the other hand, catheter ablation shows a success rate of ~50% at five years in patients with persistent AF [5]. The lack of therapeutic effect in a relatively high percentage of patients limits its clinical application, and might itself be responsible for atrial fibrosis and remodeling, eventually leading to permanent AF [6][7]. Unfortunately, in these patients the successful epicardial ablation by sinus rhythm restoration could cause a reduction of left atrial diameters and volumes [6][7][8][9]. In this setting, epicardial AF ablation could induce the modulation of the complex electro-anatomical arrhythmic atrial substrate in patients with persistent AF [6]. Conversely, the unsuccessful of AF ablation could be explained by the advanced atrial electrical/anatomical remodeling [6][7][8][9], as the result of an enhanced trigger activity and reentry mechanisms [10]. These mechanisms are both implied in the genesis and perpetuation of persistent AF [11]. Alterations in the regulation of intracellular calcium (Ca^{2+}) have been linked to an abnormal trigger activity and reentry in AF patients [10][12]. Moreover, in human atrial myocytes altered Ca^{2+} fluxes have been shown to induce delayed after depolarizations (DADs) [9][10][11][12].

2. SERCA

Sarcoplasmic Endoplasmic Reticulum Ca^{2+} ATPase (SERCA) is considered a major player in these processes [10]. Indeed, patients with AF have lower SERCA levels compared to patients with sinus rhythm [13]. Of note, SERCA levels can be assayed in peripheral blood lymphocytes, as their levels correlate with SERCA levels obtained in specimens of cardiac tissue [13]. Mechanistically, a reduced Ca^{2+} uptake in the endoplasmatic/sarcoplasmatic reticulum, which is mediated by SERCA, results in intra-cytoplasmic Ca^{2+} overload, which is known to be arrhythmogenic [10][14]. Moreover, the abnormal Ca^{2+} handling along with cellular DAD-mediated triggered activity could promote AF persistence [10][11][12][13][14][15]. Indeed, the persistence of abnormal Ca^{2+} handling can activate ion channels and trigger Ca^{2+} -dependent signaling pathways, eventually promoting atrial remodeling and the progression of AF to more persistent forms [10]. Therefore, we speculate that alterations in SERCA levels might play a central role in AF persistence and in its recurrence following an epicardial ablation. To our knowledge, these aspects have never been investigated before. Our hypothesis is that lower SERCA levels might be linked to higher rates of failure of epicardial ablation in patients with persistent AF. To verify such hypothesis, we designed a prospective, multicenter, observational study to evaluate AF recurrences at one year of follow-up after epicardial ablation, correlating this clinical outcome to SERCA expression in patients with sinus rhythm restoration (responders group) vs. patients with AF (nonresponders group) after an epicardial ablative approach.

References

1. Sumeet S. Chugh; Rasmus Havmoeller; Kumar Narayanan; David Singh; Michiel Rienstra; Emelia J. Benjamin; Richard F. Gillum; Young-Hoon Kim; John H. McAnulty; Zhi-Jie Zheng; Mohammad H. Forouzanfar; Mohsen Naghavi; George A. Mensah; Majid Ezzati; Christopher J. L. Murray; Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study.. *Circulation* **2013**, 129, 837-47, 10.1161/CIRCULATIONAHA.113.005119.
2. Kirchhof, P.; Benussi, S.; Kotecha, D.; Ahlsson, A.; Atar, D.; Casadei, B.; Castella, M.; Diener, H.C.; Heidbuchel, H.; Hendriks, J.; et al. Document Reviewers: 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS: The TaskForce for the management of atrial fibrillation of the European Society of Cardiology(ESC)Developed with the special contribution of the European Heart Rhythm Association(EHRA) of the ESCEndorsed by the European Stroke Organization (ESO). *Eur. Heart J.* **2016**, 37, 2893–2962.
3. Michel Haïssaguerre; Pierre Jaïs; Dipen C. Shah; Atsushi Takahashi; Mélèze Hocini; Gilles Quiniou; Stéphane Garrigue; Alain Le Mouroux; Philippe Le Metayer; J. Clémenty; Spontaneous Initiation of Atrial Fibrillation by Ectopic Beats Originating in the Pulmonary Veins. *New England Journal of Medicine* **1998**, 339, 659-666, 10.1056/nejm199809033391003.
4. Gaetano Santulli; Catheter ablation improved quality of life more than drug therapy at 1 y in symptomatic atrial fibrillation.. *Annals of Internal Medicine* **2019**, 171, JC10, 10.7326/ACPJ20190

7160-010.

5. Anand Ganesan; Nicholas J. Shipp; Anthony G. Brooks; Pawel Kuklik; Dennis H. Lau; Han S. Lim; Thomas Sullivan; Kurt C. Roberts-Thomson; Prashanthan Sanders; Long-term Outcomes of Catheter Ablation of Atrial Fibrillation: A Systematic Review and Meta-analysis. *Journal of the American Heart Association* **2013**, *2*, e004549, 10.1161/jaha.112.004549.
6. Bisleri, G.; Rosati, F.; Bontempi, L.; Curnis, A.; Muneretto, C. Hybrid approach for the treatment of long-standing persistent atrial fibrillation: Electrophysiological findings and clinical results. *Eur. J. Cardiothorac. Surg.* **2013**, *44*, 919–923.
7. Marrouche, N.F.; Wilber, D.; Hindricks, G.; Jais, P.; Akoum, N.; Marchlinski, F.; Kholmovski, E.; Burgon, N.; Hu, N.; Mont, L.; et al. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: The DECAAF study. *JAMA* **2014**, *311*, 498–506.
8. Agnes Pump; Luigi Di Biase; Justin Price; Prasant Mohanty; Rong Bai; Pasquale Santangeli; Sanghamitra Mohanty; Chintan Trivedi; Rachel Xue Yan; Rodney Horton; Javier E. Sanchez; Jason Zagrodzky; Shane Bailey; G. Joseph Gallinghouse; J. David Burkhardt; Andrea Natale; Efficacy of Catheter Ablation in Nonparoxysmal Atrial Fibrillation Patients with Severe Enlarged Left Atrium and Its Impact on Left Atrial Structural Remodeling. *Journal of Cardiovascular Electrophysiology* **2013**, *24*, 1224-1231, 10.1111/jce.12253.
9. Agustín Bortone; Serge Boveda; Jean-Luc Pasquié; Pénélope Pujadas-Berthault; Eloi Marijon; Anthony Appetiti; Jean-Paul Albenque; Sinus rhythm restoration by catheter ablation in patients with long-lasting atrial fibrillation and congestive heart failure: impact of the left ventricular ejection fraction improvement on the implantable cardioverter defibrillator insertion indication. *Europace* **2009**, *11*, 1018-1023, 10.1093/europace/eup167.
10. Mary Margot Catherine Maleckar; Andrew G Edwards; William E Louch; Glenn T Lines; Studying dyadic structure–function relationships: a review of current modeling approaches and new insights into Ca²⁺ (mis)handling. *Clinical Medicine Insights: Cardiology* **2017**, *11*, , 10.1177/1179546817698602.
11. Jessica Gambardella; Daniela Sorriento; Michele Ciccarelli; Carmine Del Giudice; Antonella Fiordelisi; Luigi Napolitano; Barbara Trimarco; Guido Iaccarino; Gaetano Santulli; Functional Role of Mitochondria in Arrhythmogenesis.. *Advances in Experimental Medicine and Biology* **2017**, *982*, 191-202, 10.1007/978-3-319-55330-6_10.
12. Leif Hove-Madsen; Anna Llach; Antoni Bayés-Genís; Santiago Roura; Enrique Rodriguez Font; Alejandro Arís; Juan Cinca; Atrial Fibrillation Is Associated With Increased Spontaneous Calcium Release From the Sarcoplasmic Reticulum in Human Atrial Myocytes. *Circulation* **2004**, *110*, 1358-1363, 10.1161/01.cir.0000141296.59876.87.

13. Joanna E. Kontaraki; Fragiskos I. Parthenakis; Eva G. Nyktari; A.P. Patrianakos; Panos E. Vardas; Myocardial gene expression alterations in peripheral blood mononuclear cells of patients with idiopathic dilated cardiomyopathy. *European Journal of Heart Failure* **2010**, *12*, 541-548, 10.1093/eurjhf/hfq057.

14. Kerry Davia; Elena Bernobich; Hardeep K. Ranu; Federica Del Monte; Cesare M. Terracciano; Kenneth T. MacLeod; Dawn L. Adamson; Babar Chaudhri; Roger J. Hajjar; Sian E. Harding; SERCA2a Overexpression Decreases the Incidence of Aftercontractions in Adult Rabbit Ventricular Myocytes. *Journal of Molecular and Cellular Cardiology* **2001**, *33*, 1005-1015, 10.1006/jmcc.2001.1368.

15. J. H. King; Y. Zhang; M. Lei; A. A. Grace; C. L.-H. Huang; James Fraser; Atrial arrhythmia, triggering events and conduction abnormalities in isolated murineRyR2-P2328Shearts. *Acta Physiologica* **2012**, *207*, 308-323, 10.1111/apha.12006.

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