



Editorial

Reduction in left atrial and pulmonary vein dimensions after ablation therapy is mediated by scar



1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia worldwide with significant impact on morbidity and mortality [1]. Therefore, current research focuses on strategies aiming at risk reduction of occurrence and progression of AF. Several established cardiovascular risk factors are also independent risk factors of AF, such as age, hypertension, congestive heart failure, coronary artery disease, valvular heart disease, and diabetes mellitus [1]. AF patients often have enlarged atria and a reduced atrial contractile function, which is mainly considered to be caused by structural remodeling involving fibrosis [2]. Furthermore, structural remodeling has other components such as connexin dysfunction or myolysis, that likely also contribute to the occurrence of AF even in the absence of left atrial (LA) enlargement [3]. The vicious circle initiates when LA remodeling occurs, which itself is a surrogate for arrhythmia recurrence after catheter ablation [2,4]. On the other hand, successful restoration of sinus rhythm (SR) has been shown to impact on the reversibility of atrial remodeling and, either as a consequence or in addition, on reduction of pulmonary vein (PV) and LA diameters [5,6]. Catheter ablation has become an effective treatment option for AF patients and is therefore set as a first-line therapy according to the recent guidelines [1]. However, time course and pattern of reversal of LA remodeling following catheter ablation is still poorly understood.

2. Atrial structural and functional reverse remodeling

Remodeling is defined as a change in LA size, molecular structure or function and is largely induced by development of tachyarrhythmias or consequence to alteration in atrial structure secondary to pressure or volume overload [2,3]. Elimination of predisposing factors, such as AF or mitral valve regurgitation, may result in partial or complete normalization of atrial tissue texture and recovery of atrial function and therefore confirms the hypothesis of atrial reverse remodeling.

Indeed, previous studies have shown reverse structural remodeling of the LA not only after ablation, but also after successful electrical cardioversion, indicating a relationship between restoration of SR and tissue remodeling.

In 2005 Reant et al. analyzed 85 patients with AF without additional risk factors by serial echocardiographic studies at baseline and at 1-, 3-, 6-, 9-, and 12-month intervals after radiofrequency ablation. LA dimensions and mechanical function as well as left ventricular (LV) systolic and diastolic function were evaluated at each time interval. Reverse remodeling of the LA and improvement of LV diastolic and systolic functions were demonstrated after restoration of SR by ablation [6].

These results were confirmed by Maille et al., who demonstrated early structural reverse remodeling after pulmonary vein isolation (PVI) with a significant decrease in LA volume. Interestingly, patients with significant LA volume reduction had a shorter AF history prior to ablation and were less likely to experience early AF recurrence indicating the role of early restoration of SR in this process. In their analysis, LA volume reduction was not related to reduced contractility of ablated tissue, as radiofrequency ablation duration did not differ between patients with and without volume remodeling [7]. This hypothesis is also supported by the results of the RACE (RATE Control versus Electrical Cardioversion for Persistent Atrial Fibrillation) trial. In this study echocardiography was performed in 335 patients at baseline and at a 1- and 2-years follow-up. Echocardiographic findings were compared between patients randomized to rate ($n = 160$) and rhythm control ($n = 175$). The findings of the study suggest, that restoration of SR via electrical cardioversion is associated with improvement of LV function and reduction of atrial size [5].

However, an experimental study including 8 dogs with chronic AF demonstrated, that despite complete reverse electrophysiological remodeling at 7–14 days after cardioversion, the LA remained enlarged, LA function was depressed and no corresponding reverse remodeling of the cellular ultrastructure was observed [8].

3. PVI-induced decrease in PV- and LA-dimensions due to ablated tissue

Patients suffering from AF often have enlarged LA and PVs compared to control patients, and structural remodeling due to AF is considered to be the main cause [3,4]. Therefore, a reverse structural remodeling by cessation of AF after successful PVI has been proposed to cause a decrease of LA and PV diameters. This contrasts with recently published data of a study analyzing cardiac magnetic resonance imaging (MRI) in 21 paroxysmal AF patients before and 3 months after PVI and in healthy sheep ($n = 12$) before and after isolation of the right PVs only. Gottlieb et al. could show, that the PV diameter reduction after PVI was similar in patients with AF and in healthy sheep without AF, and was associated with PV scar extent. They summarized that the PVI-induced PV-downsizing is caused by the ablative energy and subsequent ablation-induced scar formation. Furthermore, Gottlieb et al. demonstrated, that the volume of the RA, in which no RF energy was delivered, remained unchanged 3 months after successful PVI [9]. Although these findings are an important contribution to a better understanding, this study remains hypothesis generating as the results are obtained from a cohort of limited size and should therefore interpreted with caution. Nonetheless,

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another interesting study on the reversibility of changes in ultrastructure and gap junctions of the LA after restoration of SR revealed, that reverse remodeling is a slow process and might be still incomplete after a 4-months period in stable sinus rhythm [10]. Although various studies confirm acute reduction of LA-size, normalization of LA structure and recovery of atrial function after catheter ablation, the direct effect of catheter ablation on LA volume reduction seen after PVI must be considered besides potential benefits of restoration of SR itself.

4. Conclusion

Observations of counteracting processes in the atria and PVs have been made upon restoration of SR, and this phenomenon has been termed reverse remodeling. Catheter ablation of AF has been shown to impact on the reversibility of atrial remodeling and on reduction of pulmonary vein (PV) and LA diameters. However, the latter seems not only to be caused by restoration of SR via catheter ablation but also at least partially by chronic effects of ablation lesions, especially in patients with higher AF-burden or longer AF history.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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