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Review

Adenosine-guided radiofrequency catheter ablation of atrial fibrillation: A meta-analysis of randomized control trials

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ABSTRACT

Background: The prognostic significance of adenosine-mediated dormant pulmonary vein conduction, and whether such dormant conduction should be eliminated, remains controversial. We sought to perform a meta-analysis of data from eligible studies to delineate the prognostic impact of adenosine-guided radiofrequency catheter ablation of atrial fibrillation.

Methods: A systematic literature search was performed using online databases in order to identify relevant studies from January 2004 to September 2016. Ten studies [six observational and four randomized control trials (RCTs)] were included in the analysis.

Results: Five studies (two observational and three RCTs) compared the efficacy of adenosine-mediated elimination of dormant conduction versus no adenosine test. Overall, the adenosine-guided ablation strategy displayed better long-term outcomes as compared with no adenosine testing (RR 1.08, 95% CI 1.01–1.14, $p=0.02$; Heterogeneity: $I^2=42\%$, p: 0.14). The meta-analysis of only RCTs failed to show any differences between the two strategies (RR 1.03, 95% CI 0.96–1.11, $p=0.37$; Heterogeneity: I^2 0%, p: 0.41). Eight studies (five observational and three RCTs) addressed the efficacy of adenosine-induced dormant conduction and additional ablation versus no dormant conduction during adenosine challenge. Overall, a trend towards a better outcome in those without dormant conduction during drug challenge was noted (RR 0.89, 95% CI 0.77–1.03, $p=0.11$; Heterogeneity: I^2 65% p: 0.006). The pooled analysis of RCTs failed to show any differences between the two arms (RR 0.90, 95% CI 0.62–1.30, $p=0.57$; Heterogeneity: I^2 88%, p: 0.0002).

Conclusions: Adenosine-guided radiofrequency catheter ablation of atrial fibrillation does not provide additional benefit in terms of freedom of arrhythmia recurrence.

Contents

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1. Introduction

Pulmonary vein isolation (PVI) has become the procedural endpoint in patients undergoing left atrial ablation for symptomatic drug-refractory atrial fibrillation (AF) [1]. The aim of PVI is abolishment of all conducted electrical activity beyond the isolating lesions. Pulmonary vein recovery of conduction in at least one vein has been verified in up to 80% of patients undergoing a second ablation procedure, and seems to be the dominant mechanism of AF recurrence [2]. Acute pulmonary vein reconnection within 30 min after ablation is also commonly seen and has been associated with late AF recurrence [3]. Furthermore, pulmonary vein reconnection has been associated with histopathological evidences of non-transmural lesions along the ablation line. Non-transmural ablation may create a dynamic cellular substrate with features of reversible injury; interestingly, the reversibility of the thermal injury appears to be an important determinant of recovery of conduction and recovery from injury that may explain recurrences of AF following PVI [4]. Adenosine administration following acute PVI may unmask residual—so-called "dormant"—conduction between the pulmonary veins and the left atrium [5]. Observational studies have offered conflicting results about the prognostic significance of dormant pulmonary vein conduction revealed by adenosine, and whether such dormant conduction should be eliminated [5,7–12]. Four recent randomized control trials (RCTs) have also given opposing results [13–16]. In the light of such conflicting information, a systematic review of published data, including the recent randomized trials, appears to be timely and may provide the best way to determine the prognostic impact of adenosine-guided ablation of AF.

2. Methods

2.1. Search strategy

A systematic literature search was performed by two investigators (K.P.L. and S.G.) using the online databases of PubMed, Embase and the Web of Science in order to identify relevant studies from January 2004 to September 2016. We used the following keywords: "atrial fibrillation," "ablation," "adenosine," "ATP," "pulmonary vein isolation," "pulmonary vein reconnection" and "dormant conduction." Study titles and abstracts as well as reference lists were manually checked independently by two investigators. All potentially relevant reports were retrieved as complete manuscripts, and then their eligibility assessed according to the inclusion criteria. Any disagreements or uncertainties between the two investigators were resolved through consensus after rechecking the source data and consultation with a third investigator (T. L.).

2.2. Inclusion/exclusion criteria

This meta-analysis included observational and RCTs studies on human subjects published in the English language with the following primary objectives: (1) freedom from arrhythmia recurrence in patients who undergo additional radiofrequency ablation to eliminate adenosine-mediated dormant conduction compared to those who did not receive adenosine; and (2) freedom from arrhythmia recurrence in patients with adenosine-mediated dormant conduction and additional radiofrequency ablation as compared with those without pulmonary vein reconnection during adenosine testing. Patient characteristics (age, gender); AF status (paroxysmal AF, persistent AF, duration of AF); echocardiographic markers (left atrial size, left ventricular ejection fraction); details of the ablation procedure (PVI strategy, prior ablation, outcomes, duration of follow-up); and the adenosine protocol used were carefully assessed. For the purpose of this article, we used the term "adenosine" for all chemical preparations of adenosine that were clinically applied [e.g. adenosine triphosphate (ATP)]. Studies using single-shot ablation devices for AF ablation (cryoballoon and/or multielectrode phased-radiofrequency catheters) were excluded from the analysis.

2.3. Data extraction

The following information was extracted from the selected studies: (1) study characteristics (name of the first author, year of publication, journal, PMID, study design, mean follow-up duration); (2) baseline characteristics of study subjects (number of patients, age, sex, type of cardiomyopathy, type of AF, echocardiographic markers, other comorbidities, medication); (3) the incidence of dormant conduction provoked during adenosine testing; and, finally, (4) the main outcomes of each study (incidence of recurrent atrial tachyarrhythmias during the follow-up in each group).

2.4. Statistical analysis

Data analysis was performed using the Review Manager (RevMan) software, version 5.3. The risk ratio (RR) and corresponding 95% confidence interval (CI) were separately calculated by using the provided crude data to account for the arrhythmia-free survival of adenosine-guided PVI with or without dormant conduction, as well as conventional PVI. The statistical heterogeneity of the study was assessed by using the I^2 index. We considered values around 25% ($I^2=25$), 50% ($I^2=50$) and 75% ($I^2=75$) to be low, medium and high heterogeneity, respectively [17]. A random effect model was used in cases in which we had $I^2 > 50\%$. Funnel plots were constructed by using RevMan software to assess publication bias. P-values < 0.05 were considered to be statistically significant.

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