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Adenosine-guided pulmonary vein isolation versus conventional pulmonary vein isolation in patients undergoing atrial fibrillation ablation: An updated meta-analysis

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ABSTRACT

Background: Recurrent atrial fibrillation episodes following pulmonary vein isolation (PVI) are frequently due to reconnection of PVs. Adenosine can unmask dormant conduction, leading to additional ablation to improve AF-free survival. We performed a meta-analysis of the literature to assess the role of adenosine testing in patients undergoing atrial fibrillation (AF) ablation.

Methods: PubMed, EMBASE, and Cochrane databases were searched through until December 2015 for studies reporting on the role of adenosine guided-PVI versus conventional PVI in AF ablation.

Results: Eleven studies including 4099 patients undergoing AF ablation were identified to assess the impact of adenosine testing. Mean age of the population was 61 ± 3 years: 25% female, 70% with paroxysmal AF. Follow up period of 12.5 ± 5.1 months. A significant benefit was observed in the studies published before 2013 (OR = 1.75; 95%CI 1.32–2.33, $p < 0.001$, $I^2 = 11\%$), retrospective (OR = 2.05; 95%CI 1.47–2.86, $p < 0.001$, $I^2 = 0\%$) and single-centre studies (OR = 1.58; 95%CI 1.19–2.10, $p = 0.002$, $I^2 = 30\%$). However, analysis of studies published since 2013 (OR = 1.41; 95% CI 0.87–2.29, $p = 0.17$, $I^2 = 75\%$) does not support any benefit from an adenosine-guided strategy. Similar findings were observed by pooling prospective case-control (OR = 1.39; 95%CI 0.93–2.07, $p = 0.11$, $I^2 = 75\%$), and prospective randomized controlled studies (OR = 1.62; 95%CI 0.81–3.24, $p = 0.17$, $I^2 = 86\%$). Part of the observed high heterogeneity can be explained by parameters such as dormant PVs percentage, use of new technology, improvement of center/operator experience, patients' characteristics including gender, age, and AF type.

Conclusions: Pooling of contemporary data from high quality prospective case–control & prospective randomized controlled studies fails to show the benefit of adenosine-guided strategy to improve AF ablation outcomes.

1. Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia with significant morbidity and mortality [1]. Catheter ablation has a class I indication for drug-refractory symptomatic AF patients [2,3]. However, AF can recur in a significant proportion of patients requiring either ongoing medical treatment with *anti*-arrhythmic drugs or repeat ablation procedure [4]. Pulmonary vein isolation (PVI) is the cornerstone of AF catheter ablation and most of the recurrent AF episodes are due to reconnection of PVs [2].

Studies have shown that intra-operative adenosine can potentially unmask dormant pulmonary vein conduction, resulting from failed PVI, and thereby guide further ablation to improve procedural success and AF-free survival [5,6].

A previous meta-analysis [7] of studies published before 2013 aimed to determine the impact of routine adenosine administration on clinical outcomes in patients undergoing PVI. However, it was inconclusive as the available data were sparse and contradictory [6,8,9]. Therefore, we performed an updated systematic review and meta-analysis of the

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literature to assess the impact of adenosine-guided PVI on the outcome of AF ablation.

2. Methods

2.1. Study selection

We undertook searches on MEDLINE (via PubMED), EMBASE, clinicaltrials.gov and COCHRANE databases (from inception to 1st December 2015) using the following search string: "atrial fibrillation" AND "adenosine" AND "catheter ablation" (Fig. 1). Even though we included all potentially eligible entries from inception to 1st December 2015, this updated meta-analysis focused on studies following that of McLellan et al. [7]. This meta-analysis [7] included studies before 2013, when no randomized controlled or multi-centre studies were available. Importantly, the authors included only 3 studies [10–12] assessing the role of adenosine infusion in AF recurrence post PVI with favorable results for adenosine testing (HR: 1.25 95%CI: 1.12–1.40, $p < 0.001$, I2 = 0.0%, $p = 0.784$). Further to that, random effects modeling was performed demonstrating a non-significant trend to a reduction in freedom from AF in patients with adenosine/ATP-induced PV reconnection who underwent additional catheter ablation compared with patients without adenosine-induced PV reconnection with a pooled relative risk of 0.91 (95% CI: 0.81–1.03, $p = 0.145$).

Reference lists of all accessed full-text articles were further searched for sources of potentially relevant information. Authors of full-text papers and congress abstracts were also contacted by email to retrieve additional information.

Only longitudinal studies performed in humans were considered for inclusion. The population, intervention, comparison and outcome (PICO) approach was used [13]. The population of interest included AF patients and the intervention was catheter ablation of AF. The comparison was adenosine-guided PVI vs. standard PVI. Relapse of AF or atrial tachycardia following ablation and after a blanking period of no less than 2 to 3 months was the primary outcome assessed.

Minimum study follow-up duration was five months. Both registries and randomized trials were considered eligible for analysis. The methods sections of evaluated studies were reviewed to confirm the suitability and composition of the reported endpoint.

In order to be eligible, studies needed to:

1. Present matched control-groups with the only difference in the treatment strategy being adenosine administration (with or without concomitant isoproterenol infusion) in one group with ablation if reconnection occurred & no adenosine administration in the control group.
2. Adenosine administration in the active treatment group or in both groups, but further ablation only in the active adenosine-guided strategy group (i.e. as an active-treatment was considered this group where in the event of reconnection following adenosine infusion further ablation was performed. The control group consisted of patients where either no adenosine testing was done, or if it was performed, no further ablation was delivered).

If other differences with regard to treatment were present in the study protocol, namely additional ablation of lines or other triggers in the active treatment group alone, the study was not considered appropriate for inclusion. Full-text articles remaining

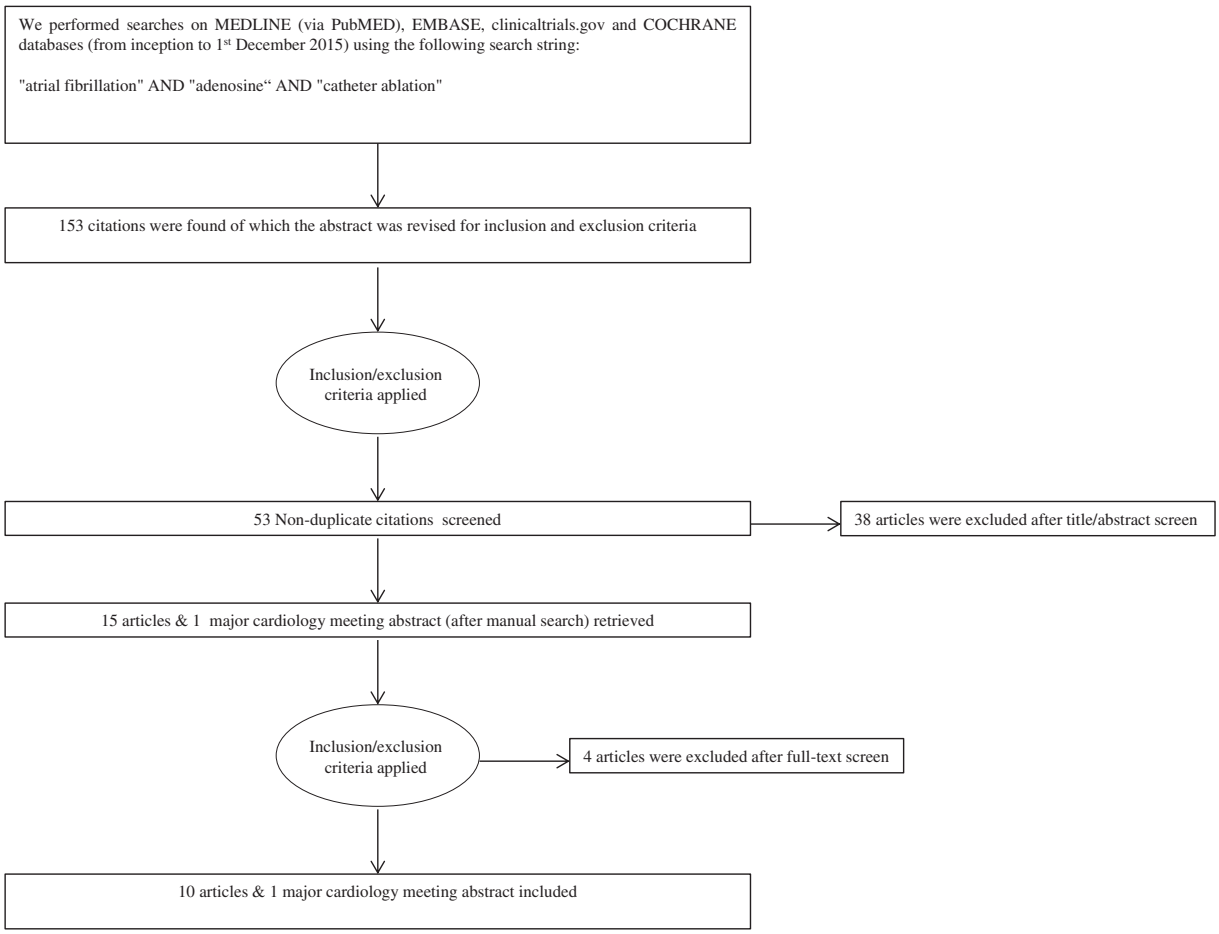

Fig. 1. Flowchart diagram illustrating study selection methodology.