INPLASY PROTOCOL

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Corresponding author:
David Reiners

david.reiners@immanuelalbertinen.de

Author Affiliation:
Department of Cardiology, Heart Center Brandenburg, Bernau / Berlin Brandenburg Medical School (MHB) "Theodor Fontane", Neuruppin, Germany.

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None declared.

Protocol: Ablation in patients with atrial fibrillation: A systematic review and meta-analysis of recurrence monitoring characteristics over the last decade

Reiners, D[1]; Haase-Fielitz, A[2]; Butter, C[3]; Bannehr, M[4]; Georgi, C[5]; Seifert, M[6]; Bredehorst, J[7]; Haase, R[8].

Review question / Objective - **How is the recurrence of atrial fibrillation after catheter ablation therapy defined and monitored in randomized-controlled clinical studies in the past ten years? Do the monitoring characteristics have an impact on the ablation efficacy outcomes?**
Main outcome(s) - **(Definition of) catheter ablation efficacy outcomes, such as: AF recurrence, AF burden, freedom from AF after the first ablation, quality-of-life outcomes (for example SF-36-questionnaire).**
Study designs to be included - **Included: Randomized controlled trials (RCTs), Studies in the English language, Patient collective with any kind of atrial fibrillation diagnosis, Catheter ablation therapy is performed in at least one study arm, Publication date between 2012 and 2022, Efficacy outcomes, Minimum follow-up of 6 months. Excluded: Unpublished studies (e.g., conference abstracts, trial protocols), non-RCT, only procedural outcomes, Animal Studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 February 2023 and was last updated on 27 June 2023 (registration number INPLASY202320101).

INTRODUCTION

Review question / Objective: **How is the recurrence of atrial fibrillation after catheter ablation therapy defined and monitored in randomized-controlled clinical studies in the past ten years? Do the monitoring characteristics have an impact on the ablation efficacy outcomes?**

Rationale: According to the 2020 Guidelines for Management of Atrial Fibrillation by the European Society of Cardiology, atrial fibrillation (AF) is defined as a supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and consequently ineffective atrial contraction.
Electrocardiographic characteristics of AF include:
• Irregularly irregular R-R intervals (when atrioventricular conduction is not impaired)
• Absence of distinct repeating P waves, and
• Irregular atrial activations. [1]
Catheter ablation is a well-established treatment for the prevention of AF recurrences. AF ablation approaches are based upon our current understanding of the underlying mechanisms of this complex arrhythmia. The importance of ectopic activations originating mainly in the pulmonary veins is widely recognised as the mechanism responsible for the initiation of AF. Accordingly, the electric isolation of the pulmonary veins, introduced by Haissaguerre and colleagues in the late '90s, remains the predominant ablation strategy for both paroxysmal and persistent AF. On the other hand, the mechanisms sustaining AF are only partially understood. As a consequence, ablation strategies aiming to eliminate these mechanisms vary substantially and are in general less successful in comparison to pulmonary vein isolation (PVI). These later approaches include the ablation of wide areas of atrial tissue (atrial roof, posterior wall, and mitral isthmus, left atrial appendage) to minimise the substrate required to sustain AF or the ablation of specific focal activity areas with centrifugal expansion (rotors) [2].
The definition of recurrence in the context of ablation for atrial arrhythmias is inconsistent among large studies and currently under debate. The established definition of any atrial arrhythmia documented over 30 seconds beyond the 3 months blanking time is questioned, since AF-burden or quality of life seem to be clinically more relevant. The definition of recurrence/ablation success is of crucial importance when interpreting efficacy outcomes and compare different modes of ablation in various studies.
We will include any randomized controlled trial that performed catheter ablation therapy to patients diagnosed with atrial fibrillation and monitored any efficacy outcomes for at least 6 months or longer published in the last ten years.

Condition being studied: Efficacy outcomes of catheter ablation for atrial fibrillation therapy.

METHODS

Participant or population: Patients with atrial fibrillation.

Intervention: Catheter ablation therapy.

Comparator: Ablation techniques for atrial fibrillation ablation vary regarding the type of energy used (RF, Cryo, PFA etc.), the ablation duration (High Power Short Duration, CB 180s i.e.), the extent of ablation (sole PVI vs. additional ablation). Frequently studies compare several ablation techniques or ablation vs. drug therapy.For example, studies include comparison of radiofrequency ablation (RF) and ablation with use of a cryoballoon (CB). In this review included studies must at least include one study arm performing catheter ablation therapy. Specific characteristics of the comparison groups are not predefined.

Study designs to be included: Included: Randomized controlled trials (RCTs), Studies in the English language, Patient collective with any kind of atrial fibrillation diagnosis, Catheter ablation therapy is performed in at least one study arm, Publication date between 2012 and 2022, Efficacy outcomes, Minimum follow-up of 6 months. Excluded: Unpublished studies (e.g., conference abstracts, trial protocols), non-RCT, only procedural outcomes, Animal Studies.

Eligibility criteria: Inclusion criteria: Adults with atrial fibrillation undergoing catheter ablation (radiofrequency and

cryo).Exclusion criteria: Adolescents (< 18 years of age), surgical ablation therapy.

Information sources: MEDLINE; EMBASE.

Main outcome(s): (Definition of) catheter ablation efficacy outcomes, such as: AF recurrence, AF burden, freedom from AF after the first ablation, quality-of-life outcomes (for example SF-36-questionnaire).

Additional outcome(s): Follow-up characteristics, such as: duration of follow-up, follow-up intervals, devices used for monitoring (e.g.: 12-lead-ECG; Holter-ECG, TTM), days of monitoring.

Data management:
Selection process: The first reviewer will identify eligible studies by abstract screening. A second independent reviewer will carefully review potentially relevant studies and reasons for exclusion. A third reviewer will mediate and re-review in the event of disagreement. A study will be included when first and second reviewer independently assess it as satisfying for the inclusion criteria.
Data collection process
One reviewer (DR) will collect the data using a standardized form. A second reviewer (AHF) will independently check the data for consistency and clarity.
Extracted data will include:
General information:
Study ID
Title
Lead author
Country
Basic characteristics:
Trial size
Size of each study arm
Aim of study
Inclusion criteria
Exclusion criteria
Type of AF
Ablation technique
Endpoint characteristics:
Primary endpoints
Secondary endpoints
Follow-up duration
Screening intervals
Type of follow-up monitoring
Definition of recurrence
Blanking period
Days of monitoring
Outcomes:
Number/ Percentage of patients reached primary and secondary endpoints in each study arm.

Quality assessment / Risk of bias analysis:
The Risk of bias will be assessed using the PEDro-Scale for each included study.
The AMSTAR 2 checklist will be used as an orientation regarding the targeted overall quality of this systematic review.

Strategy of data synthesis: We will provide descriptive information and statistics of all included studies. Furthermore, we aim to perform meta-analysis on the distribution of reaching the efficacy-related outcome in each study. In addition, we plan to analyze the impact of different monitoring characteristics, such as follow-up duration and intervals on the efficacy outcome and analyze subgroups divided by the used monitoring device.

Subgroup analysis: Subgroup analysis by monitoring device.

Sensitivity analysis: To be determined.

Language restriction: English only.

Country(ies) involved: Germany.

Keywords: atrial fibrillation; ablation; efficacy outcome; recurrence; monitoring; measurement characteristics.

Dissemination plans: We plan to submit the systematic review for publication in a peer-reviewed journal.

Contributions of each author:
Author 1 - David Reiners.
Email: david.reiners@immanuelalbertinen.de
Author 2 - Anja Haase-Fielitz.
Author 3 - Christian Butter.
Author 4 - Marwin Bannehr.
Author 5 - Christian Georgi.
Author 6 - Martin Seifert.
Author 7 - Julian Bredehorst.
Author 8 - Robert Haase.

References:

1: Hindricks et al: 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and 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 ESC, European Heart Journal, Volume 42, Issue 5, 1 February 2021, Pages 373–498

2: Koulouris: Catheter ablation for the management of atrial fibrillation: a treatment strategy for all patients? in: E-Journal of Cardiology Practice, Vol. 21, N° 8 - 03 Nov 2021.