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Radiofrequency Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation

Meta-Analysis of Quality of Life, Morbidity, and Mortality

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ABSTRACT

OBJECTIVES The aim of this study was to perform a collaborative meta-analysis of published and unpublished quality-of-life, morbidity, and mortality data from randomized controlled trial comparisons of radiofrequency ablation (RFA) and antiarrhythmic drug therapy (AAD) in symptomatic atrial fibrillation.

BACKGROUND RFA is superior to AAD in decreasing recurrences of atrial fibrillation, but the effects on other clinical outcomes are not well established.

METHODS The primary investigators of eligible randomized controlled trials were invited to contribute standardized outcome data. Random-effects summary estimates were calculated as standardized mean differences and risk ratios with 95% confidence intervals for continuous and binary outcomes, respectively. Fixed effects were used in subgroup analyses.

RESULTS Twelve randomized controlled trials (n = 1,707 patients) were included. RFA led to greater improvements in 4 36-Item Short Form Health Survey areas and the symptom frequency score from baseline to 3 months. In all quality-of-life metrics, there was a trend toward diminution of the differences between the 2 approaches with follow-up. There were 7 of 866 (5 in a study using phased RFA) and 0 of 704 strokes in the RFA and AAD arms, respectively ($p = 0.02$, Fisher exact test). Bleeding and mortality events were not significantly different between the 2 arms. There was high heterogeneity for hospitalizations, with decreased hospitalization risk with RFA when it was not first-line therapy (risk ratio: 0.34; 95% confidence interval: 0.24 to 0.46) and increased risk as first-line therapy (risk ratio: 1.22; 95% confidence interval: 1.03 to 1.45).

CONCLUSIONS RFA demonstrates an early but nonsustained superiority over AAD for the improvement of quality of life. There are no obvious differences in other clinical outcomes, and the periprocedural stroke risk is non-negligible. (J Am Coll Cardiol EP 2016;2:170–80) © 2016 by the American College of Cardiology Foundation.

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The optimal therapeutic approach for atrial fibrillation (AF) is still debated. A beneficial effect of radiofrequency ablation (RFA) on quality of life (QoL) has been suggested by several studies (1,2), but it is unclear whether the effect of RFA on QoL is sustained, because long-term follow-up data have been limited (3). Also, previous retrospective analyses have demonstrated conflicting results with regard to stroke and hospitalization risks with RFA and antiarrhythmic drug therapy (AAD) (4,5), and no randomized controlled trials (RCTs) have been sufficiently powered to address these issues. Finally, given the demonstrated superiority of RFA over AAD in rhythm control, and the potential ensuing decreased need for anticoagulation (6,7), long-term bleeding should theoretically be less frequent with an RFA strategy. However, this remains unproved.

Meta-analyses have demonstrated the superiority of RFA in maintaining sinus rhythm compared with AAD (8–16). However, only 1 study analyzed limited published QoL data in nonstandardized scales and demonstrated superiority of RFA, without addressing the longevity of this effect. Three meta-analyses assessed the safety of RFA and AAD and considered all adverse events related to the interventions collectively, ranging from minor events to death, without specifically focusing on clinically important outcomes such as stroke and bleeding (8,11,14). Only 1 meta-analysis synthesized limited published data from 3 RCTs on the risk for cardiovascular hospitalization and demonstrated favorable RFA effects (15). Also, a recent meta-analysis of 3 studies assessed the safety and effectiveness of RFA only as first-line treatment (16). No meta-analysis has been previously aimed at addressing specifically the long-term risks for stroke, bleeding, or death with RFA and AAD strategies.

We have therefore conducted a systematic review and meta-analysis of all published RCTs comparing RFA with AAD in paroxysmal or persistent AF with regard to QoL outcomes, hospitalization, stroke, bleeding, and mortality. We attempt to overcome the limitations imposed by the limited or nonstandardized published QoL and clinical event data by including unpublished primary trial data. Differences in AF recurrence were not within the scope of this study, because all previous meta-analyses have addressed this outcome convincingly (17).

ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug therapy
AD = arcsine difference
AF = atrial fibrillation
CI = confidence interval
QoL = quality of life
RCT = randomized controlled trial
RFA = radiofrequency ablation
RR = risk ratio
SF36 = 36-Item Short Form Health Survey

METHODS

DATABASE SEARCH. Using the OVID search engine and the generic terms *atrial fibrillation*, *atrial flutter*, and *ablation*, 2 independent reviewers searched the MEDLINE, Embase, and Cochrane Central Register of Controlled Trials databases (limited to RCTs) without year or language restrictions (accessed March 18, 2015). We also searched ClinicalTrials.gov (accessed March 18, 2015) and the most recent major pertinent meetings (American College of Cardiology Scientific Sessions, American Heart Association Scientific Sessions, European Society of Cardiology Congress, Heart Rhythm, European Heart Rhythm Association/Cardiostim) for ongoing trials that were not yet published in journals. References of eligible papers were further scrutinized for additional eligible studies.

ELIGIBILITY OF STUDIES. We considered trials that randomly assigned patients with paroxysmal or persistent AF to any type of RFA versus AAD. Trials were eligible regardless of whether RFA was used as first-line therapy or not. Studies examining RFA versus AAD in patients with AF and heart failure were excluded because of the distinct QoL and overall prognostic characteristics of this patient population. We also excluded trials comparing the 2 modes of therapy following failure of previous ablation attempt, trials comparing different ablation techniques without medical management arms, trials evaluating RFA versus rate control, and trials comparing AAD with no AAD after ablation.

DATA COLLECTION AND ENDPOINTS OF INTEREST. For each eligible RCT, we documented general study

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