JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER

VOL. 68, NO. 11, 2016
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2016.06.036

ORIGINAL INVESTIGATIONS

Ganglion Plexus Ablation in Advanced Atrial Fibrillation

The AFACT Study

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ABSTRACT

BACKGROUND Patients with long duration of atrial fibrillation (AF), enlarged atria, or failed catheter ablation have advanced AF and may require more extensive treatment than pulmonary vein isolation.

OBJECTIVES The aim of this study was to investigate the efficacy and safety of additional ganglion plexus (GP) ablation in patients undergoing thoracoscopic AF surgery.

METHODS Patients with paroxysmal AF underwent pulmonary vein isolation. Patients with persistent AF also received additional lines (Dallas lesion set). Patients were randomized 1:1 to additional epicardial ablation of the 4 major GPs and Marshall's ligament (GP group) or no extra ablation (control) and followed every 3 months for 1 year. After a 3-month blanking period, all antiarrhythmic drugs were discontinued.

RESULTS Two hundred forty patients with a mean AF duration of 5.7 ± 5.1 years (59% persistent) were included. Mean procedure times were 185 ± 54 min and 168 ± 54 min ($p = 0.015$) in the GP ($n = 117$) and control groups ($n = 123$), respectively. GP ablation abated 100% of evoked vagal responses; these responses remained in 87% of control subjects. Major bleeding occurred in 9 patients (all in the GP group; $p < 0.001$); 8 patients were managed thoracoscopically, and 1 underwent sternotomy. Sinus node dysfunction occurred in 12 patients in the GP group and 4 control subjects ($p = 0.038$), and 6 pacemakers were implanted (all in the GP group; $p = 0.013$). After 1 year, 4 patients had died (all in the GP group, not procedure related; $p = 0.055$), and 9 were lost to follow-up. Freedom from AF recurrence in the GP and control groups was not statistically different whether patients had paroxysmal or persistent AF. At 1 year, 82% of patients were not taking antiarrhythmic drugs.

CONCLUSIONS GP ablation during thoracoscopic surgery for advanced AF has no detectable effect on AF recurrence but causes more major adverse events, major bleeding, sinus node dysfunction, and pacemaker implantation. (Atrial Fibrillation Ablation and Autonomic Modulation via Thoracoscopic Surgery [AFACT]; NCT01091389)
(J Am Coll Cardiol 2016;68:1155–65) © 2016 by the American College of Cardiology Foundation.

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Manuscript received April 20, 2016; revised manuscript received June 7, 2016, accepted June 8, 2016.

JACC VOL. 68, NO. 11, 2016
SEPTEMBER 13, 2016:1155–65

ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug

AF = atrial fibrillation

APD = action potential duration

AT = atrial tachycardia

AV = atrioventricular

GP = ganglion plexus

HFS = high-frequency stimulation

LA = left atrial

LAVI = left atrial volume index

PV = pulmonary vein

PVI = pulmonary vein isolation

The most common arrhythmia, atrial fibrillation (AF) is associated with increased morbidity and mortality. Ablation is indicated for patients remaining symptomatic despite a trial with antiarrhythmic drugs (AADs) (1,2). Therefore, catheter ablation and stand-alone thoracoscopic surgery are increasingly being used. The arrhythmogenic trigger from the pulmonary veins (PVs) is the target for ablation in patients with paroxysmal AF without concomitant atrial or cardiac disease; the mechanism is less well established in patients with advanced AF, defined as persistent AF, enlarged left atria, or previously failed catheter ablation. Various treatment strategies have been advocated, combining more extensive myocardial ablation and ablation of non-PV and nonmyocardial targets, including stepwise catheter ablation approaches (3), in which PV isolation (PVI) is followed by linear left atrial (LA) ablation, ablation of continuous fractionated atrial electrograms (4), or ablation of rotors (5). As it has become clear that the autonomous nervous system plays a central role in initiating AF and in atrial autonomic remodeling (6,7), partial atrial denervation through ablation of the major autonomic ganglion plexus (GP), either alone or in combination with PVI, has been pursued (8,9).

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GP stimulation promotes AF by a combined parasympathetic and sympathetic action resulting in action potential duration (APD) shortening and increased sarcoplasmic reticulum calcium release in PV myocardium, allowing early after-depolarizations to emerge and trigger AF (10). Aside from AF induction, GP stimulation affects local and global LA conduction time, consistent with a predominantly parasympathetic effect (11). Thus, the stimulation of the autonomic nerves within the GPs, beyond triggering AF, may also have a proarrhythmic effect on the atrial myocardium that perpetuates the arrhythmia (11).

Studies investigating the role of GP ablation in addition to PVI have demonstrated mixed results (8,12,13), as have nonrandomized studies during concomitant cardiac surgery (14,15). The GPs reside in epicardial fat pads and cannot be ablated endocardially without (much) more atrial myocardial ablation. This may induce post-ablation atrial tachycardias (ATs). However, more rigorous myocardial ablation around the PVs may also lower the chance of reconnection. Second, most studies have focused on patients with paroxysmal AF with few cardiovascular comorbidities. Epicardial ablation during thoracoscopic surgery for AF may allow more selective GP ablation without ablating the underlying atrial myocardium; however, only observational data on thoracoscopic GP ablation are available (16–19).

The aim of the prospective, randomized, controlled AFACT (Atrial Fibrillation Ablation and Autonomic Modulation via Thoracoscopic Surgery) study was to investigate epicardial GP ablation during thoracoscopic surgery for advanced AF. We hypothesized that GP ablation in these patient results in a higher percentage of freedom from AF, without inducing more periprocedural or late complications.

METHODS

AFACT is a single-center study, performed at the Academic Medical Center in Amsterdam, that enrolled patients between April 2010 and January 2015. The study conformed to the Declaration of Helsinki and was approved by the Institutional Review Board. All patients provided written informed consent.

PRE-OPERATIVE WORKUP. The inclusion and exclusion criteria are listed in the Online Appendix.

All patients had electrocardiographic documentation of AF and underwent the following pre-operative tests: nontriggered cardiac magnetic resonance imaging angiography for LA anatomy, 24-h Holter recording for AF burden and rate control assessment, transthoracic echocardiography for LA diameter and volume (determined using the Simpson method), spirometry for vital capacity and forced expiratory volume in 1 second to assess the ability to undergo perioperative single-lung ventilation, and treadmill testing to exclude clinically significant coronary artery disease (followed by coronary angiography when appropriate). Hepatic and renal failure, as well as clinically relevant anemia, were excluded. All patients were adequately anticoagulated with vitamin K antagonists or non-vitamin K oral anticoagulant agents (NOAC) ≥4 weeks prior to surgery.

Randomization was computer guided and performed in blocks with varying block sizes at the time of pericardial opening. With 110 patients in each arm (α = 0.8, 2-sided significance level = 0.05), AFACT was powered to detect a 17.5% difference in AF absence after 1 year, on the basis of previous studies (16,20,21). We enrolled 240 patients to allow for about 10% of patients not completing follow-up.

SURGICAL PROCEDURE. The surgical procedure has been described previously (16). In short, bilateral video-assisted thoracoscopy was performed. Oral