

Catheter ablation of symptomatic atrial fibrillation: Sex, ethnicity, and socioeconomic disparities



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Catheter ablation for treatment of atrial fibrillation (AF), AF ablation, is more effective than antiarrhythmic drugs in reducing AF burden, reducing symptoms and increasing health-related quality of life. Although females more often experience AF-related symptoms, and have more severe symptoms, have lower quality of life, and experience more serious adverse effects of antiarrhythmic drugs than males, they are less likely to undergo AF ablation. Potential explanations for the disparity include older age at diagnosis, longer AF duration, a greater number of comorbidities, more extensive atrial fibrosis, and presumed lower success rate and more complications after AF ablation in women. Studies have failed to show sex-related differences in AF recurrence or serious complications following AF ablation but show more nuisance bleeds in women. Ethnic minorities, such as African Americans and Latin Americans, and individuals of low socioeconomic status are also less likely to

undergo AF ablation, possibly associated with greater numbers of comorbidities, lack of patient advocacy, healthcare costs, and inadequate insurance coverage. Inclusion of marginalized patient groups in clinical trials of AF treatment and a personalized, patient-centered approach may expand equality in utilization of AF ablation.

KEYWORDS Atrial fibrillation; Catheter ablation; Ethnicity; Healthcare system; Sex; Socioeconomic factors

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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, with a prevalence of approximately 3% in adults. The arrhythmia is more frequent in males than in females among all age groups.^{1–3} Prevalence and incidence of AF is increasing, and by 2030 an estimated 14–17 million Europeans and 12 million in the United States will be affected.^{2,4} AF is associated with an increased risk of all-cause mortality and stroke, and is a major reason for cardiovascular hospitalization.^{5–7} Hospitalizations for AF are increasing worldwide, for example in Australia, where they increased 5.2% annually from 1993 to 2013, compared with 2.2% increase for myocardial infarction and no increase for heart failure.^{7–9} AF is associated with higher all-cause mortality and morbidity in females than in males.^{5,6,10} Recent reports argue that sex differences in AF-related outcomes are driven by an age-related greater cardiovascular risk factor burden in women.^{11,12}

Over the past 3 decades, catheter ablation of AF (hereafter AF ablation) has become an important therapy to reduce AF symptoms and improve quality of life.^{13,14} Females undergo electrical cardioversion less frequently and are more likely to receive rate control therapy,^{10,15} and also undergo AF abla-

tion less often despite more often reporting symptoms, increased symptom severity, and lower health-related quality of life than males.^{15–18} AF ablation is also less common in ethnic minorities such as African Americans, Latin Americans, and individuals of low socioeconomic status.^{19,20}

In this topical review, we explore current research of sex, ethnicity, and socioeconomic disparities that affect the likelihood of AF ablation. We highlight research gaps to be addressed to make this significant therapy accessible to more patients.

Catheter ablation

Pulmonary vein isolation via catheter ablation using radiofrequency energy or cryoenergy is an expanding therapy for the management of patients with symptomatic AF.^{21,22} The alternative treatment of rhythm control with antiarrhythmic drugs is inferior with respect to efficacy and has potentially serious side effects.^{13,23–26} AF ablation is the recommended treatment strategy for both symptomatic paroxysmal and persistent AF refractory to antiarrhythmic drugs and may be first-line therapy in paroxysmal AF.^{21,27}

Sex disparities

Females more often experience AF-related symptoms and report greater symptom severity and poorer quality of life,

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KEY FINDINGS

- There is unequal provision of atrial fibrillation (AF) ablation.
- Female sex, African American and Latin American ethnicity, and low socioeconomic status are associated with reduced likelihood of undergoing AF ablation.
- Outcomes and serious complications of AF ablation are not proven poorer in females and ethnic minorities.
- Adequate analyses of outcomes and complication rates considering sex and marginalized patient groups are warranted in trials of AF ablation.

as well as more frequent and serious side effects and reduced efficacy of antiarrhythmic drugs compared to males.^{15,28} Hence, AF ablation seems to be an appropriate choice for rhythm control in females. Females are, however, less often referred for rhythm control via electrical cardioversion or AF ablation and are more likely to receive rate control therapy, including pacemaker implantation and atrioventricular junction ablation.^{15,16,20,29} Females undergoing AF ablation are generally older and have a higher prevalence of hypertension as well as a longer history of AF.^{18,30} The lower rates of females undergoing AF ablation may be partly attributed to presentation with AF at an older age and with more comorbidities, possible factors in reluctance of physicians to refer for advanced treatment. This supposition is contradicted by the expanded indications and number of AF ablation procedures conducted over the past decade in patients of increased age and with presence of comorbidities without a corresponding increase in the proportion of women.³¹ In a consensus document of sex differences in cardiac arrhythmias from the European Heart Rhythm Association, Linde and colleagues²⁹ suggested that there might also be a reluctance among female patients to choose invasive treatment. Some studies have suggested less favorable results of AF ablation in females, which may be related to longer AF duration imposing a greater risk of AF progression.^{32–34} Pathophysiological differences between females and males with AF, with females exhibiting a greater extent of left atrial fibrosis and more non-pulmonary vein-mediated AF, may be a source of poorer outcomes of AF ablation.^{29,33,35,36} These findings can possibly be related to level of disease progression before referral for the AF ablation procedure, with advanced left atrial remodeling associated with long-standing persistent AF.³³ Data from an AF ablation improvement registry showed that women with nonparoxysmal AF were more likely to receive adjunctive lesion sets compared with men, which could indicate more complex disease.³⁷ More advanced atrial remodeling and a greater number of recurrences have been shown after AF ablation in females despite AF duration similar to males.³⁸ In contrast, a systematic review reported that none of the more than 20 included

studies found female sex to be a predictor of AF recurrence after AF ablation.³⁹ Furthermore, the AXAFA-AFNET 5 study showed similar improvement in quality of life in both sexes after ablation.¹⁸

Higher rates of procedure-related complications were observed in women in some AF ablation studies, 1 of which reported a 1.8-fold risk of tamponade in females compared to males.^{20,32,40,41} Data from the German AF Ablation Registry showed that women had greater rates of in-hospital complications related to major bleeding events than men.³² In contrast, the AXAFA-AFNET 5 study showed no higher rate of serious complications such as tamponade and intracranial hemorrhage in females, but female sex was associated with longer hospital stay and higher rates of nuisance bleeds.¹⁸ The Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation trial (CABANA) showed no sex differences in adverse events in patients who underwent AF ablation⁴² (Table 1). Females have smaller atria, thinner atrial walls, and smaller blood vessels than males, which may increase risk for vascular complications when using instruments developed for, and adapted to, male patients.^{43,44}

Reports of less favorable results and greater rate of complications in AF ablation may affect physician referral patterns for females in general.⁴⁵ Current guidelines do not differ in class of recommendation for rhythm control therapies, including AF ablation, in females and males.^{21,46}

Socioeconomic factors

AF ablation is a resource-intensive procedure and cost may affect access. Low socioeconomic status is associated with reduced likelihood of undergoing AF ablation.^{47,48} In countries lacking a universal healthcare system, physicians might be reluctant to offer AF ablation to patients without insurance or adequate insurance coverage.²⁰ Cost might well affect a patient's decision to decline referral. Even in countries with universal health care and free in-hospital treatment, patients with a lower level of education and low income are less often treated with AF ablation.¹⁹ One explanation may be the association of educational level with the ability to comprehend and discuss treatment options with the physician and make informed health-related decisions (patient advocacy).^{19,48} Differences in clinical practice, physician preferences, and proximity to a center that performs AF ablations may also explain some differences in AF ablation.¹⁹

Ethnicity disparities

The prevalence of AF is different among different ethnic populations. AF is less common in Latin Americans and African Americans in the United States, and in persons of South Asian descent in the United Kingdom, than in White individuals, despite a higher burden of AF risk factors in non-Whites than in White individuals.^{20,48,49} A meta-analysis of 2 studies

Table 1 Atrial fibrillation ablation trials comparing patient demographics, outcomes, and safety in females and males

| Author, year | Study type, n (% F) | Age (y), F vs M | AF history (y), F vs M | Paroxysmal AF, F vs M | Follow-up (mo) | Free from AF, F vs M | Improvement in PROs | Complications, F vs M |
|---------------------------------------|------------------------------|------------------------------|---------------------------|--------------------------------|----------------|---|------------------------|---|
| Forleo et al, 2007 ³⁰ | Observ, 221 (32%) | 62 vs 57 <i>P</i> = .002 | 5 vs 4 <i>P</i> = .04 | 56% vs 61% NS | 23 | 83% vs 83% NS | Equal | 6% vs 5% NS |
| Zylla et al, 2016 ³² | Observ, 3652 (33%) | 64 vs 59 <i>P</i> < .0001 | - | 72% vs 61% <i>P</i> < .0001 | 12 | 50% vs 55% <i>P</i> = .02 | - | 5.9% vs 3% <i>P</i> = .02 [†] |
| Kloosterman et al, 2020 ¹² | RCT, 633 (33%) | 66 vs 63 <i>P</i> < .001 | Women > men | 64% vs 55% <i>P</i> = .03 | 3 | 66% vs 72% NS | Equal | 9% vs 6% NS [‡] |
| Kuck et al, 2018 ³⁴ | RCT, 750 (39%) | 64 vs 57 <i>P</i> < .001 | 5 vs 5 NS | 100% vs 100% NS | 18 | 58% vs 65% <i>P</i> = .01 | - | 16% vs 10% <i>P</i> = .02 |
| Cheng et al, 2019 ⁴¹ | Meta-analysis, 151,370 (34%) | 63 vs 59 <i>P</i> < .001 | 6 vs 5 NS | 70% vs 63% <i>P</i> < .0001 | 29 | 61% vs 69% <i>P</i> < .0001 | - | Women > men |
| Pak et al, 2021 ³⁶ | Cohort, 443 (25%) | 59 vs 58 NS | 6 vs 6 NS | 66% vs 60% NS | 31 | 59% vs 66% <i>P</i> = .02 [§] | - | 5% vs 4% NS |
| Russo et al, 2021 ⁴² | RCT, 1046 (37%) | 69 vs 67 NS | 1 vs 1 NS | 50% vs 39% <i>P</i> < .001 | 12 | 59% vs 66% [¶] | - | 6% vs 6% NS |
| Yunus et al, 2022 ³⁷ | Observ, 5356 (37%) | 67 vs 63 <i>P</i> < .0001 | - | 59% vs 50% <i>P</i> < .0001 | - | - | - | 5% vs 4% NS |
| Wong et al, 2022 ³⁸ | Cohort, 116 (36%) | 63 vs 61 NS | 4 vs 5 NS | 50% vs 46% NS | 22 | 54% vs 75% <i>P</i> = .03 | - | - |

Figures denote comparisons between females and males.

AF = atrial fibrillation; F = females, M = males; NS = not significant; Observ = observational; PRO = patient-reported outcomes; RCT = randomized controlled trial.

[†]In-hospital.

[‡]From AF procedure to 3 months after ablation.

[§]Repeat AF ablations.

[¶]No *P* value stated.

Table 2 Research gaps that warrant further trials

- Reasons for the lower rates of AF ablation in females, ethnic minorities, and individuals of low socioeconomic status.
- Pathophysiological differences in sex and ethnicity in susceptibility and mechanisms of AF.
- Sex differences in outcomes and complication rates of AF ablation—inherent or instrument-dependent.
- Ethnic differences in outcomes of AF ablation and antiarrhythmic drugs.

AF = atrial fibrillation.

of AF in African Americans also showed that every 10% increase in European ancestry increased the risk of AF by 13%, indicating that ethnicity may affect susceptibility or even mechanisms of AF.⁵⁰ African Americans and Latin Americans have lower likelihood of undergoing AF ablation than white Americans even after adjusting for insurance status and income.^{20,48} However, the lower prevalence of AF in African Americans and Latin Americans cannot fully explain the observed differences in AF ablation rates.⁴⁷ Traditionally, the adoption of advanced cardiovascular therapies has been slower in the above-mentioned groups, but studies show these inequalities to persist even though AF ablation has been in clinical use for several decades.^{20,48,51} Fewer patient cardiologist visits is independently associated with lower likelihood of undergoing AF ablation, which may further explain the observed ethnic differences, as African Americans and Latin Americans are less likely to be under cardiologist care.^{48,52}

In the CABANA trial, ethnic minorities in North America who underwent AF ablation had a substantial reduction in mortality not observed in the overall trial population. The difference in mortality compared to ethnic minority patients on antiarrhythmic drugs seems to be mostly related to worse outcomes in the drug therapy group.⁵³ This suggests that AF ablation should be preferred before antiarrhythmic drugs in ethnic minorities.

Conclusions and future implications

AF ablation is recommended in clinical guidelines as therapy for symptom amelioration. There is increasing evidence of inequality in the implementation of AF ablation for rhythm control favoring males, white individuals, and persons of high income and education level. Evidence of sex, ethnic, and socioeconomic differences in success rates of AF ablation is insufficient. The slightly higher complication rate in females, driven primarily by nuisance bleeds, should not be a reason to withhold ablation. Randomized clinical trials of AF ablation with adequate representation of females, ethnic minorities, and patients of low socioeconomic status are urgently warranted, as is also a more personalized patient-centered approach regardless of sex, ethnicity, or socioeconomic status for patient involvement, and shared decision-making at all

phases of AF management. Identified research gaps are outlined in [Table 2](#).

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