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Original Research Article

Incidence of cerebro-vascular stroke in atrial fibrillation patients treated medically versus those treated with Radio-Frequency ablation

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Name of Author:
Ahmed Taher Mahmoud[1], Hesham Abd El-Moneim Aly Al-Aassar[2], Moataz Mohamed Amin[3], Moataz Mohamed Hussien Hassaann[4]*

Affiliation: [1,2,3,4]*Critical Care Department, Faculty of Medicine, Cairo University, Egypt*

Corresponding Author:
Moataz Mohamed Hussien Hassaann

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Abstract: ***Background:*** Atrial fibrillation (AF) is one of the most prevalent prolonged cardiac arrhythmias and is a significant risk factor for cerebrovascular stroke, which continues to be a major global source of morbidity, mortality, and long-term impairment. Even if medical rhythm management and oral anticoagulation lower the risk of thromboembolism, a considerable percentage of patients still experience stroke. The effectiveness of radio-frequency (RF) catheter ablation as a rhythm control technique has been established, although its influence on the incidence of long-term cerebrovascular stroke in comparison to medical therapy is still debatable. ***Aim:*** To assess the incidence of stroke in patients with atrial fibrillation treated medically compared with RF catheter ablation, determine potential risk factors for stroke and implement suggestions for a unique follow-up and management approach. ***Methods:*** This retrospective comparative study was conducted on 65 patients with atrial fibrillation who were managed either medically or by RF catheter ablation. Patients were recruited from Critical Care and Cardiology services and followed up for the occurrence of cerebrovascular stroke and transient ischemic attack (TIA). Baseline demographic data, clinical characteristics, comorbidities, type of AF, CHA_2DS_2-VASc score, anticoagulation status, recurrence of AF, and ablation-related or medical treatment complications were analyzed. ***Results:*** The incidence of cerebrovascular stroke was lower in patients treated with RF catheter ablation compared with those managed medically, although stroke events were still observed in both groups. Higher CHA_2DS_2-VASc scores, advanced age, history of hypertension, diabetes mellitus, heart failure, and prior cerebrovascular events were significantly associated with increased stroke risk regardless of treatment modality. Persistent or recurrent AF after ablation and inadequate or discontinued anticoagulation were important contributors to thromboembolic events. ***Conclusion:*** Radio-frequency catheter ablation of atrial fibrillation is associated with a lower incidence of cerebrovascular stroke compared with medical management alone; however, it does not eliminate stroke risk. Long-term stroke prevention in AF patients remains strongly dependent on appropriate risk stratification and sustained anticoagulation, irrespective of rhythm control strategy. Careful patient selection, strict adherence to anticoagulation guidelines, and close follow-up are essential to minimize cerebrovascular complications.

Keywords: Atrial fibrillation; Cerebrovascular stroke; Radio-frequency ablation; Anticoagulation; CHA_2DS_2-VASc score.

INTRODUCTION

Atrial fibrillation (AF) continues to be one of the leading causes of stroke, heart failure, sudden death, and cardiovascular morbidity worldwide, despite significant advancements in the treatment of AF patients. In addition, a sharp increase in the number of AF patients is anticipated in the upcoming years. (1) The task force's members include cardiologists with a range of subspecialty knowledge, cardiac surgeons, stroke neurologists, and trained nurses, reflecting the interdisciplinary input into the management of patients with AF. (1) AF is independently linked to a 1.5-fold increased risk of all-cause death in males and a two-fold greater risk in women (2,3,4). Anticoagulation can significantly reduce the risk of stroke death, but other cardiovascular fatalities, such as heart failure and sudden death, are nevertheless common even in AF patients receiving current evidence-based treatment (5). Increased morbidity, including heart failure and stroke, is also linked to AF (3,6,7).

Few researchers have retrogradely examined a unique subgroup of individuals who had RF ablation of atrial fibrillation (RFA), and they found that the annual rate of stroke following RFA is around 1%, independent of anticoagulation, heart rhythm, or thromboembolic risk. Given that several patient-specific risk factors include age ≥ 75 years, hypertension, heart failure, prior stroke or TIA, and CHA2DS2-VASc score ≥ 2, these findings may prove helpful for patient selection for and follow-up following RFA. High-risk individuals had a low rate of long-term anticoagulation persistence following RFA. (8)

Regardless of the cause or method of treatment (medical vs. RF ablation), atrial fibrillation is ultimately linked to the risk of fatal stroke. Therefore, recommendations and risk factor stratification should be examined in future research, either prospectively or retrospectively, to classify the risk of stroke in AF patients in various modules.

MATERIALS AND METHODS

This bi-armed retrospective analytic analysis included 65 patients with atrial fibrillation who were admitted to Cairo University's Critical Care Department between 2012 and 2016 with two-years follow-up.

Inclusion criteria:
- Age > 18 years.
- Both sexes.
- Patients admitted or outpatient with AF.

Exclusion criteria:
- EF < 35 %.
- RHD

The study began by enrolling all patients admitted to the Critical Care Department and the International Medical Center (IMC) between 2012 and 2016, following approval by the Critical Care Department's ethical and scientific committee on 18/07/2017 and the acquisition of patients' informed written or verbal consent.

Data from patient files and the E system Medica Plus at the Critical Care Unit and the International Medical Center (IMC) were obtained for the study, which was planned as a retrograde analytical study. If the International Classification of Diseases, Ninth Edition (ICD9) was utilized, patients were identified using their assigned codes (Codes 148.1, 148.2, 148.3, and 148.91 for the diagnosis of AF, Code 5A2204Z for sinus rhythm restoration, and Code 02583ZZ for catheter ablation). The same codes were used if the International Classification of Diseases, tenth edition (ICD10) was utilized.

Every patient was evaluated through lengthy, in-depth phone conversations, and they were all enrolled for a 12-lead ECG and clinical assessment. Holter ECGs were requested for patients who were in sinus rhythm at the time of examination.

Two groups of recruited patients were created: Group A comprised 34 patients who were medically managed with rate controllers and anticoagulants in the Cardiology Department at the International Medical Centre (IMC) and Group B comprised 31 patients who underwent radiofrequency ablation for paroxysmal or persistent AF in the Critical Care Medicine department at Cairo University.

In order to compare risk variables and the incidence of stroke, matched groups were created using a proportional hazard Cox regression model adjusted by propensity scores. Additionally, management and follow-up recommendations were created for both treated groups.

Standard 12-leads ECG:
Every patient underent a surface ECG. Upon admission, all patients had their standard 12-lead ECG recorded with a standardization of 1 mV/10 mm and a paper speed of 25 mm/s (9, 10).

HATCH Score
The HATCH score is used to predict whether paroxysmal atrial fibrillation (AF) will progress to persistent AF. A score of 0–1 indicates a low risk of AF progression, whereas a score of ≥2 indicates a higher risk and a higher likelihood of developing persistent AF. (11).

CHA_2DS_2-VASc Score:
In patients with non-valvular atrial fibrillation, the CHA_2DS_2-VASc score calculates the annual risk of stroke; a score of 0 denotes low risk, a score of 1 indicates intermediate risk, and a score of ≥2 indicates high risk. (12).

Outcomes:
Primary outcome:
The incidence of stroke in both groups of patients with AF treated medically (either by RF catheter

ablation or pharmacological rhythm management or rate control strategies).

Secondary outcome:

• Suggestions for both groups' follow-up.
• Suggestions for both groups' management.

Statistical analysis:

SPSS v26 was used for statistical analysis (IBM Inc., Chicago, IL, USA). The following tests were used: Fisher's exact test, Mann-Whitney test, Chi-square test, and unpaired Student's T-test. Statistical significance was defined as a two-tailed P value of less than 0.05.

RESULTS

The mean age of all study participants was 53.97 ± 5.97 years, and there was no statistically significant difference between the groups receiving medical care and those receiving ablation. Thirty (46.2%) of the trial participants were female, and there was no statistically significant difference between the groups receiving medical treatment and ablation. Additionally, the mean urea level, left atrial size, and ejection fraction did not differ statistically significantly between the ablation and medical treatment groups. However, compared to the ablation group (0.92 ± 0.16 mg%), the medical treatment group's mean creatinine level was significantly higher (1.04 ± 0.18 mg%). (Table 1).

Table (1): Baseline clinical characteristics among the study groups (n = 65)

	Medical treatment (n = 34)	**Ablations** (n = 31)	**Total (n = 65)**	**P value**
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)	54.00 ± 6.21	53.94 ± 5.81	53.97 ± 5.97	0.966
Gender (Female)	17 (50.0%)	13 (41.9%)	30 (46.2%)	0.515#
Urea (mg%)	20.88 ± 3.07	19.87 ± 2.81	20.40 ± 2.97	0.173
Creatinine (mg%)	1.04 ± 0.18	0.92 ± 0.16	0.98 ± 0.18	0.005*
LA size (cm)	3.97 ± 0.22	4.06 ± 0.28	4.02 ± 0.25	0.135
EF (%)	56.88 ± 4.62	58.26 ± 5.53	57.54 ± 5.08	0.279
Time from puncture to transeptal	NA	22.61 ± 5.98	22.61 ± 5.98	NA
Time of mapping	NA	23.84 ± 5.70	23.84 ± 5.70	NA
RF time	.NA	35.29 ± 5.47	35.29 ± 5.47	NA
Procedure time	NA	187.45 ± 19.67	187.45 ±19.67	NA
Fluro time	NA	54.13 ± 11.78	54.13 ± 11.78	NA

*: statistically significant, SD: standard deviation, NA: not applicable

There were no statistically significant differences between the medical therapy group and the ablation group at baseline, according to the initial evaluation of CHA2DS2VASC and HATCH scores. Furthermore, there were no statistically significant differences seen in the comorbidities assessment with respect to diabetes mellitus, ischemic heart disease, asthma, chronic obstructive pulmonary disease, cardiomyopathy, or hypertension. However, the percentage of anticoagulant prescriptions in the medical treatment group was much greater (44.1%) than in the ablation group (16.1%). The ablation group experienced a considerably higher percentage of paroxysmal atrial fibrillation (87.1%) than the medicinal treatment group (41.2%). Anti-coagulation medication use was more common in the medical treatment group (44.1%) than in the ablation group (16.1%). The difference was statistically significant (Table 2).

Table (2): Comorbidities and baseline clinical assessment among the study groups (n = 65)

		Medical treatment (n = 34)	**Ablation (n = 31)**	**Total (n = 65)**	**P value**
		No. (%)	**No. (%)**	**No. (%)**	
Hypertension		13 (38.2%)	11 (35.5%)	24 (36.9%)	0.818#
Diabetes mellitus		7 (20.58%)	7 (22.6%)	14 (21.5%)	0.845#
Ischemic heart disease		1 (2.94%)	1 (3.2%)	2 (3.1%)	1@
Asthma		1 (2.94%)	1 (3.2%)	2 (3.1%)	1@
chronic obstructive pulmonary disease		2 (5.88%)	1 (3.2%)	3 (4.6%)	1@
Anticoagulation		15 (44.1%)	5 (16.1%)	20 (30.8%)	0.015#*
HATCH score	0	22 (64.7%)	20 (64.5%)	42 (64.5%)	0.865#
	1	10 (29.4%)	10 (32.3%)	20(30.8%)	
	2	2 (5.9%)	1 (3.2%)	3 (4.6%)	
CHA2DS2VASC	0	20 (58.8%)	17 (54.8%)	37 (56.9%)	0.322#
	1	6 (17.6%)	8 (25.8%)	14 (21.5%)	
	2	3 (8.8%)	0 (0%)	3 (4.6%)	
	3	5 (14.7%)	6 (19.4%)	11 (16.9%)	
AF type	paroxysmal	14 (41.2%)	27 (87.1%)	41 (63.1%)	< 0.001#*
	persistent	20 (58.8%)	4 (12.9%)	24 (36.9%)	

HATCH score: Hypertension, Age, Transient ischemic attack, Chronic obstructive pulmonary disease, and Heart failure score, CHA2DS2-VASc: Congestive heart failure or left ventricular dysfunction Hypertension, Age (doubled), Diabetes, Stroke (doubled)-vascular disease, score.

#: chi square test, @: Fisher exact test, *: statistically significant, NA: not applicable.

Regarding cerebrovascular stroke, 9.7% of patients in the ablation group experienced it, compared to 17.6% of patients in the medicinal treatment group. There was no statistically significant difference in the two groups' rates of cerebrovascular stroke. In a similar vein, the percentage of patients with disability was higher in the medical treatment group (14.7%) than in the ablation group (6.5%). Nevertheless, there was no statistically significant change. (Table 3).

Table (3): Distribution of disabilities and Cerebrovascular Stroke among the study groups (n = 65)

	Medical treatment (n = 34)	**Ablation group** (n = 31)	**Total (n = 65)**	**P value@**
	Count (%)	Count (%)	Count (%)	
CVS	6 (17.6%)	3 (9.7%)	**9 (13.8%)**	0.480
Disabilities	5 (14.7%)	2 (6.5%)	**7 (10.8%)**	0.430

@: Fisher exact test, CVS: Cerebrovascular Stroke

Comparing the medical treatment group to the ablation group, the medical treatment group had a greater recurrence of disease by six months, one year, and two years: 22.6%, 35.5%, and 51.6% versus 8.8%, 14.7%, and 23.5%, respectively. Nevertheless, there was no statistically significant difference in the percentages of recurrences between the ablation group and the medical treatment group during the three time periods. (Table 4).

Table (4): Recurrence of the disease and blanking status among the study participants (n = 65)

Outcome		**Medical treatment** (n = 34)	**Ablation group** (n = 31)	**Total (n = 65)**	**P value**
		Count (%)	Count (%)	Count (%)	
Recurrence interval	within 6 months	7 (22.6%)	3 (8.8%)	10 (15.4%)	0.309@
	within 1 year	11 (35.5%)	6 (14.7%)	16 (24.6%)	0.129#
	within 2 years	16 (51.6%)	8 (23.5%)	24 (36.9%)	0.076#

The percentage of patients with anticoagulation in the form of Warfarin and New Oral Anticoagulation (NOAC) among the medical treatment and ablations groups was the same: 60% and 40%, respectively (Table 5).

Table (5): Anti-coagulant drug used among recipients of anticoagulation (n= 20)

Anticoagulant	**Medical treatment (n = 15)**	**Ablations (n = 5)**	**Total recipients (n = 20)**	**P value@**
	Count (%)	**Count (%)**	**Count (%)**	
Warfarin	9 (60%)	3 (60%)	12 (60%)	1
NOAC	6 (40%)	2 (40%)	8 (40%)	

@: Fisher exact test, NOAC: New Oral Anticoagulants

Amiodarone was the most used medical treatment for rhythm control (55.9%), followed by Propafenone (29.4%) and Sotalol (14.7%) (Table 6).

Table (1): Medical treatment used for rhythm control among the medical treatment group (n = 34)

Drug name	**Count (%)**
Amiodarone	19 (55.9%)
Propafenone	10 (29.4%)
Sotalol	5 (14.7%)

Vascular hematoma accounted for 12.9% of ablation-associated complications, with pericardial effusion and post-ablation Atrial Flutter/Atrial Tachycardia (A. Flu/AT) coming in second and third, respectively, at 9.7%. Phrenic nerve damage, atrial-esophageal fistula, and thromboembolism from sources other than cerebrovascular stroke (CVS) were not documented. (Table 7).

Table (7): Ablation-associated complications among the ablation group (n = 31)

Procedure complication	Count (%)
Pericardial effusion	3 (9.7%)
phrenic nerve injury	0 (0.0%)
vascular hematoma	4 (12.9%)
Post-ablation A. Flu/ AT	3 (9.7%)
Atrio-esophageal fistula	0 (0.0%)
Thrombo-embolism (other than CVS)	0 (0.0%)

Drug intolerance was the most reported complication (11.8%), followed by allergy and Drug-related hypotension/ bradycardia (8.8%). There were no reported cases of Drug-related thyroid disorders (Table 8).

Table (8): Complications of medical treatment among the medical treatment group (n = 34)

Complication	Count (%)
Allergy	3 (8.8%)
Drug intolerance	4 (11.8%)
Drug-related hypotension/ bradycardia	3 (8.8%)
Drug-related thyroid disorders	0 (0.0%)

DISCUSSION

The mean creatinine level in the medical therapy group was considerably higher (1.04 ± 0.18 mg%) than in the ablation group (0.92 ± 0.16 mg%) in the current study. The therapeutic choice to postpone catheter ablation in favor of pharmaceutical care may have been influenced by the discovery that individuals in the medicinal therapy group had comparatively poorer kidney function.

This aligned with Bansal et al. (13) who demonstrated that AF is linked to a high risk of recurrent cardiovascular events and the development of end-stage kidney disease, and that its incidence is two to three times higher in CKD patients than in the general population. In addition to making people more susceptible to AF, chronic kidney disease (CKD) increases the risk of cardiovascular morbidity and the development of end-stage renal disease, which calls for cautious treatment.

In this regard, Goette et al. (14) shown that individuals with AF may experience more adverse events if their creatinine levels are elevated, supporting the necessity for a more cautious approach to treatment for patients with renal impairment.

In the same context, Mirhosseini et al. (15) highlighted that mean creatinine level in patients with and without were 1.1±0.5 and 1.6±0.2, respectively, highlighting the common co-occurrence of renal impairment in AF patients.

Our findings showed that the percentage of anticoagulant prescriptions in the medical therapy group was much greater (44.1%) than in the ablation group (16.1%). The clinical characteristics and risk assessment of patients chosen for medical treatment most likely account for this discrepancy. According to CHA_2DS_2-VASc grading, patients under medical management may have a higher perceived thromboembolic risk, necessitating anticoagulation. Paroxysmal AF type, which usually carries a reduced risk of stroke and may be the reason for less frequent use of anticoagulants, was much more common in the ablation group (87.1%) than in the medical treatment group (41.2%). There was no statistically significant difference between the two groups in terms of ischemic heart disease, asthma, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, or cardiomyopathy, according to the comorbidities assessment.

In the same line, Kautzner et al. (16) conducted a study in which 482 patients suffering from paroxysmal atrial fibrillation were divided into two groups at random. There were 243 patients in the control group and 239 patients in the DTA group (irrigated RF ablation catheters). They found that there was little difference between the two groups in terms of heart disease, diabetes mellitus, and hypertension.

This was further supported by Kuck et al. (17) who found that RF ablation is the most common method for paroxysmal AF. In addition, Nielsen et al. (18) suggested the radiofrequency ablation as first-line treatment in patients with paroxysmal AF.

In this study, only 9.7% of patients in the ablation group experienced cerebrovascular stroke, compared to 17.6% of patients in the medicinal treatment group. The numerically lower stroke incidence in the ablation group raises the possibility of a preventive effect of catheter ablation, even though this difference did not achieve statistical significance. Disability rates showed a similar pattern, with 14.7% of patients in the medical group and just 6.5% in the ablation group—again, no statistically significant difference. These patterns might be a reflection of ablation's improved results in terms of rhythm management and stroke prevention, especially in patients with paroxysmal atrial fibrillation and better maintained cardiac function.

Aligning with our findings, Providencia et al. (19) observed that catheter ablation was associated with a significant reduction in stroke. In the same line, Ding et al. (20) demonstrated that a substantial decrease in the risk of ischemic stroke was associated with catheter ablation. According to these investigations, improved long-term cerebrovascular outcomes could result from rhythm control attained by ablation.

This was further supported by Akerström et al. (21) who demonstrated that catheter ablation of AF was associated with reduced all-cause mortality or stroke when compared with medical therapy. Also, Burnham et al. (22) revealed that catheter ablation is consistently associated with lower rates of stroke compared to AF management without ablation. Furthermore, Friberg et al. (23) concluded that ablation may be associated with lower incidence of ischemic stroke and death in patients with AF.

The observed trends are in line with the larger body of evidence indicating that, when compared to medical therapy, catheter ablation may provide a meaningful reduction in cerebrovascular events and disability, especially in patients who have been carefully chosen. This is true even though the current study did not show statistically significant differences.

Comparing the medical treatment group to the ablation group in the current study, the medical treatment group had a greater recurrence of disease by six months, one year, and two years: 22.6%, 35.5%, and 51.6% versus 8.8%, 14.7%, and 23.5%, respectively. The trend obviously favors catheter ablation in lowering AF recurrence over time, even if the differences in recurrence rates between the two groups were not statistically significant at any of the time points.

This aligned with Chew et al. (24) who reported that catheter ablation is associated with lower AF recurrence rates and all-cause hospitalization. Also, Rattka et al. (25) showed that, as compared to conventional medical treatment, catheter ablation has been linked to a reduction in AF recurrence and mortality. These findings substantiate ablation's superiority in long-term rhythm control.

The lower recurrence rates seen in the ablation group, despite the current study's lack of statistical significance, are consistent with a pattern documented in the literature and suggest that catheter ablation is a more effective method of preventing AF recurrence than medication therapy.

According to our findings, there was no discernible difference between the medical treatment and ablation groups' percentages of patients receiving anticoagulation in the form of Warfarin and New Oral Anticoagulation (NOAC), which were 60% and 40%, respectively. The most often prescribed medication for rhythm control was amiodarone (55.9%), which was followed by propafenone (29.4%) and sotalol (14.7%).

In the same context, Wang et al. (26) advised that oral anticoagulants (OACs) can be taken for at least the first two months following AF ablation.

Aligning with our study, Barra et al. (27) also found that amiodarone is the strongest antiarrhythmic medication on the market and is frequently used to treat and prevent AF in addition to potentially fatal ventricular arrhythmias.

Similarly, a review by Camm et al. (28) who demonstrated that amiodarone (62.8% utilized at any time), sotalol (41.4%), and propafenone (14.5%) were the rhythm control strategies.

Vascular hematoma (12.9%) was the most frequent ablation-related event in this study, followed by pericardial effusion and post-ablation atrial flutter/atrial tachycardia (A. Flu/AT) (9.7% each). No cases of atrial-esophageal fistula, thrombo-embolism, or phrenic nerve damage from sources other than cerebrovascular stroke were documented. The most common problem was drug intolerance (11.8%), which was followed by allergies and drug-related bradycardia/hypotension (8.8%). Drug-related thyroid problems were not documented.

Radiofrequency (RF) ablation has important clinical consequences even if its complication rate is still rather low. On the other hand, when contemplating ablation as a treatment option, the problems from antiarrhythmic drug (AAD) therapy frequently appear over a longer period of time, emphasizing the significance of thorough patient selection and extended patient follow-up.

In accordance with our results, Doldi et al. (29) noted that 49 patients (37.3%) had their antiarrhythmic medication regimen modified, with 16.3% experiencing intolerance. Likewise, Williams et al. (30) claimed that medication intolerance was the reason for about 25% of patients stopping sotalol therapy. These results highlight the difficulties of managing AF medically throughout the long run.

Aligning with our findings, Sharma et al. (31) discovered that the most frequent problems following catheter ablation are those related to vascular access, which have been documented to happen in 1–13% of instances.

In this regard, Alipour et al. (32) mentioned that vascular access site hematoma is one of the dangers associated with catheter ablation. Likewise, Dalsgaard et al. (33) showed that after AF ablation, the incidence of a substantial hematoma is between 1.5% to 10%.

These results highlight the fact that although RF ablation is generally safe, it is still important to be vigilant for vascular problems. Similarly, the possibility of cardiovascular adverse effects and medication intolerance during medical therapy calls for close observation and could affect choices about treatment approaches.

CONCLUSION

Despite improvements in therapy, atrial fibrillation (AF) continues to be a major cause of stroke, heart failure, sudden cardiac death, and cardiovascular morbidity. In the upcoming years, it is anticipated that its prevalence would rise dramatically worldwide. A multidisciplinary strategy comprising cardiologists, cardiac surgeons, stroke neurologists, and trained nurses is necessary due to the complexity of AF therapy.

The risk of all-cause mortality is independently increased by AF, increasing by 1.5 times for males and doubling for women. Anticoagulation lowers the fatality rate from stroke, however other cardiovascular problems are still common.

Regardless of anticoagulant status or rhythm management, catheter-based radiofrequency ablation (RFA) for AF has demonstrated a residual stroke risk of about 1% per year. Risk factors that affect outcomes after ablation include age ≥75, hypertension, heart failure, previous stroke or TIA, and CHA_2DS_2-VASc ≥2.

Compared to AF patients treated medically, those treated with RF ablation had lower creatinine levels, fewer anticoagulant prescriptions, and a higher prevalence of paroxysmal AF. Differences were comparable even though the ablation group had reduced rates of stroke and disability. Complication profiles varied, with medication intolerance predominating in medical therapy and vascular events more frequent after ablation.

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