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Patients Treated with Catheter Ablation for Atrial Fibrillation have Long-Term Renal Function Similar to Patients without Atrial Fibrillation

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Abstract

Background: Atrial fibrillation (AF) has been reported to worsen renal function over time. Renal dysfunction in the setting of AF decreases response to rhythm control approaches and increases risk of cardiovascular morbidity and mortality. Aggressive rhythm control approaches, such as catheter ablation, may interrupt this cycle and impact renal function favorably over time.

Methods: Patients were enrolled from the large ongoing prospective Intermountain Cardiovascular Health Study. A total of 1,983 consecutive patients who underwent AF ablation that has serial assessment of kidney function were compared to a cohort of 4,996 patients with AF (no ablation) and 19,154 without AF derived from the catheterization database.

Results: Ablation patients were older compared to catheterization controls (66.2 vs. 56.7, p<0.0001). Ablation patients compared to no ablation patients had lower rates of dyslipidemia (40.3% vs. 28.8%, p<0.0001), heart failure (32.5% vs.12.2%, p<0.0001), and coronary artery disease (52.3% vs.31.5%, p<0.0001). Creatinine was at baseline higher and increased in AF patients not treated with ablation over time, where modest change was observed in those treated with ablation and controls. Ablation patients also had similar rates of progression to renal failure compared to the younger catheterization patients and significantly lower than the no ablation patients. These observations persisted in age-based analysis.

Conclusion: Renal function and failure rates over time in patients with AF that receive an ablation are similar to patients without AF. These data suggest that aggressive rhythm control strategies may minimize the adverse influence of the arrhythmia on long-term renal function.

Keywords

Atrium, Fibrillation, Renal dysfunction, Creatinine, Renal failure, Ablation

Introduction

Atrial Fibrillation (AF) is a common cardiac arrhythmia in clinical practice today.[1]It has been shown that more than 2 million people in the United States are affected by AF; a number expected to increase [1-3]. As the population ages, in general all types of cardiovascular diseases are increasing and their individual and accumulative impact on outcomes remain an area of increasing study.

Heart and kidney dysfunction are often correlated with each other [4,5]. Furthermore, if the function of either of these two organs begins to decline, the other may be adversely affected, causing further organ damage. For those patients that are suffering from chronic renal insufficiency, there is often a progression of renal disease despite treatment and an increased risk of myocardial infarction, heart failure and cardiovascular death [4-8]. Risk factors for both AF and renal dysfunction are very similar (i.e.: age, hypertension, diabetes mellitus, cardiovascular/structural heart disease) and approximately 18% to 21% of patients that have chronic renal insufficiency have AF [5,9]. A recent study found that long-term renal function was favorably influenced after catheter ablation for AF; a finding suggestive that AF and its' treatment may be therapeutic targets to improve long-term outcomes in patients with coexistence of arrhythmia and renal dysfunction [9].

Catheter ablation is an established treatment for AF. The worldwide multicenter success rates with ablation were reported to be greater than 70% [10,11]. With favorable observed success rates with paroxysmal AF patients, ablation has been expanded to other AF subtypes and in patients with multiple disease states [12]. Since most anti-arrhythmia drugs cannot be used long-term safely with advanced kidney disease, the question of the utility, safety, and long-term impact of catheter ablation and renal function requires additional study.

Methods

Patients were identified through review of the Intermountain

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Heart Collaborative Study database that had long-term care within the system and serial kidney function blood draws that underwent catheter ablation for symptomatic AF. Patients were considered for the catheter ablation based upon typical criteria that included failing anti-rhythmic medications and continued symptomatic arrhythmia episodes. Our radiofrequency ablation approach has been previously described in detail [13,14]. All patients had >1 baseline kidney assessments performed prior to the catheter ablation.

The ablation group was compared against two other cohorts. One group was comprised of AF patients that did not undergo ablation and another group that had no history of AF. Both groups consisted of patients within the Intermountain Healthcare system with long-term follow-up and serial assessment of kidney function. AF was diagnosed or excluded through examination of clinical notes, ICD-9 codes, and the system-wide electrocardiogram database.

In addition to age and gender, patient information collected included diabetes status (diabetes mellitus: fasting blood glucose >125mg/dL, clinical diagnosis of diabetes mellitus, or anti-diabetic medication use; insulin resistance: fasting glucose between 110-125mg/dL; and normal: fasting glucose <110mg/dL), hypertension (systolic blood pressure ≥140mmHg, diastolic ≥90mmHg, or anti-hypertensive use), and hyperlipidemia (total cholesterol ≥200mg/dL, LDL ≥130 mg/dL, or cholesterol-lowering medication use). Smoking included active smokers or those with a >10 pack-year history. Prior cerebrovascular accident (CVA), transient ischemic attack (TIA), and myocardial infarction (MI) were physician-reported or determined by previous ICD-9 discharge diagnosis codes. AF subtype (paroxysmal, persistent, or permanent) was physician-reported at ablation hospitalization. Discharge medications (i.e., statin, other lipid lowering medications, ace-inhibitors [ACEI], angiotensin receptor blocker [ARB], beta-blocker, diuretic, digoxin, plavix, coumadin) were also available.

The general methodology of ablation and the peri-procedure and follow-up care of these patients has been reported previously in detail [13-15]. Regarding follow-up, 2 weeks after the patients have the catheter ablation; they are seen in the clinic for assessment of the groin wounds, and to evaluate for any post-operation complications such as increasing chest discomfort, dyspnea or dysphagia. During the initial 3 months after the ablation, the patient's arecontinued on their anti-rhythmic medications, along with Pradaxa, Coumadin or Xarelto for appropriate anticoagulation. At the three month follow up visit, a repeat kidney function test was performed, as well as discussion in stopping the anti-rhythmic medication if indicated, and depending on the CHADS score (score ≤1), converting the patient to daily Aspirin. At all follow up visits, ECG's are performed to assess the rhythm, as well as the use of Event Monitors every 3 months over the first year and thereafter based upon symptoms. In regards to repeat AF events, any atrial tachyarrhythmia (AF or atrial flutter) event that occurred after the medications have been discontinued, that lasts longer than 30 seconds, is considered as a recurrence of the arrhythmia. Regarding renal function, serial assessment of kidney function (every 3 months) was compared as well as new ICD-9 coding of chronic renal failure.

Statistical Analysis

The total population was separated into three groups for comparison: those that had no history of AF, those that had AF and underwent the RF catheter ablation and those that had AF and no RF ablation. The differences in baseline characteristics between the groups were determined by the chi-square statistic for discrete variables and the unpaired t-test and analysis of variance (ANOVA) for continuous variables. The change in creatinine (follow-up creatinine minus baseline creatinine) was calculated and compared between the three groups using ANOVA and intergroup comparisons were made using the Tukey's HSD test. The Kaplain Meier Survival estimate and the log rank statistic was used to determine longitudinal associations with follow-up renal failure. A p-value of <0.05 was deemed statistically significant.

Results

A total of 26,133 patients were studied. Of these, there was a total of 1,983 consecutive patients who underwent AF ablation that had serial assessment of kidney function that were compared to a cohort of 4,996 patient with history of AF that had no catheter ablation performed, and 19,154 without AF. Baseline demographics and ejection fraction of the population are shown in Table 1. Of the study patients within the three groups, those patients that had AF and catheter ablation were older compared to the catheterization controls, (66.2 vs. 56.7). It was interesting to view that AF study group had a higher risk of heart failure (32.5% vs. 12.2%) compared to the AF ablation group, as well as hyperlipidemia (40.3% vs. 28.8%) and CAD (52.3% vs. 31.5%). Regarding outcomes of those that received an AF ablation, at 1 year 82.9% and at 3 years 64% had no documented episode of recurrent AF after their last ablation procedure (27% required more than one ablation procedure).

The serial creatinine blood draws, indicated that the creatinine at baseline was higher in the AF with no ablation, and increased when not treated with ablation over time when compared to those that had the ablation (1.26 ± 0.86mg/dl vs. 1.06 ± 0.48mg/dl). These changes to the creatinine levels were observed in those that were treated with the ablation procedure as well as the controls (1.06 ± 0.48mg/dl ablation, and 1.05 ± 0.77mg/dl control). This data indicates that for those patients that have had the ablation for AF, the creatinine levels improved and are relatively close to those in the control group, that do not have complications due to arrhythmias.

In regards to the progression of kidney function when associated with AF, the study results demonstrated that the AF group, who had the ablation, had similar rates of progression to renal failure compared to the younger control patients. At three months, control was +0.03mg/dlvs.+0.03mg/dl in the ablation group, and six months +0.02mg/dl vs. +0.03mg/dl compared to baseline measurements. The

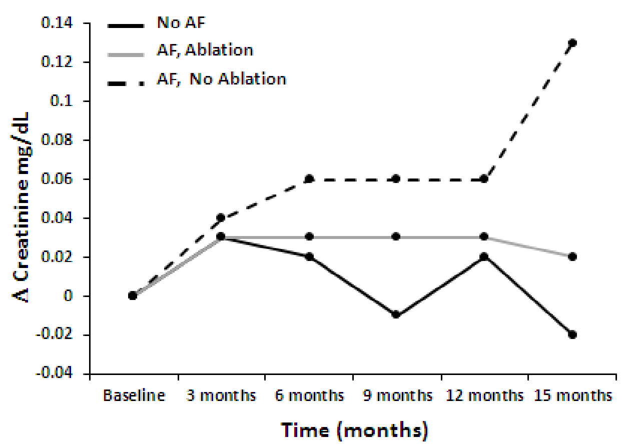

Figure 1: The figure displays the change in creatinine relative to the baseline at time of study enrollment. Overall, there was no-modest change in the no AF and AF ablation patients over time. In contrast, patients with AF not treated with ablation had consistent elevations in creatinine over time.

Table 1: Baseline characteristics of patients with serial renal function separated and compared by atrial fibrillation status.

Characteristic	Control	AF	Ablation	p-value
Age (years)	56.7 ± 16.1	70.7 ± 12.5	66.2 ± 11.2	<0.0001
Sex (male)	54.0%	60.5%	58.3%	<0.0001
Hypertension	41.7%	50.6%	51.6%	<0.0001
Hyperlipidemia	38.4%	40.3%	28.8%	<0.0001
Diabetes	16.4%	19.3%	12.3%	<0.0001
Smoking	10.0%	8.4%	3.1%	<0.0001
Family history	25.9%	20.5%	0.3%	<0.0001
Heart failure	10.1%	32.5%	12.2%	<0.0001
Prior MI	4.2%	12.8%	4.6%	<0.0001
Prior CAD	25.5%	52.3%	31.5%	<0.0001
EF (%), n=13,857	57.9 ± 16.0	51.6 ± 16.2	51.6 ± 12.4	<0.0001

Table 2: Renal function characteristics of patients with serial renal function separated and compared by atrial fibrillation status.

Variable	Control	AF	Ablation	Global p-value
Baseline creatinine (n=26,133)	1.05 ± 0.77*(median: 0.90) (n=19,154)	1.26 ± 0.86*† (median: 1.07) (n=4996)	1.06 ± 0.48†(median: 1.00) (n=1983)	<0.0001
Δ 3 months (n=4150)	0.03 ± 0.65 (n=2571)	0.04 ± 0.56 (n=1250)	0.03 ± 0.50 (n=329)	0.91
Δ 6 months (n=3485)	0.02 ± 0.69 (n=2195)	0.06 ± 0.65 (n=958)	0.03 ± 0.44 (n=332)	0.34
Δ 9 months (n=2992)	-0.01 ± 0.79 (n=1883)	0.06 ± 0.74 (n=824)	0.02 ± 0.39 (n=285)	0.10
Δ 12 months (n=2941)	0.02 ± 0.91 (n=1916)	0.06 ± 0.78 (n=768)	0.03 ± 0.37 (n=257)	0.44
Δ 15 months (n=2680)	-0.02 ± 1.05* (n=1713)	0.13 ± 0.84* (n=740)	0.02 ± 0.41 (n=227)	0.002
Renal failure Diagnosis				
3 months	3.0%* (576/19,357)	9.3%*† (469/5058)	2.9%† (57/1957)	<0.0001
6 months	3.7%* (695/18,898)	11.9%*† (582/4875)	4.1%† (76/1865†)	<0.0001
1 year	4.8%* (860/17,771)	15.3%*† (692/4535)	5.9%† (99/1687)	<0.0001
2 years	6.2%*‡ (947/15,300)	19.5%*† (753/3856)	8.8%†‡ (117/1335)	<0.0001
Long-term (n=26,592)	9.8%*‡ (1908/19,506)	26.0%*† (1327/5102)	11.7%†‡ (232/1984)	<0.0001

*control vs. AF p<0.05; †ablation vs. AF p<0.05; ‡control vs. ablation p<0.05.

Table 3: Multivariable odd ratios (OR) and hazard ratios (HR) for 3 month, 6 month, 1 year, 2 year, and long-term renal failure risk among those without a history of AF (control) versus patients with AF but that have and have not undergone an ablation. The control group served as the referent in all comparisons.

	3 month	6 month	1 year	2 year	Long-term
AF, no ablation vs. control	OR=3.29, p<0.0001	OR=2.25, p<0.0001	OR=2.21, p<0.0001	OR=2.06, p<0.0001	HR=1.77, p<0.0001
AF, ablation vs. control	OR=0.97, p=0.85	OR=0.97, p=0.80	OR=1.02, p=0.90	OR=0.96, p=0.72	HR=0.94, p=0.38

results were also lower than the AF no ablation patients (+0.04mg/dl, and six months +0.06mg/dl) (Figure 1).

Table 2 shows the three study groups creatinine levels at different draw times. The rates of renal function change and new onset renal failure were fairly similar among the patients in the AF group that had the ablation when compared to the control group. 576 patients out of 19,357 (3.0%) of the control group and 57 of the 1957 (2.9%) AF ablation patients had a new onset of renal dysfunction at three months when compared to the AF group with no ablation, the new onset of renal dysfunction was 9.3% (469/5058 patients).Over the entire length of follow-up (3.6 ± 2.6 years), the control population did have a significantly lower rate of renal failure compared to both the AF group with no ablation (p<0.0001) and the AF group with ablation (p=0.007). However, after adjustment by risk factors and medications, the risk for long-term renal failure between the control group and the AF ablation group was attenuated and no longer significant (Table 3).

We then examined creatinine clearance in the AF and control groups to determine the reliability of serialcreatinine assessment and ICD-9 diagnosis of renal failure. Over long-term follow-up in 74 patients with serial creatinine clearance data entries, 10% of the control population versus 35.2% of the AF, no ablation group versus 11.1% of the AF ablation group developed a creatinine clearance < 30mL/min (p<0.0001) values similar to the long-term rates of renal failure determined by creatinine alone (Table 2).

Finally, examining only the AF ablation group, there was a clear benefit in renal function outcomes in those patients that did not have recurrences of AF or atrial flutter. In regard to the development of renal failure, recurrence of AF or atrial flutter increased risk significantly (HR 1.48, p<0.0001). In a similar manner, recurrence of AF was associated with an increase in creatinine over time (HR 1.39, p<0.0001).

Discussion

AF is an arrhythmia that will continue to progress as the population ages and as the patient population is living longer with comorbid conditions due to the advancements in treatments. These population-based trends suggest the need for careful surveillance of potential end-organ injury related to or in part to AF, cardiovascular disease states, and pharmacologic therapies. In regard to kidney disease, progressive dysfunction places AF patients at unique risk as many of the antiarrhythmic medications and novel anticoagulants are dependent completely or partially on renal elimination.

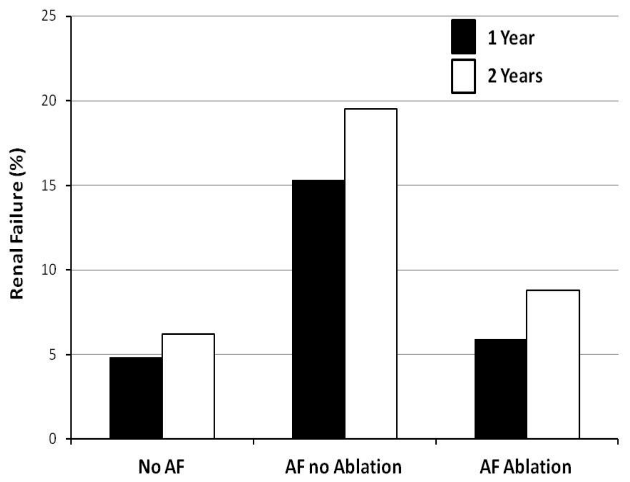

Figure 2: The figure displays the percent of patients at 1 and 2 years that develop renal failure based upon ICD-9 codes divided into 3 groups (AF patients that underwent ablation, AF ablation patients, and patients with no history of AF).

In this context, the current study has several important clinic findings. First, in AF patients not treated with ablation there is a relatively higher incidence and progression of renal dysfunction. In addition, more of these patients progress to a characterization of kidney failure. In patients that undergo ablation, the progression of renal dysfunction or progression to kidney failure is favorably influenced and tracks closely with those patients that have no history of AF. The data are in accordance with the study by Takahashi et al. [9] who reported that changes in glomerular filtration rate at 1 year were significantly better in those patients that maintained sinus rhythm after catheter ablation compared to those that did not (3 ± 8 versus -2 ± 8mL·min(-1) · 1.73m(-2); P<0.0001).

There are several potential mechanisms that may underlie our findings and those previously reported. First, restoration of sinus rhythm provides more uniform vascular dynamics compared to atrial fibrillation [16,17]. Along these lines of enhancing cardiac output, atrial fibrillation ablation has been shown to favorably influence cardiac function over time, which when worsening can negatively influence kidney function over time [18,19]. Next, both atrial fibrillation and the presence and progression of renal dysfunction are correlated with higher levels of systemic inflammation [20,21]. Another potential mechanism is AF is associated with both macroemboli and microemboli [22]. The impact of chronic microemboli may also result in progressive injury to other organs, such as the kidney with renal dysfunction. At minimum the risk of vascular events is heightened in patients that have a combined state of renal dysfunction and AF [23]. We have previously shown that stroke is favorably influenced after AF ablation and tracks along with the risk of patients that have never had AF [13]. As stroke is a marker of systemic macroembolism in patients with AF, we anticipate that if restoring sinus rhythm can favorably reduce stroke (embolism) it should also favorably reduce ischemic kidney injury. Finally, chronic mircobleeds in AF patients on long-term anticoagulation has been shown to result in brain injury, but this same mechanism may result in repetitive injury to the kidney cortex and chronic, but progressive dysfunction [24]. AF ablation that may influence long-term anticoagulation dependency in lower risk patients may reduce this risk.

Our study has several limitations. It is an epidemiologic study of select AF patients treated with ablation versus no ablation that can only be used to identify associations, but unable to establish causality or mechanisms. This study relies on the medical records and as such that ability of physicians to make and document the disease states. In the constraints of the retrospective review, additional analyses of creatinine clearance or glomerular filtration rate levels over time were not available in the complete population and the limited data available are presented for reference comparison. Creatinine alone is an inferior measurement as change can reflect both environmental influences and disease risk factors. The treatments of these patients differed and as such, individualized therapy or lack of therapy may have influenced risks of morbidity and mortality. Next, patients chosen for an ablation may have been healthier as they were selected for an elective procedure. However, in this regard the comparison to those with no history of AF is more important as there was no higher risk over time or renal dysfunction in the ablation group. Finally, including only those patients with serial creatinine assessment may also have introduced bias as these patients may have been receiving more frequent care, but we would anticipate the bias to expand to all study groups.

Conclusion

AF is ever increasing in today's society. With this, comes the risk of increasing renal dysfunction and failure. Our results in this study suggest that patients that have AF that do not undergo aggressive rhythm control, by having the catheter ablation are at increased risk of having renal complications, compared to those patients that have AF with the ablation. This study supports that renal function and failure rates over time in patients with AF that receive an ablation are similar to patients without AF. This suggests that aggressive rhythm control strategies may minimize the adverse influence of the arrhythmia on long-term renal function.

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