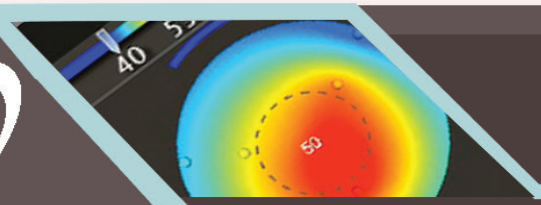
Issn : 1941 - 6911

Apr - May 2021
Volume 13 - Issue 6



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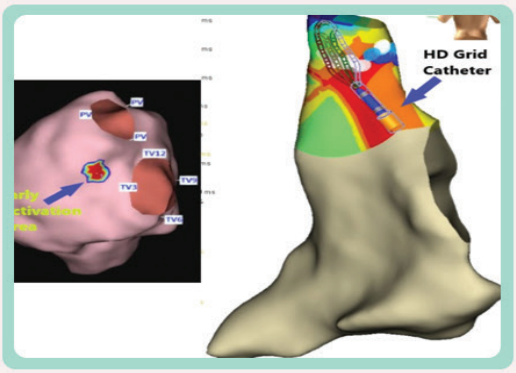

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Editorial

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The Unveiling of a Modern Pandemic!

Journal of Atrial Fibrillation (JAFIB)

Apr - May 2021

Issue 6

Volume 13

Dear Colleagues

Welcome to the current issue of the Journal of Atrial Fibrillation. The pandemic unveils itself into its second year and the end doesn't seem to be anywhere near. It is incredible to see how effectively our leaders have succeeded in making into a political issue than that of health. Thanks to you all we are making slow but steady progress we have made in understanding and managing COVID.

I am very excited to be the interim for the journal as we continue the search for the next Editor-in-Chief continues. I want to thank Dr. DJ Lakkireddy for his service as the immediate past Editor-in-Chief of the journal. His contributions behind and in-front of the screen helped us build this journal. We have some very exciting and thought provoking articles spanning the entire spectrum of Electrophysiology. There has been a significant delay in the release of this issue due to many unavoidable circumstances. Several of our staff members were affected by COVID and the team was significantly short-handed. We have now regrouped and ready to go on publishing and providing high quality scientific material completely free of charge for our readers.

We have adopted new electronic manuscript management system which should help us process the manuscripts much faster. The turn around times should improve as well. With the resurgence of COVID many of you might be affected in many ways. Please continue to encourage your unvaccinated patients to take the jab and contribute to the overall herd immunity. If you are eligible for the 3rd shot (booster) please go on take it. In Q4 of this year we will announce a new editorial team including the Editor-in-Chief. The scope of the journal will expand and will accept articles from all areas of Electrophysiology covering ablation, devices, left atrial appendage closure devices and basic research. We are considering makingthe journal into a monthly release over the next year. I strongly encourage you to submit your applications to join the editorial team as the selection process starts in a few weeks from now.

I once again appreciate the opportunity to present the current and future issues of the journal and your continued support and patronage.

Sincerely

Amin-Al-Ahmad

Amin-Al-Ahmad
MD, FACC, FHRS

Interim Editor-in-Chief
Journal of Atrial Fibrillation

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Editorial

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Physical Inactivity Among Older Adults with Atrial Fibrillation: Prime Time to Get Active!

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Introduction

Atrial fibrillation (AF) affects more than 3 million Americans, with estimated prevalence of nearly 10% in 65 years and older[1]. The prevalence of the disease increases steeplyin the elderly, affecting nearly 12% in 75–84 years, and approximately 1/3 in 80 years or older. The current estimated global burden of the disease is more than 33.5 million[2]. With increasing disease incidence by approximately 5 million each year worldwide, there is urgent need to identify and address associated risk factors [3]. In the recent CABANA trial, with over 2100 patients, the median Atrial Fibrillation Effect on Quality of Life (AFEQT) score was just 63 (Interquartile 25-75%: 48-80) suggesting more than 75% of the patients were moderate to severely symptomatic affecting their quality of life[4]. The toll of AF in overall health and quality of life that it poses cannot be overemphasized.

Over the last two decades, our understanding on AF has much advanced and a number of risk factors have been identified[1,5]. While some risk factors are non-modifiable such as age, male gender, single or polygenic (heritable or de-novo) inheritance, important modifiable risk factors have also been identified. In addition to metabolic syndrome, obesity, sleep apnea, hypertension, chronic kidney disease, diabetes mellitus, cigarette smoking, and depression, physical inactivity has been identified among the most potent modifiable risk factor[1,6]. In a the CARDIO-FIT study, Pathak et al have shown that employing a tailored exercise program designed for age and physical ability involving combination of aerobic and resistance/strength exercises for progressive fitness, every METs gained from baseline was associated with 9% decline in risk of AF recurrence[7]. Hence the role of risk factors management including structured moderate physical activity and weight loss cannot be over stated.

In this issue of JAFIB, Mehawej, J et al report on factors associated with lower levels of moderate intensity physical activity in a cohort of elderly patients. Assessing physical activity in real life is challenging as it is associated with inaccuracies and often exaggerated due to recall bias. A strength of the study is the use of the Minnesota Leisure Time Physical Activity questionnaire to assess the level of physical activity[8]. This instrument has been validated and correlates positively with level of cardiorespiratory fitness[9]. The use of the Cardiovascular Health Study frailty scale is another strength of the study. This instrument was developed based on the Cardiovascular Health Study, where frailty phenotype (defined as presence of ≥ 3: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed and low physical activity) was independently predictive of incident falls, worsening mobility, hospitalization and deaths (adjusted HR: 1.29–2.24)[10]. Depending on the tool of assessment, prevalence of frailty has been described in up to 75% of the elderly patients with AF[11]. Evaluating frailty in patients with AF is important as it has been associated with increased mortality, higher symptom burden, poor success to ablation therapies, and higher incidence of bleeding on oral anticoagulation[11,12].

Another strength of this study is the gender makeup of the population, with nearly 50% of the study participants being women. While the age adjusted prevalence of AF in US has been reported to be 0.9% in females compared to 2.4% in male, female gender has been underrepresented in the majority of major clinical trials[13]. In the CABANA trial assessing the effect of catheter ablation vs medical therapy on quality of life in AF patients, only 37% of the subjects were female[4]. Similarly, in the HUNT study, assessing the physical activity and cardiovascular outcome in AF patients, only 31% were females[14]. The Cardiovascular Health Study which assessed the physical activity and incidence of AF in older adults had better female participation, about 56%. In that study women had lower rate of participation in recommended physical activity and were older compared to males[14,15]. It is important to highlight that the level of physical activity can have gender specific impacts on outcome. In a recent meta-analysis, women were shown to benefit from all level of physical activities, whereas in males, up to moderate physical activity was beneficial but vigorous activities were associated with higher incidence of AF[16].

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As in most trials, African American, Asian American and Hispanics are underrepresented in this study also. With little data, the true incidence and prevalence of the disease in these population is hard to ascertain. Despite higher prevalence of known risk factors as hypertension, obesity, diabetes in African Americans and Hispanics, the incidence of AF may be lower in these population although these populations are underrepresented in majority of trials and population-based studies[1]. In The Cardiovascular Health Study assessing physical activity and incidence of AF in older population, only 17% of the participants were nonwhite15. Even in the Multiethnic Study of Atherosclerosis (MESA), only 42.9% of the participants were non-white highlighting the disparity in representing these population, with AF incidence of 3.4% over a median follow-up of 5.3 years[17].

Too many Americans are sedentary. In a Center for Disease Control (CDC) survey from 2014, nearly 27% of individuals between ages 65-74 years old and nearly 35% aged ≥75 years old were physically inactive or reported no physical activity outside of their work18. In current study by Mehawej, J et al, the results are even more sobering as nearly 50% of the adults above 65 years are engaged in less than the recommended physical activity. Regardless, both of these studies highlight the importance of exercise as a readily available tool that is highly effective in improving AF outcomes yet is much underutilized. In the same CDC survey, as the number of chronic diseases, identified as stroke, coronary heart disease, arthritis, cancer (excluding skin cancer), chronic obstructive pulmonary disease (COPD) and depression burden increased, the level of physical activity was more limited[18]. Besides the CDC identified risk factors for reduced physical activity in elderly population, the investigators have identified factors pertaining to elderly AF patients that includes morbid obesity, renal disease, slow gait speed, cognitive impairment and social isolation.

As in any cross-sectional study, it is a limitation that direction of cause-and-effect can not be determined and relationships may be complex. Obesity has been associated with poor self-esteem, depression, and social isolation which in turn likely limit the much-needed physical activity in these patients and perpetuate obesity and its related complications[19]. On the other hand, there is increasing evidence that depression and physical inactivity interact in both directions leading to poor cardiovascular health outcomes[20].

This study has clearly identified that physical inactivity is rampant in elderly patients with AF. How to improve this? In patients with multiple forms of cardiovascular disease including acute myocardial infraction, congestive heart failure, coronary artery bypass and open-heart surgery, cardiac rehabilitation programs with graded exercise are safe and effective. A number of smaller studies have shown cardiac rehabilitation in patients with AF is also safe and effective in improving cardiovascular outcomes[7,21,22]. As evidence builds of the safety and efficacy of moderate intensity physical activity in patients with AF, it is prime time to institute it in our practice. Increasing awareness of potential benefits of physical activity in this population is critical. Adults who remain physically active in their mid-life are likely to remain active and have better health outcomes later in their life so promoting these activities in early or mid-adulthood will have a lasting impact in our growing elderly population[23]. As shown by Pathak R et al, aggressive risk factors reduction such as weight loss, moderate intensity physical activity, blood pressure, lipid and sleep disorder management were associated with long term arrhythmia free survival[24]. Programs designed to engage individuals at community level such as community fitness programs, peer delivered physical activity, neighborhood group walks programs can be effective to encourage physical activity and break social isolation to improve cardiovascular health outcomes[25,26]. Also, similar programs to increase awareness and incorporate routine scheduled physical activities in long term care facilities can benefit substantial elders as approximately 6% of the US population get help or live in some form of assisted or long-term care facilities.

It has been reported that excessive endurance activities can lead to increased incidence of AF. But how much should we be concerned about urging increasing activity, given the evidence that "excessive endurance exercise" can worsen AF? In Finnish veteran orienteers with history of high endurance activity (an average military training history of 36 years), the incidence of lone AF was 5.3% compared to control of 0.9%and those between the age of 63-70 years had an incidence of 6.6%[27]. In a study of elderly Norwegian men between the age of 65-90 years with history of long-term endurance sport (average 33 years of systematic endurance training, in average competed 17cross-county ski races)had 6% (95% CI: 0.8-11.1) added risk compared to general population of the similar age group[28]. These vigorous activities included long range cycling, marathon running and high endurance sports, are not applicable to most of our elderly patients[29]. Several studies have shown a U-shaped response with the intensity of physical activity and increased risk of AF when cumulative hours of vigorous endurance sports activity are >1500-2000 hours or >5 hours per week[30-32]. Very few elderly patients are engaging in these high levels of endurance activity. While recognizing this impact is important for the tiny minority of AF patients who run marathons or involve in high endurance activity, for the vast majority of our patients, helping them get off the couch and get moving is one of the most important interventions we can offer.

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Rate Control Versus Rhythm Control in Patients with Left Ventricular Assist Devices and Atrial Fibrillation

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Abstract

Background: Atrial fibrillation (AF) is a common comorbidity in patients with left ventricular assist devices (LVAD) with no defined guideline treatment strategy of rate versus rhythm control. The purpose of this study is to determine the effects of rate versus rhythm control for AF on the outcomes of patients with LVAD at our institution.

Methods: Consecutive patients who underwent LVAD implantation at St Vincent Hospital from January 1, 2015 to December 31, 2017 were retrospectively evaluated. Patients with AF were identified and divided into rate control or rhythm control groups. The primary outcome evaluated was a composite of death, heart failure admission, gastrointestinal bleed, ventricular tachycardia, cerebrovascular accident, hemolysis, and pump thrombosis. Secondary outcomes included the individual variables from the primary outcome.

Results: Out of 201 patients that underwent LVAD implantation, 81 had AF after implantation and were included with a median follow-up period of 384 days. The rate control group (n = 31; 38%) and the rhythm control group (n = 51; 62%) had no difference in composite outcomes (61% vs 59%, p = 0.83). When taken individually there was no difference in outcomes between the two groups. Thirteen patients underwent electrical cardioversion and successful conversion to normal sinus rhythm occurred in 71% of cases with a 60% recurrence rate.

Conclusions: There was no difference in primary outcome between rate and rhythm control groups. These data suggest that maintenance of sinus rhythm may not be necessary in all patients with LVAD.

Introduction

Atrial fibrillation (AF) is present in up to 50% of patients with congestive heart failure (CHF). [1,2,3] For patients with advanced CHF, left ventricular assist device (LVAD) has become a viable management strategy as a bridge to transplantation or destination therapy. The effect of AF on the outcomes of patients with LVADs is unknown.[1, 4,5,6,7] Specifically, current evidence remains equivocal on whether AF increases thromboembolic events, heart failure events or mortality in this population [8, 9, 10, 11] Furthermore, when AF is present in the LVAD patient, it is unclear whether rate or rhythm control is the most appropriate strategy. We retrospectively evaluated the effect of rate versus rhythm control for AF on the outcomes in our LVAD population.

Methods

Study Design and Participants

A retrospective single center review was performed of all 201 patients who underwent LVAD implantation at St Vincent Hospital in Indianapolis, IN from January 1, 2015, through December 31, 2017. Follow-up ended July 31, 2018. Patients were identified using the mechanical circulatory support database managed by our LVAD research team. Inclusion criteria consisted of any patient with AF post LVAD implantation irrespective of whether AF was present pre-operatively. Patients under the age of 18 were excluded. The primary outcome evaluated was a composite of death, CHF admission, gastrointestinal bleed (GIB), ventricular tachycardia (VT), cerebral vascular accident (CVA), hemolysis, and pump thrombosis. Secondary outcomes included the individual rates of death, CHF admission, GIB, VT, CVA, hemolysis and pump thrombosis. This study was approved by the local Institutional Review Board.

Study Arms and Clinical Data

Patients were separated into two groups based on AF management strategy: rate control vs. rhythm control. The definition of rate control included patients that did not receive therapy in attempts to restore normal sinus rhythm (NSR), while rhythm control included patients that received an antiarrhythmic drug (AAD) or electrical cardioversion in an attempt to restore and maintain NSR. Because many patients with LVAD are on AAD for ventricular tachycardia, only individuals treated with AAD with the intent to restore NSR were included in the rhythm control group; this intent was deduced by two independent

Key Words
Atrial Fibrillation, LVAD, Rhythm Control.

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chart reviewers and in the case of disagreement adjudicated by a third study member. AF was initially ascertained by chart review, but then confirmed by electrocardiogram, inpatient telemetry or data from cardiac implantable electronic device (CIED). CVA was defined as having a stroke, transient ischemic attack or intracranial hemorrhage diagnosed by the treating physician. Congestive heart failure admission was defined as patients requiring inotropes or readmission for IV diuretics. Time in therapeutic range (TTR) with warfarin was calculated for all patients using the Rosendaal method. [12]

Statistical Analysis

Continuous variables were compared using student T-test if normally distributed or Mann-Whitney test if non-normally distributed. Categorical variables were compared using Pearson Chi-square analysis or Fischer Exact Testing and expressed as percentages. Two tailed P values <0.05 were considered statistically significant.

Results

Baseline Characteristics

From January 1, 2015, through December 31, 2017, 201 patients underwent LVAD implantation. Of these patients, 82 (41%) had AF after device implantation. Among these, 31 (38%) underwent rate control and 51 (62%) underwent rhythm control treatment approaches. The baseline demographics are summarized in [Table 1]. In the rate control group, the median (interquartile range) age was 62 (57, 66) years and only 9.7% of the patients were female, while in the rhythm control group, the median (interquartile range) age was 60 (53, 67) years and 17.6% of the patients were female, with no difference in age or sex between the two groups. The two groups had similar CHA_2DS_2VASc scores (CHF, hypertension, age ≥ 75 years, diabetes, stroke/TIA/thromboembolism, vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]) and duration of follow up. Other basic demographic characteristics were also similar between the two groups including TTR.

Antiarrhythmic Therapy and Electrical Cardioversion

Eight patients (26%) in the rate control group were taking amiodarone for VT suppression with no intention of restoring sinus rhythm (chart review agreement 100%). In the rhythm control group, 98% (n = 49) of patients received therapy with an antiarrhythmic drug (amiodarone in all but one patient who was given dofetilide) and 59% of patients had antiarrhythmic therapy long-term. Electrical cardioversion (CV) was performed in 28% of patients in the rhythm control group and immediately restored NSR in 71% (10 of 14 patients). There was a recurrence rate of 60% (n = 6) in long term follow up despite successful cardioversion.

Outcomes According to Treatment Arm

Overall, there was no difference in the combined endpoint of death, CVA, GIB, CHF admission, VT, hemolysis and pump thrombosis (p = 0.83). There was also no difference in secondary outcomes between the two groups. Ventricular tachycardia was the secondary outcome that occurred most frequently in the rate control and rhythm control group (29% and 43% respectively, p = 0.3). In the rate control group, there was a 26% mortality rate during follow-up while it was 18% in the rhythm control group (p = 0.38) The primary and secondary outcomes are summarized in [Table 2]. Additionally, a comparison of all rate control patients not taking amiodarone were compared to those in the rhythm control group. Fourteen (58%) patients in the rate control arm that were not taking amiodarone met the primary endpoint compared to the 30 (59%) patients in the rhythm control group (p = 0.95). Furthermore, we compared all patients who were taking amiodarone compared to those not taking amiodarone. Fifteen (63%) of the patients that were not taking amiodarone met the primary endpoint compared to the 33 (58%) patients taking amiodarone (p = 0.7).

Discussion

The current study adds to the limited body of literature evaluating the impact of AF management in patients with LVADs. We found that AF occurred in 41% of patients after implantation of LVAD, which was lower than previous reports.[10,11,12] There was no difference in composite outcome of death, CVA, CHF admission, GIB, VT, hemolysis and pump thrombosis between rate and rhythm control strategies (61% vs 59%, p = 0.83). To our knowledge, this is the first study to determine the acute success rate of cardioversions in AF patients with LVADs, with

Table 1: **Baseline Characteristics. Values are median (interquartile range) or n (%). Abbreviation are IMACS – International registry for mechanically assisted circulatory support; LVAD – Left Ventricular assist Device; CHADsVASc – CHF, hypertension, age >= 75 years, diabetes, stroke/TIA/thromboembolism, vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]; INR – International normalized ratio.**

	Rate Control 31 (38%)	Rhythm Control 51 (62%)	p-value
Median Age, years	62 (57, 66)	60 (53, 67)	0.49
Female Sex	3 (9.7%)	9 (17.6%)	0.32
BMI	29 (25, 33)	29 (26, 33)	0.73
Medical History			
Atrial fibrillation	23 (74.2%)	33 (64.7%)	0.37
Coronary Artery Disease	12 (38.7%)	26 (51%)	0.28
Ventricular Tachycardia	15 (48.4%)	20 (39.2%)	0.42
Hypertension	16 (51.6%)	35 (68.6%)	0.12
Diabetes	14 (45.2%)	28 (54.9%)	0.39
Hyperlipidemia	20 (64.5%)	36 (70.6%)	0.57
Stroke	4 (12.9%)	5 (9.8%)	0.66
ICD	25 (80.6%)	36 (70.6%)	0.31
Destination Therapy	15 (48.4%)	25 (49%)	0.96
IMACS profile			0.57
1	6	7	
2	1	7	
3	17	26	
4	5	9	
7	0	1	
LVAD Type			0.4
Heart Ware	16	18	
Heart Mate 2	6	18	
Heart Mate 3	8	13	
CHADsVASc Score	3 (2, 4)	3 (3, 4)	0.4
Follow-up (median LVAD days)	409 (275, 743)	343 (231, 693)	0.37
Time in Therapeutic Range, INR	67 (56, 75%)	67 (55, 75%)	0.93

Table 2: Outcomes. Values are n (%). CHF – congestive heart failure

	Rate Control	Rhythm Control	
	Events	Events	p-value
Composite Outcome	19 (61%)	30 (59%)	0.83
Ventricular Tachycardia	9 (29%)	22 (43%)	0.3
Cerebrovascular Accident	2 (6%)	9 (18%)	0.15
Gastrointestinal Bleed	6 (19%)	16 (31%)	0.23
CHF admission	5 (16%)	14 (27%)	0.24
Hemolysis	1 (3%)	2 (4%)	0.86
Thrombosis	1 (3%)	2 (4%)	0.87
Death	8 (26%)	9 (18%)	0.38

14 patients undergoing cardioversion and an acute success rate of 71%.

Primary and Secondary Endpoints

The primary outcome including a composite of death, CVA, CHF admission, GIB, VT, hemolysis and pump thrombosis revealed no statistical difference between rate versus rhythm control groups (61% vs 59%, p = 0.83). Conclusions from previously published studies evaluating whether or not AF contributes to morbidity and mortality in this unique population were equivocal. [1,4,5,6,7] As a result, clinicians caring for this group of patients have few data to identify what risk AF may pose and the best therapeutic approach. Recently, Noll et al attempted to bridge this void of literature by retrospectively evaluating what effects rhythm control may have over rate control. They concluded that a rhythm control strategy for atrial arrhythmias in patients with LVAD does not decrease the risk of mortality, thromboembolism or bleeding. [13] Our data also support that a rhythm control strategy to maintain sinus rhythm may not improve outcomes in patients with LVAD.

The secondary outcomes included the rate of death, CHF admission, GIB, VT, CVA, hemolysis and pump thrombosis and revealed no statistical difference. These secondary outcomes were selected given the putative risks of AF in this select population include blood stasis secondary to decreased atrial contractility resulting in clot formation, CVA, pump thrombosis and hemolysis; rapid and irregular ventricular contractions precipitating CHF exacerbations and ventricular arrhythmias; and treatment with additional medications, such as amiodarone, that may result in labile INRs. Amiodarone was almost exclusively used in the rhythm control group and did not result in a significant difference in TTR despite drug-drug interactions. There was no difference in rate of GIB or CVA between the two groups. However, there was a trend towards higher rate of CVA (18% vs 6%) and GIB (31% vs 19%) in the rhythm control group that did not meet statistical significance. Larger scale trials are needed to ensure this difference doesn't expand with larger numbers. This also demonstrates the importance of appropriate international normalized ratio (INR) monitoring if additional medications are prescribed with significant warfarin interactions. There was also no difference in CHF admissions between the two groups suggesting rate control for AF should suffice for heart failure mitigation.

Electrical Cardioversion for AF

To our knowledge, this is the first study to determine the success rate of cardioversions in AF patients with LVADs, with 14 patients undergoing cardioversion. The success rate of 71%, is similar to previous reports in patients without LVAD ranging from 68-90%. [14, 15] It is important to note that 71% (n = 10 of 14) of these patients were taking amiodarone at the time of electrical cardioversion. After successful cardioversion, 60% had eventual AF recurrence despite continued antiarrhythmic medication. Of the 14 patients who underwent cardioversion, 1 had a CVA within 1 month after the CV. The patient had a therapeutic INR at time of CV, and had no left atrial appendage thrombus identified on a transesophageal echocardiogram immediately prior to CV. Nine days after the CV, the patient presented with a small right middle cerebral artery infarct and a subtherapeutic INR.

Limitations

This study has the limitation of being a retrospective, nonrandomized, single-center study with a limited number of patients. As a result, we are unable to account for confounding factors that may play a significant role in the results. These confounding factors include, but are not limited to selection bias toward early cardioversion or AADs for patients perceived to have benefit from an early rhythm control strategy (e.g. patients with severe heart failure and uncontrolled ventricular rates), ventricular arrhythmias requiring anti-arrhythmic therapies that may also aid in AF rhythm control and those requiring prolonged inotropic therapy making rate control medications difficult to use.

Conclusions

In patients with AF in the setting of LVAD, there was no difference in composite or individual outcomes of death, CVA, CHF admission, GIB, VT, hemolysis and pump thrombosis between rate and rhythm control groups. Electrical CV can be accomplished with reasonable safety and efficacy in patients with LVAD.

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Demographic, Clinical, and Angiographic Characteristics of Atrial Fibrillation Patients Suffering from de Novo Acute Myocardial Infarction: A Subgroup Analysis of the MINOCA-TR Study Population

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Abstract

Background: Atrial fibrillation (AF) prevalence in patients with acute myocardial infarction (MI) ranges from 3% to 25%. However demographic, clinical, and angiographic characteristics of AF patients who admitted with de novo MI are unclear. The aim of this study was to investigate the prevalence of patients presenting with de novo MI with AF.

Methods: The study was performed as a sub-study of the MINOCA-TR (Myocardial Infarction with Non-obstructive Coronary Arteries in Turkish Population) Registry, a multicenter, cross-sectional, observational, all-comer registry. MI patients without a known history of stable coronary artery disease and/or prior coronary revascularization were enrolled in the study. Patients were divided into AF and Non-AF groups according to presenting cardiac rhythm.

Results: A total of 1793 patients were screened and 1626 were included in the study. The mean age was 61.5 (12.5) years. 70.7% of patients were men. The prevalence of AF was 3.1% (51 patients). AF patients were older [73.4 (9.4) vs. 61.0 (12.4) years, p<0.001] than non-AF patients. The proportion of women to men in the AF group was also higher than in the non-AF group (43.1% vs. 28.7%, p=0.027). Only 1 out of every 5 AF patients (10 patients, 19.6%) was using oral anticoagulants (OAC).

Conclusions: AF prevalence in patients presenting with de novo MI was lower than previous studies that issued on AF prevalence in MI cohorts. The majority of AF patients did not have any knowledge of their arrhythmia and were not undergoing OAC therapy at admission, emphasizing the vital role of successful diagnostic strategies, patient education, and implementations for guideline adaptation.

Key Words
Atrial fibrillation, Myocardial infarction, Oral anticoagulation, MINOCA-TR study.

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Introduction

Atrial fibrillation (AF) is a common arrhythmia in the general population and ranks third in incidence in patients with myocardial infarction (MI) after sinus bradycardia and sinus tachycardia [1]. Previous studies have reported a wide variety in the prevalence rates of AF in the MI population [2,3]. European Society of Cardiology (ESC) 2017 Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation (STEMI) reported prevalence rates as high as 21% for MI patients [4]. AF can result in undesired in-hospital outcomes [5] such as recurrent coronary ischemia, congestive heart failure, or stroke, as well as the need for long-term oral anticoagulation use, which increases rates of bleeding complications [6]. Preexisting, known coronary artery disease (CAD) is a well-recognized comorbidity in patients with AF. CAD and other comorbidities carry the risk for incident AF. Interestingly, there is scarce demographic and clinical information in the literature on AF in the MI population without a history of CAD and coronary revascularization. Evidence for acute management and long-term treatment strategies such as oral anticoagulation are not clear and should be identified [7].

This study aimed to determine prevalence rates of AF in de novo MI patients without revascularization history and to compare the demographic, clinical, and angiographic characteristics of patients with and without AF in the de novo MI population in Turkey.

Methods

Study design

The registry of Myocardial Infarction with Non-obstructive Coronary Arteries in the Turkish population (MINOCA-TR) is a nationwide, multicenter, prospective, and observational cohort study of patients with a de novo myocardial infarction (MI) presentation. A total of 32 invasive cardiology centers (eighteen university, ten state, and four private hospitals) around Turkey participated to the study. Patient recruitment was performed between March to October 2018. Patients without a known history of prior coronary revascularization who underwent a diagnostic coronary angiography procedure with a possible diagnosis of MI were screened and included in the study population. The aim of this screening was to obtain real-life data and prevent potential bias in the clinical context. A sub-study of the MINOCA-TR registry, this paper focuses on the prevalence of AF in the MINOCA-TR study population [8,9]. The study population was divided into two groups, the AF and non-AF groups, based on their presenting rhythm at admission. Demographic, clinical, and angiographical data of the MINOCA-TR study population was recorded and compared. The study protocol of the MINOCA-TR was approved by the Clinical Research Ethical Committee of Dokuz Eylul University and was registered with www.clinicaltrials.gov (NCT03364387).

Study population

Consecutive patients 18 years of age and older who were diagnosed with MI using the Third Universal Definition of Myocardial Infarction and who underwent a diagnostic coronary angiography were included in the study population. Each participating physician arranged the management of treatment on their own, and the study patients were not given any medical procedure other than guideline directed therapy. Potential study patients were informed about the study and asked to sign informed consent forms after coronary angiography (or percutaneous coronary interventions if needed). Patients with stable coronary artery disease, unstable angina pectoris, coronary revascularization history (PCI or CABG), or type 4 or type 5 MI and patients under the years of 18 and who did not sign the informed consent were excluded from the study.

Coronary angiographies

Coronary angiographies were performed in the individual centers involved in the study. A digital copy of each recording was sent to the MINOCA-TR adjudication committee, which was made up of three invasive cardiologists. Coronary angiographies were evaluated for the possible presence of an overlooked type 1 MI.

Statistical Analysis

Statistical analysis was descriptive, exploratory, and generally limited to frequency or summary statistics (e.g., means ± standard deviation or medians ± quartiles). Demographic information was summarized according to the type of data by descriptive statistics (n, mean, standard deviation, median, the difference between percentiles) or frequency

Table 1: Demographic and clinical characteristics of study population at admission

	AF patients(n=51)	non-AF patients(n=1575)	p value
Mean age (years), mean (SD)	73.4 (9.4)	61.0 (12.4)	<0.001
Female gender, n (%)	22 (43.1)	453 (28.7)	0.027
BMI (kg/m2), mean (SD)	26.9 (4.1)	27.6 (4.4)	0.522
Smoking, n (%)	20 (39.2)	922 (58.6)	0.006
Diabetes mellitus, n (%)	20 (39.2)	460 (30.3)	0.174
Hypertension, n (%)	33 (64.7)	744 (48.5)	0.023
Hyperlipidemia, n (%)	15 (32.6)	482 (35.9)	0.640
Systolic blood pressure (mmHg), mean (SD)	130.9 (27.3)	128.9 (23.3)	0.872
Diastolic blood pressure (mmHg), mean (SD)	78.2 (16.2)	77.3 (13.9)	0.761
Admission Killip class (≥3), n (%)	2 (3.9)	47 (2.9)	0.001
LV ejection fraction (%), median (25th-75th percentile)	45.0(30.0-50.0)	50.0(35.0-55.0)	0.008
Presence of severe (≥3rd degree) MR, n (%)	6 (11.7)	27 (1.7)	<0.001
Blood glucose (mg/dL), median (25th-75th percentile)	140.0(85.0-192.0)	123.0(81.0-176.0)	0.086
Creatinine (mg/dL), median (25th-75th percentile)	0.90(0.71-1.50)	0.85(0.67-1.31)	0.203
Hemoglobin (gr/dL), mean (SD)	12.7 (2.2)	13.6 (1.9)	0.004
hs-Troponin (ng/mL), median (25th-75th percentile)	15.2(1.4-97.1)	15.3(0.9-428.0)	0.689
NSTEMI presentation, n (%)	35 (68.6)	839 (53.2)	0.023

Abbreviations: BMI, body mass index; LV, left ventricule; MR, mitral regurgitation

Table 2: Percentages of oral P2Y12 loading at admission and preexisting use of oral anticoagulant

	AF patients(n=51)	non-AF patients(n=1575)	p value
$P2Y_{12}$ inhibitors loading, n (%)	49 (96.0%)	1446 (91.8%)	0.027
Preexisting oral anticoagulant use, n (%)	10 (19.6%)	16 (1.0%)	<0.001

distribution (n and %). The Student's t-test was used for continuous variables, the analysis of variance for categorical variables, and the Pearson's chi-square test for binominal variables. P values of <0.05 were accepted as significant.

Results

Baseline characteristics of study population

A total of 1793 patients were screened for eligibility. Of these, 1626 patients admitted with de novo acute MI were enrolled in this study. The mean (SD) age of the population was 61.5 (12.5) years and men made up 70.7% of the study population. Fifty-one (3.1%) patients were diagnosed with AF. Dramatically, the minority of patients were previously diagnosed with AF (14 patients, 27.4%) and only 1 out of every 5 AF patients (10 patients, 19.6%) was using oral anticoagulants (OAC). Demographic and clinical characteristics of the study population are presented in [Table 1]. Patients in the AF group were older than the non-AF group [mean 73.4 (9.4) vs. 61.0 (12.4) years, p<0.001]. The percentage of women in the AF group was also higher than that in the non-AF group (43.1% vs. 28.7%, p=0.027). Non-ST segment elevation MI (NSTEMI) presentation (68.6% vs. 53.2%, p=0.023) and prevalence of hypertension (64.7% vs. 48.5%, p=0.023) were more common in patients in the AF group. Conversely, fewer patients in the AF group smoked than in the non-AF group (39.2% vs. 58.6%, p=0.006). Median LV ejection fraction at admission was lower in AF patients than the non-AF patients [45.0% (30-50%) vs. 50.0% (35-55%), p=0.008]. Hemoglobin levels were also lower in the AF group [12.7 (2.2) vs. 13.7 (1.9) gr/dL, p=0.004]. A greater number of patients in the AF group were classified as Killip class 3 and 4 at admission (3.9% vs. 2.9%, p=0.001). Severe mitral regurgitation was more common in AF patients (11.7% vs. 1.7%, p<0.001). Although the STEMI rate was 46.0% for the entire study population, only 3.0% of the total population, none of which were in the AF group, received thrombolytic treatment as a reperfusion therapy before diagnostic coronary angiography. Oral $P2Y_{12}$ inhibitor loading before the index emergency admission rate was higher in AF patients (96.0% vs. 91.8%, p=0.027). Clopidogrel was the most commonly used $P2Y_{12}$ inhibitor in the study population (49.2%). On the other hand, the loading rate of oral $P2Y_{12}$ inhibitors other than clopidogrel was 31.3% in the AF and 47.6% in the non-AF group (p=0.004). Preexisting oral anticoagulant use was also higher in AF patients (19.6% vs. 1.0%, p<0.001) [Table 2].

Coronary angiography results

The majority of patients were treated via primary percutaneous intervention (1280 patients, 78.7% of the overall study population). Coronary artery bypass grafting was the preferred method for revascularization for 10.5% of cases and medical management was preferred for 10.2%. The selected treatment options were similar between the AF and non-AF patients [Table 3]. The percentages of patients diagnosed with MINOCA were also similar between gropus (7.8% vs. 6.6%, p=0.743).

Discussion

In the current study investigating the prevalence and demographic and clinical characteristics of AF in patients with de novo myocardial infarction, we found a lower prevalence rate of 3.1%, in contrast to previous studies in the literature [2,3,10,11]. Similar to our results, the HORIZONS-AMI study reported a low AF incidence (4.5%) in patients undergoing primary percutaneous coronary intervention (pPCI). Mean age in AF and non-AF groups were also similar to our study. Relatively low percentage of patients with a previous history of percutaneous or surgical revascularization (approximately 13%) in the HORIZONS-AMI study population might be the factor in low new-onset AF development [12]. The exclusion of patients with a previous history of revascularization and diagnosis of stable coronary artery disease (stable CAD) as well as the relatively younger age of the enrolled population is thought to play a main role in the lower than expected prevalence of AF in our study. Stable CAD and AF share common risk factors and patients with a long history of stable CAD and its risk factors also show increased risk of incident AF [13]. In addition, coronary revascularization procedures, particularly CABG, have been found to create a predisposition to incident AF [14]. For this reason, the authors are of the opinion that the exclusion of patients with stable CAD and revascularization history were the main factors behind the low percentage of AF patients in the study population. Furthermore, a positive correlation between age and AF has been confirmed in many registries [15,16]. The relatively young mean age (approximately 60 years old) of patients enrolled in our study may also have resulted in the lower prevalence of AF in our study population. Theoretically, patients without previous diagnosis of stable CAD and/or without history of revascularization may be younger and have fewer AF risk factors. Although ethnicity may play a role for differences in the prevalence of AF, no evidence has been reported showing different rates of AF between Turkey and the rest of the World [17,18]. However, acute coronary syndrome registries conducted in Turkey report younger average ages in patients admitted with acute MI than in European countries and the United States [19-22]. We believe that the younger age pattern may have an effect on lower AF prevalence in our study than that of other global registries [2,7].

Our study also found that non-ST-elevation myocardial infarction (NSTEMI) presentation was higher in the AF population than in patients without AF, with approximately 70% of AF patients presenting with NSTEMI. Age is a common risk factor of both AF and NSTEMI. The current literature shows a positive correlation between increasing age and the rate of NSTEMI in the MI population and a higher prevalence of AF in patients with non-ST segment elevation acute coronary syndrome (NSTE-ACS) [23]. On the other hand, AF with fast ventricular response can precipitate Type 2 MI that commonly presents with ST segment changes rather than elevation on admission ECG [24]. However, while this study did not find any differences in the prevalence of MINOCA between the AF and non-AF groups, possible type II error cannot be ignored.

Advanced age, female gender, lower LV ejection fraction (LVEF), higher Killip class, obesity, presence of multiple comorbidities, and hemodynamic instability are associated with AF [2,25-27]. Similar to previous studies, patients in the AF group were older than in the non-

Table 3: Preferred treatment strategies for coronary artery disease (p=0.884)

	AF patients(n=51)	non-AF patients(n=1575)
Percutaneous coronary intervention (PCI), n (%)	38 (74.5%)	1244 (79.0%)
Coronary artery bypass grafting (CABG), n (%)	5 (9.8%)	166 (10.6%)
Medical management, n (%)	8 (15.7%)	158 (10.0%)
Other options, n (%)	0 (0.0%)	7 (0.4%)

AF group and the proportion of women to men in the AF group was higher than that in the non-AF group. Previous registries revealed that with advanced age, gender difference in MI patients lessens and the female/male ratio increases [28]. AF patients were an average of twelve years older than non-AF patients in our study, which may explain the gender difference between the AF and non-AF groups. Additionally, smoking is more common in men than in women in the Turkish population [29]. The authors believe that the observed difference in smoking between the groups may be due to the female dominance in the AF group. Hypertension is an essential predictor of AF development [30] and higher hypertension prevalence in the AF group can play a role in the development of AF in advanced age (64.7% vs. 48.5%, p=0.023). In addition, we should pay attention to type I statistical error in evaluations of differences of gender, smoking, and prevalence of hypertension in this context. Lower LVEF in the AF group (45.0% [30.0-50.0] vs. 50.0% [35.0-55.0], p=0.008) can be explained by the higher burden of comorbidities such as advanced age and hypertension in AF patients [31]. Loss of atrial kick and possible tachycardiomyopathy are other factors that may result in lower EF and have been found to be responsible for worse hemodynamic status and increased mortality [32]. Accordingly, the ratio of Killip class 3 and 4 patients at admission was higher in the AF group in our study.

An interesting finding in our study was the relatively low percentage of patients who were initially treated by the thrombolytic therapy. ST-elevation myocardial infarction (STEMI) patients made up nearly half of the study population (46.0%) but only 3.0% of all patients received thrombolytic treatment before coronary angiography. Even in the AF group, while 31.3% of patients presented with STEMI, none received thrombolytic therapy. It is possible that the lower preference for thrombolytic therapy as an initial reperfusion choice may be related to the well-organized ambulance system and sufficient number of invasive cardiology centers which are capable of performing 7/24 primary PCI around the country.

Oral $P2Y_{12}$ inhibitor loading was common in both AF and non-AF patients. Although the AF group was found to have a higher oral $P2Y_{12}$ inhibitor loading rate (96.0% vs. 91.8%, p=0.027) than the non-AF group, this can be an incidental finding and accepted as an example of type I statistical error. The study also found the use of oral $P2Y_{12}$ inhibitors other than clopidogrel to be relatively common in the AF group, with approximately one third of patients in the AF group loaded with an oral $P2Y_{12}$ inhibitor other than clopidogrel. We believe that the relatively common use of more potent $P2Y_{12}$ inhibitors in AF population was due to the lower percentage of AF patients who had been already taken OAC therapy. It can be argued that with common OAC usage, potent $P2Y_{12}$ inhibitor loading ratios would be lower.

Ischemic stroke is a devastating complication of AF and MI patients with AF carry a significant risk of stroke. Previously, it has been reported that dual/triple therapy by adding an OAC decreases the risk of stroke [33,34]. Despite this stroke risk, most AF patients admitted with MI were discharged without any OAC therapy [3]. Many trials have focused on finding the sweet spot between stroke, stent thrombosis, and major bleeding risk and compared triple and dual therapy strategies with different duration and different regimens. Almost all of reported greater safety with dual therapy with OAC plus clopidogrel than triple therapy [35-41]. Current guidelines advise personalized management of these patients according to bleeding and thrombosis risk [42,43]. It is also important to emphasize the low percentage of oral anticoagulant usage in patients with AF before emergency admission.

Underdiagnosed/overlooked AF, particularly in asymptomatic patients, undertreatment, and compliance issues with OAC therapy may be the main reasons for the lower percentage of OAC use in the study population. These results show the importance of successful and timely diagnosis of AF, patient education on OAC therapy, and transparent performance metrics and guideline adaptation for health providers.

Limitations

The study had several limitations discussed below. Regarding the cross-sectional design of the study, it was not possible to obtain short and long-term prognostic metrics of the patient population. Due to the relatively small sample size of the AF population, possible type II statistical errors may have affected the comparative data. Some demographic and clinical characteristics of the study population may be specific to the Turkish population and thus not reflect a global perspective. MI was defined in line with the Third Universal Definition of Myocardial Infarction. However, the current Fourth Universal Definition of Myocardial Infarction was published after the starting date of study and protocol revisions were not made due to possible risks of harmonization between pre- and post-revision data. AF diagnosis was based on a[12] lead ECG performed at admission, meaning that incident AF could not be captured and differentiated from existing chronic patterns. For this reason, the organizing committee required the completion of a form from the investigators in case with suspicion of incident AF. Similarly, we did not receive any data about the patterns of AF (ie first diagnosed, paroxysmal, persistent, etc). A higher rate of first diagnosed AF patterns may explain the dramatic percentages of OAC use in the study population.

Conclusions

In conclusion, the study reports a lower percentage of AF prevalence in the de novo MI population than previous studies of enrolled unselected MI and ACS cohorts. It also demonstrated the underuse of OAC in AF patients, emphasizing the vital role of opportunistic diagnostic strategies, patient education, and implementations for guideline adaptation.

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Temperature-Controlled Catheter Ablation for Paroxysmal Atrial Fibrillation: The QDOT-MICRO Workflow Study

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Abstract

Background: A novel QDOT MICRO (Biosense Webster, Inc., Irvine, CA) catheter with optimized temperature control and microelectrodes was designed to incorporate real-time temperature sensing with contact force detection and microelectrodes to streamline ablation workflow. The QDOT-MICRO feasibility study evaluated the workflow, performance, and safety of temperature-controlled catheter ablation in patients with symptomatic paroxysmal atrial fibrillation with conventional ablation setting.

Methods: This was a non-randomized, single-arm, first-in-human study. The primary outcome was pulmonary vein isolation (PVI), confirmed by entrance block after adenosine and/or isoproterenol challenge. Safety outcomes included incidences of early-onset primary adverse events (AEs) and serious adverse device effects (SADEs). Device performance was evaluated via physician survey.

Results: All evaluated patients (n = 42) displayed 100% PVI. Two primary AEs (4.8%) were reported: 1 pericarditis and 1 vascular pseudoaneurysm. An additional SADE of localized infection was reported in 1 patient. No stroke, patient deaths, or other unanticipated AEs were reported. Average power delivered was 32.1±4.1 W, with a mean temperature of 40.8 °C±1.6 °C. Mean procedure (including 20-minute wait), fluoroscopy, and radiofrequency application times were 129.8, 6.7, and 34.0 minutes, respectively. On device performance, physicians reported overall satisfactory performance with the new catheter, with highest scores for satisfaction and usefulness of the temperature indicator.

Conclusions: Initial clinical experience with the novel catheter showed 100% acute PVI success and acceptable safety and device performance in temperature-controlled ablation mode. There were no deaths, stroke, or unanticipated AEs. Fluoroscopy and procedural times were short and similar or better than reported for prior generation catheters.

Key Words

Atrial fibrillation, Workflow, Catheter ablation, Pulmonary vein isolation, Arrhythmia.

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Introduction

Catheter ablation is a well-recognized treatment option for paroxysmal atrial fibrillation (PAF) [1], and complete electrical isolation of the pulmonary veins (PVI) from the left atrium (LA) is recommended for all atrial fibrillation (AF) ablation procedures [2].

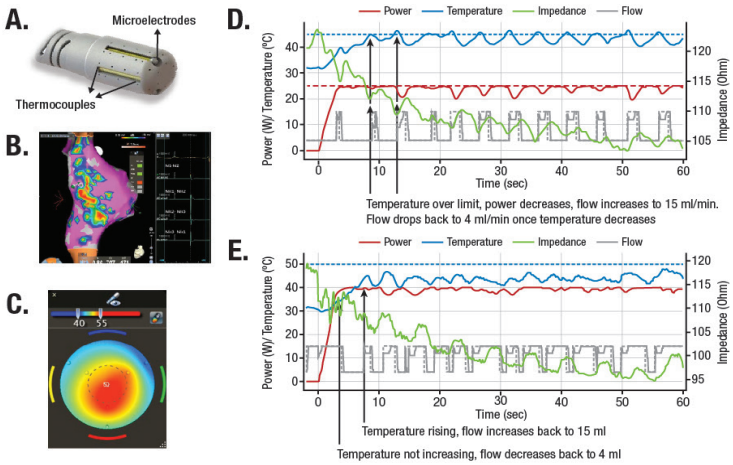


Figure 1: **(A) The QDOT MICRO catheter with 3 distal microelectrodes and 6 thermocouples; (B) visual display of the enhanced ECG signal attenuation obtained by Microelectrodes (Mic1, Mic2, and Mic3) in comparison to the traditional M1-M2 electrodes and the catheter's associated location, as shown with CARTO3 integration; (C) real-time visual display of the temperatures recorded by the catheter; (D) temperature-control QMODE module algorithm with RF power ≤35 W; and (E) temperature-control QMODE module algorithm with RF power >35 W.**

ECG, electrocardiogram; RF, radiofrequency.

Open-irrigated radiofrequency (RF) catheters are the most widely used for PAF ablation. More recently, RF catheters with real-time, contact force (CF)–sensing capability have become available, and studies have shown that these CF-sensing catheters improve procedural efficiencies and long-term success [3,4]. A newer iteration of the CF-sensing catheter that includes a 56-hole porous tip (versus 6 larger holes), permitting PVI while delivering a reduced volume of fluid [5]. However, it has been reported that uniform cooling from the porous tip resulted in attenuation of temperature change within the catheter tip, even with increasing power levels [6]. Furthermore, the temperature feedback, detected by a single thermocouple in the middle of the tip, is very poor.

A novel catheter with optimized temperature control and microelectrodes [Figure 1A] was designed to potentially enhance the safety and effectiveness of the currently available, porous tip, CF-sensing catheter by incorporating real-time temperature sensing with CF and microelectrodes to both adequately cool the catheter tip and retain optimal sensing of tissue temperature. The addition of a multi-channel RF generator and novel algorithm allows for temperature-controlled ablation by adjusting the irrigation rate and power based on temperature feedback ([Figure 1B - Figure 1E]). Microelectrodes were incorporated to enhance the quality of the near-field electrogram signals ([Figure 1A] and [Figure 1B]). Higher signal resolution gives the operator the ability to monitor signal attenuation during mapping and ablation while aiding in the identification of non-ablated tissue. The real-time temperatures recorded by the thermocouples are displayed graphically [Figure 1C]. A proprietary add-on software module was designed for the study to display and record electrocardiogram (ECG) results, temperature, location, and CF information.

The initial clinical experience with this catheter for PVI using a very high power, short duration (vHPSD) workflow (90 W, 4 seconds) has been described previously [7]. The current QDOT-MICRO (Biosense Webster, Inc., Irvine, CA) workflow feasibility study was designed primarily to evaluate the workflow, acute success, device performance, and safety of the new catheter during standard electrophysiology mapping and PAF ablation 3 months post-procedure using a standard ablation power setting (1 W-45 W) in a temperature-controlled mode.

Methods

Study design

This was a prospective, non-randomized, multi-center, clinical investigation performed in 6 clinics in Europe to evaluate the workflow and acute performance of the QDOT MICRO catheter in PAF ablation with temperature-controlled mode in the standard power setting. This temperature-controlled mode, known as the QMODE algorithm, automatically adjusts the irrigation flow rate between low flow (4 mL/min) to high flow (15 mL/min) to reach and maintain the set maximum power without exceeding the set target temperature. The maximum allowed power at the LA roof, LA ridge, and locations anterior and inferior to the pulmonary veins (PVs) were directed not to exceed 45 W. For the LA posterior wall and areas close to the esophagus, ablation was directed to begin at ≤25 W. The utilization of an appropriate strategy (i.e., esophageal temperature probe, esophageal visualization, and/or esophageal displacement) to reduce esophageal injury was also required. Outcomes were assessed at baseline, at the time of the ablation procedure, at discharge, and at 7 days and 3 months post-procedure.

The study was conducted in accordance with the Declaration of Helsinki with E6 of the International Conference on Harmonisation Good Clinical Practices, ISO 14155-2011, and all applicable local and federal regulations. The study was also approved by the ethics committees in all participating countries. All study patients provided written informed consent.

Table 1: Baseline Patient Characteristics

Characteristics	Enrolled population (N = 43)*
Age, years, mean ± SD	60.3 ± 12.6
Sex, male, n (%)	27 (62.8%)
Patient history	-
AF duration, months, median (Q1, Q3)	24 (10.0, 59.0)
Atrial flutter, n (%)	6 (14.0%)
Systemic hypertension, n (%)	24 (55.8%)
Diabetes, n (%)	2 (4.7%)
Coronary disease, n (%)	7 (16.3%)
Prior thromboembolic events/TIA, n (%)	4 (9.3%)/1 (2.3%)
Hyperthyroidism, n (%)	2 (4.7%)
CHA_2DS_2-VASc score, mean ± SD	1.8 ± 1.31
Congestive heart failure, n (%)	1 (2.3%)
Failed anti-arrhythmic drug class, n (%)	38 (88.4%)
LVEF (%), mean ± SD (min, max)	60.6 ± 5.38 (50.0, 73.0)
LA dimension, mm, mean ± SD (min, max)	38.5 ± 6.43 (24.0, 50.0)

AF, atrial fibrillation; LA, left atrium; LVEF, left ventricular ejection fraction; Q, quartile; SD, standard deviation; TIA, transient ischemic attack.
*Enrolled population including 1 patient who did not receive any treatment and excluding 8 patients who were treated with a previous version of the study device.

Table 2: Procedural Characteristics

Variable, mean ± SD (Q1, Q3)	Safety population (N = 42)
Total procedure time, minutes*	129.8 ± 27.2 (106.0, 153.0)
Total mapping time, minutes	9.5 ± 7.6 (3.0, 13.0)
Total ablation time, minutes†	67.2 ± 22.4 (47.0, 81.0)
Total RF application duration, minutes‡	34.0 ± 10.8 (27.3, 36.5)
Total fluoroscopy time, minutes	6.7 ± 9.1 (2.4, 6.1)
Fluid delivered via study catheter(s), mL	572.5 ± 296.1 (400.0, 750.0)
Number of RF applications§	62.5 ± 19.9 (49.0, 73.0)
Total RF duration per application, seconds§	31.5 ± 14.3 (21.4, 40.0)
Maximum temperature, °C§	51.4 ± 1.93 (50.4, 52.5)
Average power, W§	32.1 ± 4.13 (29.6, 33.3)

Q, quartile; RF, radiofrequency; SD, standard deviation.
*Time from first puncture until the time the catheter was removed (includes 20-minute wait time).
†Time between the first and last RF applications.
‡Total RF application duration measured by the operator.
§Measured by the generator.

Patients

Eligible patients were required to be ≥18 years of age and candidates for catheter ablation of symptomatic PAF. Patients were excluded if they had AF secondary to electrolyte imbalance, thyroid disease, or reversible or non-cardiac cause; previous ablation for AF; persistent AF; left atrial thrombus; carotid stenting or endarterectomy; LA size >50 mm; left ventricular ejection fraction <40%; uncontrolled heart failure or New York Heart Association function class III and IV; unstable angina; history of blood clotting or bleeding abnormalities or contraindication to anticoagulation; a thromboembolic event in the past 12 months; percutaneous coronary intervention for myocardial infarction in the past 3 months; cardiac surgery in conjunction with valve surgery or any valvular cardiac surgical/percutaneous procedure in the past 6 months; or expected cardiac transplantation or other cardiac surgery in the next 6 months.

In phase 1 of the study, 8 patients were enrolled. A lower electrode temperature response than anticipated, which may potentially result in less effective ablation lesions in certain ablation locations, was identified. Consequently, enrollment in the study was temporarily suspended while the design of the catheter was modified and the generator software was updated. Additional preclinical work was performed prior to subsequent enrollment to ensure that the anticipated temperature response was recorded by the electrodes. The modified device was used to perform the ablation procedure for 43 patients in phase 2 of the study.

Ablation procedure

Treatment with uninterrupted systemic anticoagulation therapy was required for at least 3 weeks prior to study treatment. During the ablation procedure, heparin was administered to achieve an activated clotting time of ≥325 seconds. Ablation was performed with the novel catheter under the temperature-controlled mode. Irrigation was automatically increased to a high flow rate up to 2 seconds before the onset through 5 seconds after termination of RF energy delivery.

Recommended temperature ranges and RF power settings were as follows: RF power range, 15 W to 45 W; target temperature setting, 47°C (range, 45°C-50°C) for ≤35 W or 42°C (range, 40°C-45°C) for >35 W; default temperature cut off for the generator, 55°C; and default ablation time, up to 60 seconds. If the temperature increased rapidly, the RF application was stopped immediately. Esophageal monitoring was required to minimize the risk of esophageal injury and was conducted for 50 patients (temperature probe for 36, barium contrast for 9, and intracardiac echocardiography for 5).

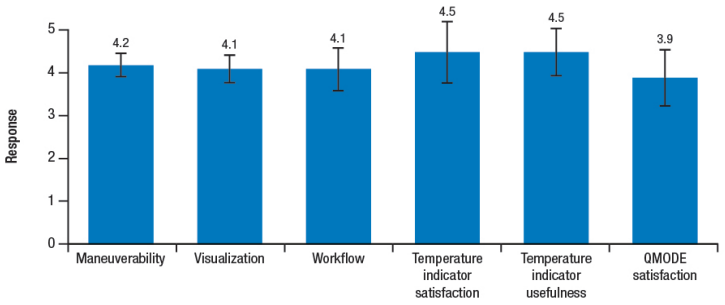
A circumferential anatomical and endocardial signals approach was used to isolate all PVs. To minimize the risk of PV stenosis, RF applications were recommended to be ≥1 cm to 2 cm outside the PV ostia to isolate the left and right PVs. In the event of spontaneous or induced AF and/or atrial flutter, additional RF lesions outside of the PV ostia were placed at the discretion of the investigator. PVI via entrance block was assessed by Lasso or PentaRay catheters (Biosense Webster, Inc., Irvine, CA).

After a required 20-minute waiting period, adenosine or isoproterenol was used to confirm PVI and rule out dormant conduction. Oral anticoagulation therapy was strongly recommended for 2 months following ablation. Thereafter, patients were advised to receive anticoagulation therapy in accordance with the 2017 Heart Rhythm Society consensus statement[8]. The administration of antiarrhythmic drugs after ablation was based on the treating physician's discretion.

Outcomes

The primary effectiveness outcome was acute success, defined as confirmed entrance block in all targeted PVs via adenosine and/or isoproterenol challenge.

The main secondary endpoint was safety assessment, as defined by the number of early-onset primary adverse events (PAEs) within 7 days of catheter ablation. In this study, PAEs were defined as death, atrioesophageal fistula (including events >7 days post-procedure), cardiac tamponade/perforation, myocardial infarction, stroke/cerebrovascular accident, thromboembolism, transient ischemic attack, diaphragmatic paralysis, pneumothorax, heart block, PV stenosis (including events >7 days post-procedure), pulmonary edema (respiratory insufficiency), vagal nerve injury, pericarditis, major vascular



Score	Rating
5	Performed better than anticipated
4	Performed adequately/met expectations
3	Accomplished task, but the catheter needs some minor redesign
2	Accomplished task with significant difficulty or partially accomplished task
1	Could not accomplish task with this design

Figure 2: Mean ± SD responses (possible score, 1-5) to the physician's device performance survey.

SD, standard deviation.

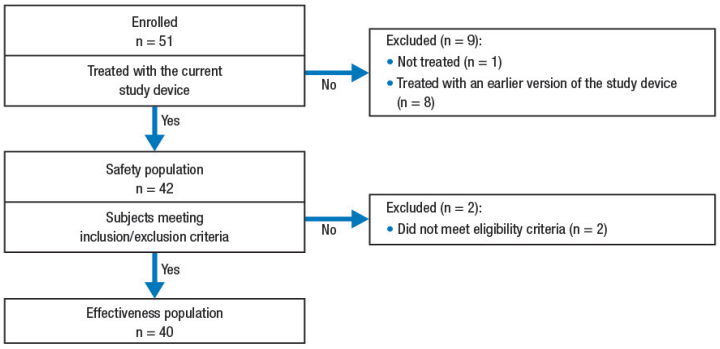


Figure 3: Patient disposition

access, and complication/bleeding. Additional serious adverse device effects (SADEs) over up to 3 months follow-up were also recorded.

Procedural endpoints included a mandatory ECG assessment at each clinical follow-up visit; rate of touch-up RF application, defined as RF applications for re-isolation of targeted PVs post adenosine and/or isoproterenol; and procedural characteristics. Device performance was assessed by a physician survey with a ranking system scoring from 1 to 5 (see table in [Figure 2]) on questions on maneuverability, visualization, workflow, temperature satisfaction, temperature indicator usefulness, and algorithm modality satisfaction.

Statistical Analysis

As this was a feasibility study, no hypothesis was tested, and all data are presented as descriptive statistics, including the number and percentage of patients who reached acute success. A total of 50 evaluable patients were deemed sufficient to characterize the workflow and acute outcomes of the study.

The effectiveness population included all enrolled patients who met all eligibility criteria and underwent ablation with the study catheter. The safety population included all enrolled patients who had the investigational device inserted, regardless of whether RF energy was delivered.

Results

Demographics and baseline characteristics

Patients were enrolled between September 28, 2016 and April 26, 2018. A total of 51 patients were originally enrolled; however, after 8 patients were treated, the device was modified and those patients were excluded from analyses of efficacy and safety. Therefore, a total of 43 patients were enrolled in the study using the updated version of the device. The safety population included 42 patients who had the investigational device inserted (1 patient did not check in for their scheduled ablation procedure). Two patients who underwent ablation were later excluded from the effectiveness population (n = 40) based on failing eligibility criteria [Figure 3].

The majority of patients were male (62.8% [27/43]) and relatively young (mean ± standard deviation [SD] age = 60.3 ± 12.6 years; [Table 1]). The most common medical comorbidities were systemic hypertension (55.8%) and coronary disease (16.3%; [Table 2]).

Procedural characteristics

Across 42 treated patients, the mean ± SD total procedure time, defined as the time from first puncture until the time the catheter was removed and including 20-minute wait times, was 129.8 minutes ± 27.2 minutes ([Figure 4]; [Table 2]). Average mapping, fluoroscopy, total ablation, and RF application times are summarized in Table 2.

On average, 62 RF applications were performed per procedure (from generator data), with an average 32-second RF duration per application Table 2. The number of applications to the left and right PVs was similar.

Average power delivered during the workflow, maximum temperature measured by the catheter, and fluid delivered via the catheter are summarized in [Table 2]. The most commonly selected CF working ranges were 3 g to 40 g (35.7% [15/42]) and 5 g to 30 g (35.7% [15/42]), and the average CF applied was 15.3 g ± 4.0 g.

Acute success

Of the 40 patients in the effectiveness population, 39 were evaluated via adenosine and/or isoproterenol challenge after entrance block confirmation; 1 patient did not have the adenosine challenge and was removed from the primary performance analysis. Entrance block in all targeted PVs was achieved in all 39 (100%) treated and evaluated patients per the endpoint definition. Entrance block was confirmed at the end of the procedure for all PV targets independently of adenosine and/or isoproterenol challenge (n = 40). At the 3-month follow-up visit, 92.7% (38/41) of patients with an ECG were in sinus rhythm and did not report any arrhythmia recurrence.

Safety results

Adverse events (AEs) are summarized in Table 3. Of the 42 patients in the safety population, 2 (4.8%) experienced PAEs: 1 pericarditis and 1 vascular pseudoaneurysm. Both events resolved without sequelae and were considered to be related to the procedure but not the device. There was an additional SADE of localized infection that was considered to be probably related to the procedure but not the device and resolved without sequelae. No SADEs were reported beyond 7 days after the investigational procedure. There were no strokes, device-related deaths, or unanticipated serious AEs.

Rate of touch-up RF application and repeat ablation

Eight patients required touch-up application after adenosine challenge, the majority (n = 6) of which were at the right PV. PV touch-up ablation sites included 1 site in the posterior left PV, 1 in the anterior right PV (RPV), 6 in the posterior RPV, and 1 in the ridge

Table 3: Summary of Safety

Event	Classification	Severity	Causality	Outcome
Vascular pseudoaneurysm	PAE/SADE	Mild	Definitely procedure related	Resolved without sequelae
Pericarditis	PAE/SADE	Moderate	Definitely procedure related	Resolved without sequelae
Localized infection	SADE	Moderate	Probably procedure related	Resolved without sequelae

PAE, primary adverse event; SADE, serious adverse device effect.

RPV. No patients had a repeat ablation procedure during the 3-month follow-up period.

Physician surveys on device performance

Results of the physician survey indicated that the catheter performed adequately and met expectations in all aspects of device performance, including catheter maneuverability, visualization, interaction with other devices in the current ablation workflow, usefulness of/satisfaction with the temperature indicator, and satisfaction with the novel algorithm [Figure 2]. The usefulness of and satisfaction with the temperature indicator each received the highest mean score of 4.5 out of 5. Specifically, operators provided feedback that the temperature indicator was useful in confirming heating (mean, 4.4/5) and providing confidence in catheter stability (mean, 4.5/5). The operators also indicated a satisfactory learning curve for the catheter in terms of maneuverability (mean, 4.4/5).

Discussion

The results of our study demonstrate that the new catheter with automatic irrigation modulation allows for temperature-controlled ablation in the standard power setting and achieved acute success in all treated patients. The low rates of PAEs (4.8%) suggested an acceptable initial safety profile, with similar or better procedural efficiency than reported in previous studies [Figure 4] [3,5,9].

The complication rate reported in this initial study is consistent with rates from standard power-controlled ablation [8]. In addition, all complications (vascular access complication, pericarditis, infection) reported were related to the procedure and unrelated to the device. The previous porous tip catheter was designed to provide more uniform cooling of the electrode tip for more efficient RF delivery and reduced fluid delivery [10]. However, it has been suggested that the catheter tip maintains a constant temperature throughout the RF application and lacks the usual temperature feedback commonly used to monitor safe and efficient RF delivery [11]. The novel catheter investigated in this study incorporates a number of surface thermocouples (6) with proximity to the cardiac tissues, which enables enhanced and localized temperature measurement. This feature allows a marked reduction in the risk of char formation; indeed, even when the tip pushes on the tissue, closing some of the irrigation holes, very accurate temperature feedback protects against blood and tissue overheating. In addition, the ability of the novel proprietary algorithm, which allows for modulation of the irrigation and power to maintain target temperatures, may have contributed to the observed low PAE rate in the temperature-controlled ablation mode. Other than the 3 reported PAEs/SADEs, there were no reports of serious AEs of stroke, thromboembolism, or other unanticipated AEs.

In addition to safety, the combination of improved temperature sensitivity and availability of the temperature graphic indicator may reduce the number of RF applications, as well as ablation and procedure times. The physicians' survey suggested that the temperature indicator [Figure 1B] provides useful feedback in confirming heating and catheter stability, potentially facilitating workflow efficiencies. In fact, procedure, fluoroscopy, ablation, and RF times reported in this study were short, generally shorter than in a previous study (SMART SF) using the previous porous tip catheter [5] ([Figure 4]; procedure time, –28%; fluoroscopy time, –64%; ablation time, –36%; RF ablation time, –31%). Of note, the fluoroscopy time achieved in the current study was minimal. The study protocol did not stipulate a specific workflow to target lowering the fluoroscopy time, and all operators had extensive prior experience in RF ablation. The quality of the endocavitary signals were improved by the microelectrodes [Figure 1], likely contributing to the efficiency of the procedure. Specifically, the microelectrodes, which selectively record local potentials, allow for a reduction in RF time by displaying the disappearance of the potential in real time, thus avoiding unnecessary RF delivery to far-field potentials. Taken together, the differences in procedural efficiencies between the current and prior studies are therefore likely attributable, at least in part, to the new catheter design and algorithm. For example, while the operators may have to vary CF and adjust power using existing catheters, the novel algorithm automatically titrates power and/or adjusts irrigation based on a predefined target temperature (47°C for ≤35 W or 42°C for >35 W), thereby simplifying the ablation workflow and leading to the gain in efficiencies.

Ultimately, the temperature-sensing capability reintroduces verification of the end goal of RF ablation - tissue heating - by measuring the temperature at the tip-tissue interface, a capability long held by conventional RF catheters that was lost with the introduction of irrigated tip catheters. In addition, the incorporation of the 6 thermocouple temperature sensors to the electrode tip of this catheter was associated with lower flow rates than previous catheter designs and led to a reduction in total fluid volume delivered. This temperature indication may therefore help improve long-term effectiveness. As previously shown, catheter stability is important in optimizing the long-term success rate [12]. The ability to consistently reach the target temperature and to maintain desired power levels at a safe temperature could be key to creating effective and durable lesions. The effectiveness is also increased by the ability of this catheter to create deep lesions when needed, such as on the anterior wall of the left and right PVs. New and emerging technologies, such as bipolar RF, high-power RF,

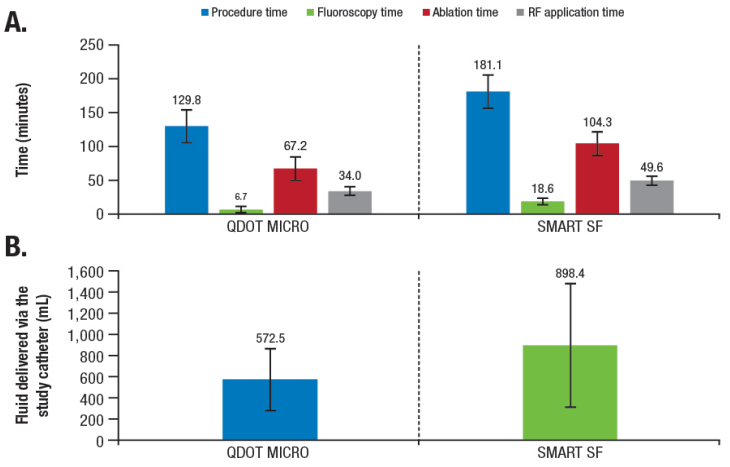


Figure 4: **(A) Mean procedure,* fluoroscopy, ablation,† and RF application duration times; and (B) fluid delivery via the study catheter in the QDOT-MICRO and SMART SF studies.[5]**

PV, pulmonary vein; RF, radiofrequency.
*Including a 20-minute wait time in QDOT-MICRO.
†Including a 30-minute wait time for PV entrance block confirmation in SMART SF.

and electroporation, are more limited in producing deep lesions. Since this study was limited to a 3-month follow-up, this hypothesis will need to be tested in future studies with longer follow-up.

Although not evaluated in this study, the novel catheter is capable of ablating in vHPSD mode during the same ablation procedure. Clinical study using this catheter for vHPSD (90 W, 4 seconds) ablation showed a similarly low fluoroscopy time of 6.6 minutes and an even lower procedure time of 105.2 minutes ± 24.7 minutes in PVI procedures[7]. However, unlike the QDOT-FAST study [7], the current study used standard power ablation settings, with a mean power of 32.1 W± 4.1W and mean RF duration of 31.5 seconds ± 14.3 seconds. In addition, the target temperature for the current study was lower compared to the QDOT-FAST study (40˚C-50˚C versus 60˚C).

The PAE rate associated with the vHPSD ablation mode (3.8%) was similar to that with the standard power ablation mode in the current study. The ability to choose between vHPSD ablation for PVI or standard temperature-controlled ablation for PVI or extra PVI ablation, as needed, is an added clinical benefit of the new catheter/algorithm that allows for versatility in adapting to different ablation workflows. Other temperature-sensing irrigated catheters that are currently under clinical investigation only allow a maximum power of up to 50 W but have shown similar short, average RF application times of 26.3 minutes ± 5.2 minutes [13].

There are several limitations to this study. The single-arm, non-randomized design precluded direct comparisons to other devices. Additionally, the study results and conclusion are based on descriptive analyses for a relatively small sample size of patients, and follow-up was performed only up to 3 months. Larger studies with a formal hypothesis and statistical power calculations are needed to confirm the safety and long-term effectiveness of the new catheter.

Conclusions

The novel catheter with a microelectrode system and enhanced temperature sensing reintroduced temperature-controlled ablation to a porous-tip irrigated catheter, with an acceptable safety profile. Initial clinical experience showed high acute success, with efficient workflow and low fluoroscopy exposure time.

Acknowledgments

The authors wish to express their appreciation to all of the QDOT-MICRO trial investigators. The QDOT-MICRO study (ClinicalTrials.gov Identifier: NCT02944968) was sponsored by Biosense Webster, Inc. The authors wish to thank the following individuals for their efforts in execution of the trial, statistical analysis, medical writing, and providing valuable input/contribution to the development of the manuscript: Carmen Rousseeuw, Lee Ming Boo, Shelley Wells, Bharat Kumar Janapala, and Baohui Zhang. Medical writing support was provided by Megan Knagge, of MedErgy, and was funded by Biosense Webster, Inc. The authors retained full control of the manuscript content development, including revisions, as well as the decision to submit the manuscript. The authors had full access to sponsor-provided data that were collected during execution of the study protocol.

Disclosure Statement

T.D.P. received non-financial support from J&J during the conduct of the study. M.G. has a licensed patent agreement with J&J, unrelated to the current data. H.K.J. received grants from Biosense Webster during the conduct of the study; grants from Novo Nordisk Foundation (NNF18OC0031258); and personal fees from Biosense Webster and Abbott, outside the submitted work. J.K. received personal fees and/or other from Biosense Webster, Boston Scientific, EPIX, MicroPort, Medtronic, and Abbott (SJM) outside the submitted work. P.N. has nothing to disclose. J.V. has nothing to disclose. A.N. has nothing to disclose. S.B.K. has nothing to disclose. P.L. received grants and personal fees from Biosense Webster. P.P. has nothing to disclose. V.Y.R. reports receiving consulting fees from Biosense Webster. He also has conflicts of interest with other companies not related to this manuscript; a comprehensive list is included as a Supplemental Appendix.

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A Comparison of Cardiac Computed Tomography, Transesophageal and Intracardiac Echocardiography, and Fluoroscopy for Planning Left Atrial Appendage Closure

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Abstract

Background: Left atrial appendage (LAA) closure (LAAC) is accompanied by a high risk of complications. Due to the complex anatomy of the LAA and the oval-shaped ostium, the proper sizing of the device is often difficult.

Purpose: To assess individualized fluoroscopy viewing angles using pre-procedural CT analysis and to compare the results of landing zone measurements obtained from CT, transesophageal echocardiography (TEE), intracardiac echocardiography (ICE), and fluoroscopy.

Methods: Patients with indications for LAAC were enrolled. Cardiac CT and TEE were done before the procedure; ICE and fluoroscopy measurements were done peri-procedurally. Multiplanar reconstruction of CT images, using FluoroCT software, was done, and optimal "personalized" viewing angles for fluoroscopy were determined. Moreover, a mean (using multiplanar CT reconstruction, derived from the LAA perimetr) amd maximum (using all four imaging modalitities) landing zone (LZ) of the LAA were masured.

Results: Twenty-five patients were analyzed. Despite significant correlation between LZs obtained from different imaging modalities, the values of LZs differed significantly; the mean LZ diameter on CT was 20.60 ± 3.42 mm, the maximum diameters were 21.99 ± 4.03 mm (CT), 18.72 ± 2.44 mm (TEE), 18.20 ± 2.68 mm (ICE), and 17.76 ± 3.24 mm (fluoroscopy). The mean CT diameter matched with the final device selection in 92% patients, while fluoroscopy or TEE maximum diameters in only 72% patients. Optimal viewing angles differed significantly from the fluoroscopy projections usually recommended by the manufacturer in 3 patients.

Conclusions: CT provides the best measurement of the LZ and the best prediction of the optimum fluoroscopy projections for the implantation procedure.

Introduction

Three randomized trials have shown the non-inferiority of left atrial appendage (LAA) closure (LAAC) to oral anticoagulation in patients with atrial fibrillation (AF). [1] The number of LAAC procedures worldwide has been growing rapidly. Despite the progress in technology, development of new generations of devices, and increased procedural experience, LAAC remains an interventional procedure with one of the highest reported adverse event rates. [2] Since the anatomy of LAA differs significantly among patients, the correct morphological assessment of the LAA is one of the key factors for a safe and effective LAAC. Choosing the proper device size is crucial for optimal procedural outcomes. Choosing an undersized device can result in device embolization or a peri-device leakage, while oversizing can cause tamponade or device embolization. Additionally, recapture and changing the device due to initial under or oversizing can increase procedural risks. The LAA varies significantly in volume, 3D-shape, and neck length; additionally, the LAA ostium can be oval to varying degrees, all of which can make a precise assessment of the landing zone (LZ) difficult. The anatomy and dimension of the LAA can be assessed using several different methods, such as transesophageal echocardiography (TEE), cardiac computed tomography (cCT), peri-procedural intracardiac echocardiography (ICE), or angiography. Different operators use different techniques based on their experience, subspeciality, and training. The cCT examination has been proposed

Key Words

Atrial Fibrillation, Left Atrial Appendage Closure, Computed Tomography, Intracardiac Echocardiography, Transesophageal Echocardiography.

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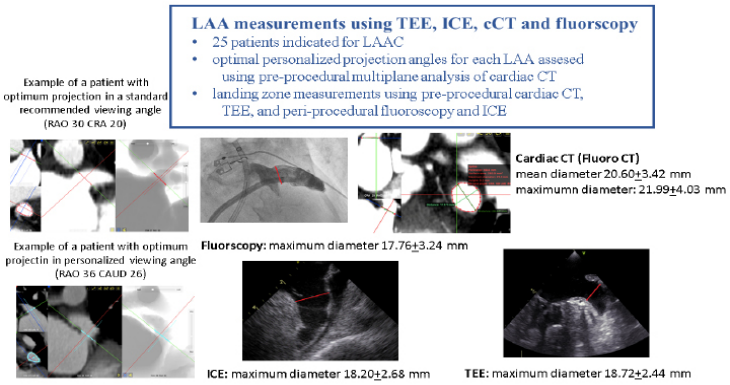

Figure 1: The figure shows the summary of results

Left side: optimal personalized projection fluoroscopic angles are shown of patients with "common" superiorly-anteriorly (A) and less often superiorly-posteriorly located LAA (B).
Right side: the maximum diameters obtained on TEE, ICE, and fluoroscopy, and the mean and maximum diameters obtained on cCT

as the most accurate by several authors.[3] In this paper, we refer our experience with preprocedural planning and LAA measurements using cCT and visualization using FluoroCT software. Preprocedural cCT images were analyzed regarding (1) the optimal personalized fluoroscopic viewing angles for a given appendage and (2) LZ measurements.

Material And Methods

We report on a group of consecutive AF patients who underwent a LAAC at our institution between January 2019 and September 2020, that included all pre-procedural cCT and TEE examinations, as well as peri-procedural fluoroscopy and ICE measurements. Indication for LAAC was a higher stroke risk, which was defined as CHA2DS2VASc ≥ 2, and a history of bleeding that contraindicated the patient for long-term oral anticoagulation therapy. Patients without a pre-procedural cCT or TEE, or without a peri-procedural ICE (i.e. in whom the procedure was navigated using TEE) were excluded from the study. Similarly, patients with significant peri-device leaks (≥ 5 mm), which indicates improper device sizing, were also excluded. This retrospective study, albeit of prospectively collected data, was approved by the hospital's Ethics Committee, and all patients signed informed consent.

Cardiac CT protocol (image acquisition)

cCT was performed 7–30 days before the implantation procedure. The c CT was performed using a Siemens Drive CT scanner, 2×128 row (Siemens Healthineers, Erlangen, Germany), a tube voltage of 100 kV, a tube current of 230 reference mAs using CARE Dose 4D (automated exposure control) (i.e., depending on the patient's body mass index), collimation of 128×0.62 mm, a pitch of 0.17, and a slice thickness of 0.6 mm. A tri-phasic injection of 80 mL of contrast media (Iomeron, Bracco Imaging, Konstanz, Germany) was used. The first 60 mL of contrast agent was administered at a flow rate of 4.0 mL/s; this was followed by 40 mL of a 25% contrast/saline mixture (flow rate of 4.0 mL/s). Lastly, a saline flush of 30 mL was administered at a flow rate of 4.0 mL/s. Automated bolus tracking, which allowed scanning of the region of interest (ascending aorta) to be synchronized with the injection of the contrast medium, was triggered at 100 Hounsfield units. Retrospective ECG triggered helical technique with pulsing modulation of mAs was used, scanning with full mAs depended on heart rate, with image reconstruction typically during the end-diastolic phase (at 70% or R-R interval).

cCT image analysis

cCT images were analyzed using FluoroCT version 3.2 for OS X 10.11 (application published by P. Theriault-Lauzier). FluoroCT is dedicated software for the simulation of fluoroscopic anatomy using volumetric rendering. [4] Multi-planar reconstructions were used to obtain orthogonal views of the neck of the LAA. The LAA ostium was defined by the line that connects the end of the coumadin ridge superiorly to the inferior junction of the LA/LAA at the circumflex artery, i.e., the echocardiographic ostium. The LZ was measured 10 mm distal to the LAA ostium (i.e., within the LAA). First, the axis of the LAA was carefully checked to improve coaxial measurements of the LZ; then, the orthogonal en face view of the LAA, at the level of the LZ, was obtained ([Figure 1] and [Figure 2]) and used for the measurement. In each measurement, the minimum and maximum diameter, as well as the perimeter, were measured. The mean diameter was then calculated based on the perimeter of the LZ. The optimal, individualized projection angle was defined using FluoroCT software ([Figure 3] and [Figure 4]). The software creates simulated views from various fluoroscopic positions. The so-called "banana view" of

Table 1: Baseline parameters

Variable (n = 25)	
Age (yrs.)	73.08+8.95
Female sex (%)	9 (36 %)
BMI	29.45+6.03
Congestive heart failure (%)	8 (32%)
Hypertension (%)	24 (96%)
Uncontrolled hypertension (%)	2 (8%)
Diabetes mellitus (%)	4 (16%)
Stroke (%)	21 (84%)
Vascular disease (%)	11 (44%)
Abnormal liver/kidney function (%)	1 (4%)
Bleeding history of predisposition (%)	25 (100%)
Labile INR (%)	20 (80%)
Drugs increasing bleeding risk (%)	4 (16%)
CHA2DS2VASc score	4.28+1.46
HAS-BLED score	2.08+0.64
Pacemaker	7 (28 %)
LV EF (%)	58.2+6.1
LA size (mm)	45.6+5.5
Medication	
Warfarin (%)	2 (8%)
NOAC /of which reduced (%)	10/7 (12%/28%)
Antiplatelet (%)	9 (36%)
No antithrombotic (%)	5 (20%)
Laboratory results	
Hemoglobin (g/L)	127.2+19.1
Hematocrit (%)	38.3+5.5
Platelet (x109/L)	161.8+58.1
Creatinine (µmol/L)	88.2+29.3
Urea (mmol/L)	5.7+2.9
ALT (µkat/L)	0.41+0.23
AST(µkat/L)	0.49+0.42

Table 2: The differences in measurements obtained by different imaging modalities

	TEE	Fluoroscopy	ICE
Mean CT diameter	-1.88 + 1.97	-2.84 + 2.21	-2.40 + 2.77
Maximum CT diameter	-3.13 + 2.90	-4.22 + 3.21	-3.79 + 3.86
Minimum CT diameter	2.62 + 2.22	1.66 + 2.75	2.10 + 2.63

the LAA was assessed first, i.e., the projection of the LAA in which the maximum length of the LAA is visible. Then, using a perpendicular projection, the LZ was drawn. Lastly, individual optimal projection angles, i.e., combinations of the right anterior oblique (RAO) + cranial (CRA) or caudal (CAUD) projections, were tested to determine which provided the best visualization of LAA. An example of two patients with very different optimal projection angles is shown in [Figure 3] and [Figure 4].

TEE examination and measurements

A TEE was done one day before the procedure, or on the morning of the day of the procedure, using a 3D probe with x-Plane imaging (i.e., two simultaneous planes) using a Vivid E95 echocardiograph (GE Vingmed Ultrasound, Horten, Norway). Patients were in a fasting state for at least 4 hours before the examination. The orifice of the LAA was measured between the end of the coumadin ridge and the circumflex artery. The LZ was measured as the widest distance (at a position 10 mm inside the LAA) using the mid- and high-esophageal views, from 0° to 135°, most often along the short-axis and long-axis projections. [Figure 1] All measurements were done from 2D projections, and maximum distances (used in this article) were measured mostly during mid-diastole, which is the current standard for sizing.

Fluoroscopy measurement

Fluoroscopic measurements were done after the transseptal puncture (TSP), i.e., when both the delivery and CHANNEL™ sheaths were in the LA. Using a 5F pigtail catheter, either a 12F or 14F delivery sheath was introduced in the LAA. At least two cineangiographic projections were made in all patients using projections recommended by the manufacturer (i.e., RAO30° + CRA10–20° and RAO 30° + CAUD10–20°. If the expected personalized optimal visualization proposed by cCT analysis differed significantly from the standard recommended projections, additional angiographic injections into the LAA were carried out using the best-expected personalized projection(s). Calibration was done using the contours of the delivery sheath (12F or 14F), and the maximum measurements were taken. [Figure 1].

ICE measurements

ICE measurements (Vivid q, GE Ultrasound, Horten, Norway) were done with an ICE probe (Accuson AcuNav, Siemens Healthcare, Germany) positioned in the LAA. Measurements were taken using an ICE probe position that optimally visualized the LAA. Typically, the ICE probe was positioned in the left superior pulmonary vein, but in some patients, the LAA was best visualized from the middle of the LA; as such, measurements in these patients were done from the LAA position [Figure 1].

Left atrial appendage closure

LAAC was performed under mild sedation (fentanyl, midazolam) and under ICE and fluoroscopy guidance. A saline infusion of 500 ml was administered in the early morning hours on the day of the procedure. The left femoral vein was used for the introduction of one (9F or 11F) sheath for the ICE probe (Accuson AcuNav, Siemens Healthcare, Germany). The ICE probe was inserted first into the right ventricular outflow tract to exclude thrombi in the LAA, and then in the right atrium to navigate the TSP and the procedure. The right femoral vein was used for the introduction of two (8.5F) transeptal sheaths (SL-1, Abbott, Plymouth, MN, USA). Five-thousand IU of heparin was administered before the TSP. After that, two TSPs were done under ICE navigation using a BRK-1 XS needle (Abbott, Plymouth, MN, USA), which was followed by the administration of another bolus of heparin to achieve a heparin level of 70–100 IU/kg. Activated clotting time (ACT) was measured every 20 min, and additional heparin boluses were given to achieve and maintain an ACT > 300. Both TSPs were done as inferiorly as possible, with the first TSP being more anterior (the aim was to see the shadow of the LAA with the ICE probe during the TSP) and the second TSP more towards the left pulmonary veins. The first SL1 sheath was replaced by an F12 or F14 delivery sheath (Abbot, Plymouth, MN, USA) and the second by a 9F CHANNEL Steerable Sheath (Boston Scientific, Marlborough, MA, USA) both using extra stiff wire (Amplatzer Guidewire, 9-GW-002, Abbot, Plymouth, MN, USA). The tip of the CHANNEL sheath was left in the left superior pulmonary vein to achieve stabil position during the procedure. After that, the ICE probe was inserted in the CHANNEL sheath. The advantage of the CHANNEL sheath is its ultrasound transparency, i.e., in contrast to SL1 sheath, we can "see" through the sheath having the ICE probe inside the sheath. The LZ of the LAA was repeatedly measured using ICE. Using a 6F Impulse™ pigtail catheter (Boston Scientific, Marlborough, MA, USA), the LAA was intubated (as "over-the-wire"), and the delivery sheath was inserted into the LAA. LAA cineangiography was performed using the delivery sheath from at least two different projections. Device sizing was based on an agreement between two of the three imaging modalities (i.e.,

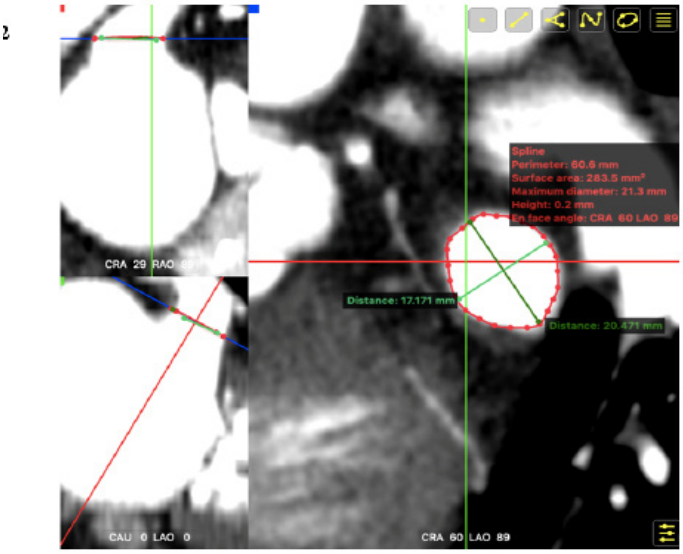

Figure 2: Examples of LZ measurement from all four modalities

Using cCT, the LZ was measured as the maximum and minimum LZ in en face view of the ostium of the LAA (the plane of measurements had to be perpendicular to the LAA axis). The mean LZ was derived from the LZ perimeter.

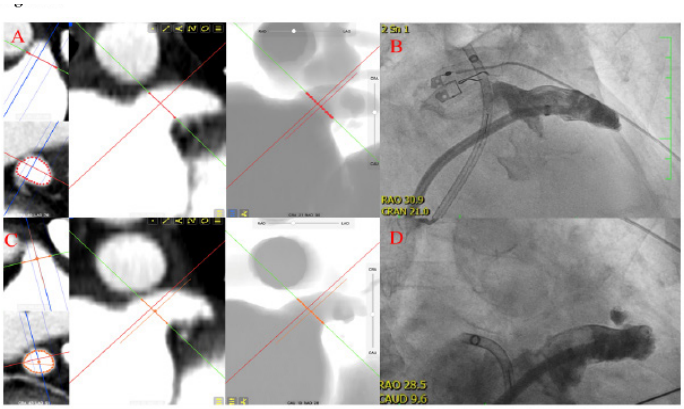

Figure 3: **Example of the fluoroscopic projection angles of a patient with a typically located LAA**

In a patient with a typically (superiorly-anteriorly) located LAA, the optimal fluoroscopic projection angles (as assessed using cCT analysis) well corresponded with the generally recommended fluoroscopic projection in RAO 30° - CRA or CAUD 10-20°)
A: cCT reconstruction using Fluoro CT with expected fluoroscopic image at RAO30°-CRA21°, B: real LAA angiography at RAO30°CRA21 C: cCT reconstruction using Fluoro CT with expected fluoroscopic image at RAO28°-CAUD10° D: real LAA angiography at RAO28°CAUD10°

cCT, TEE, or angiography) considering the maximumt (TEE, ICE and angiography) or mean LZ (cCT). The degree of device oversizing was chosen by the operator. Based on our previous experience using the manufacturer's recommendations for device sizing, in relation to the maximum LZ diameter obtained from TEE and fluoroscopy, these two modalities were preferred in case of agreement. In the absence of agreement, ICE and CT measurements were also considered, and the final decision was based on all four imaging modalities and a discussion between both operators and the company's technical support team. After Amulet (Abbott, Plymout, MN, USa) implantation, we strived to achieve the 5 signs of proper device deployment (tire-shaped lobe, separation of the lobe from the disc, the concavity of the disc, axis of the lobe perpendicular to the neck axis of the LZ, and width of the lobe of ≥ 2/3 within the circumflex artery. Peri-device leakage was checked using ICE and contrast dye injection before device delivery. Aspirin was given I.V. immediately after device delivery, and clopidogrel (P.O.) was given within 30 min after the procedure. The antithrombotic regimen after the LAAC consisted of aspirin + clopidogrel for three months. After that, a TEE was done, and in the absence of any peri-device leakage, clopidogrel was withdrawn.

Statistical Analysis

Continuous variables are expressed as mean ± SD, or median as appropriate, and categorical variables as absolute numbers and percentages. Variables were compared using the t-test or the Wilcoxon test, as appropriate. Bland-Altman plots were used to determine bias and limits of agreement of measurements relative to image modality. Correlations were tested using Pearson´s correlation coefficient. A statistical significance threshold of 0.05 was accepted. All analyses were done using IBM software.

Results

Baseline and procedural characteristics

Since February 2019 to September 2020, LAAC was performed on 28 patients. Two of them were done using TEE navigation, and in 1 of them, significant leak was present on 3 month TEE. Thus, 25 patients were finally analyzed; the mean age was 73.08 ± 8.95, 9 (36%) were females, the mean CHA_2DS_2VASc was 4.28 ± 1.46, and the mean HAS-BLED score was 2.08 ± 0.64. The indication for a LAAC, in all patients, was a history of significant bleeding, and all patients were deemed unsuitable for long-term anticoagulation. Baseline characteristics of the cohort, including antithrombotic treatment at the time of the procedure, are shown in [Table 1]. The implantation was successful in all patients; the mean procedure length was 98.4 ± 16.8 min, fluoroscopy time was 11.3 ± 3.7 min, and the mean Amulet size was 22.6 ± 3.5. No significant peri-device leakage was present 3 months after the procedure (based on TEE examinations). The TEE assessment of device position and compression at 3-months was "very good." Regarding complications, there was one pericardial effusion that occurred roughly 3 hours after the procedure; it resolved with a good outcome and without the need for cardiac surgery.

The mean duration of the 25 analyzed patients was 17.1+8.8 months. During the follow-up, two patients (8%) died (both from heart failure). Stroke occurred in 1 patient (15 months after the procedure, on aspirin, with good clinical outcome, mRankin = 2), and 1 patient underwent clinically-relevant non-major bleeding. All patients were on antiplatelet monotherapy at last available control. Regarding the follow-up of three non-analyzed patients, two were on antiplatelet monotherapy and one on apixaban (patient with leak), and none underwent either stroke or significant bleeding.

Landing zone measurements

There were good correlations relative to LZ measurements with all 4 imaging modalities; R = 0.84 ($p < 0.001$) for the mean CT vs. TEE, R = 0.79 ($p < 0.001$) for the mean CT vs. fluoroscopy, R = 0.62 ($p = 0.001$) for the mean CT vs. ICE, R = 0.78 ($p < 0.001$) for fluoroscopy vs. TEE, R = 0.60 ($p = 0.002$) for fluoroscopy vs. ICE, and R = 0.57 ($p = 0.004$) for TEE vs. ICE. The correlations between the mean CT diameter and values obtained from the other 3 imaging modalities are shown in [Figure 5]. However, the LZ obtained from these different modalities were significantly different [Figure 1]. The mean diameter on CT was 20.60 ± 3.42 mm, and the maximum diameter on CT was CT, 21.99 ± 4.03 mm. Because the LAA mean diameter on CT best matched with the final size of implanted device, all other diameters were compared to this one. The maximum diameter on TEE was 18.72 ± 2.44 mm ($p<0.001$, if compared to mean CT diameter), the maximum diameter on ICE was 18.20 ± 2.68 mm ($p<0.001$, if compared to mean CT diameter), and the maximum on fluoroscopy was 17.76 ± 3.24 mm ($p< 0.001$, if compared to mean CT diameter).

Bland-Altman plots comparing mean CT diameter with maximum diameters obrained from TEE, ICE and fluoroscopy are shown in [Figure 6]. If we used the mean diameter from CT as the best and most accurate standard, then the least discrepancy was found between the mean CT and the maximum TEE diameter (–1.88 mm), next was the mean CT and the maximum ICE diameter (–2.40 mm), and the greatest discrepancy was found between the mean CT and the maximum fluoroscopy diameter (–2.84 mm). The discrepancies between TEE, ICE, and fluoroscopic measurements, compared to cCT values, are shown in [Table 2]. Importantly, the values obtained from TEE and fluoroscopy were constantly ~ 2 lower compared to cCT; however ICE values differed, some of them were lower and some other

higher than cCT values.

In terms of device size selection relative to the sizing based on maximum fluoroscopy or TEE diameter, per the manufacturer's recommendations, if only a single modality had been used, 18 (72%) of the fluoroscopy, 18 (72%) of the TEE , and 12 (48%) of the ICE measurements would have been correct in terms of selecting the device size that was finally implanted. When using the CT mean diameter and then choosing the next larger-sized LAAC device, 23 (92%) of the CT measurements were correct in selecting the optimal device size relative to what was actually implanted. Of the 2 CT outlier measurements, both would have led to implantation of an oversized device; of the 7 TEE outlier measurements, 4 would have led to oversizing and 3 to undersizing; of the 7 fluoroscopic outlier measurements, 5 would have led to undersizing and only 2 to oversizing, and of the 13 ICE outlier measurements, 5 would have led to oversizing and 7 to undersizing (again, all comparisons are between predicted sizes the actual size of the implanted devices).

Optimal fluoroscopic projection assessment (personalized fluoroscopic viewing angles)

On cCT, personalized viewing fluoroscopy angles were searched for each particular LAA in different combinations of RAO projections with different cranial and caudal projections. The aim was to test for how many patients the fluoroscopic projections recommended by the manufacturer will be acceptable. The RAO 30°, in combination with CRA 10–20° or CAUD 10–20° provided at least one acceptable projection in most patients (22 pts., 88%), although FluoroCT analysis allowed to find the best personalized viewing angle in this relatively broad angle range. However, in patients with the LAA lying superiorly and posteriorly, i.e. LAA with an early posterior angulation lying "backward" on the roof of the left atrium and instead lying superiorly-anteriorly and pointing toward the left ventricle, the optimal fluoroscopic projections differed substantially with greater RAO and CAUD angles being needed. An example of a posteriorly oriented LAA is shown in [Figure 4]; in this particular patient, the optimal viewing angle, analyzed using FlouroCT, was RAO36° - CAUD 26° that was also finally used for implantation [Figure 4].

Discussion

Cardiac CT provided the most accurate LZ diameter measurements and was optimally correlated with the actual size of the implanted device. The maximum diameters measured using TEE, fluoroscopy, and ICE correlated well with values obtained from cCT, but all these measurements systematically underestimated the LZ diameter. Moreover, preplanning of the implantation procedure using cCT analysis enabled the preprocedural determination of the optimum personalized fluoroscopic viewing angles for the best visualization of the LAA, something which is valuable for the operator and can make the procedure more convenient.

LZ measurements

In a few, mostly retrospective, single-center studies, CT LAA measurements have been shown to be larger than those obtained using angiography and 2D-TEE. 3567 Recent evidence suggests that landing zones determined using CT are 2–3 mm larger than those determined using angiography and 2D TEE. [8] Saw et al. showed (which agrees with our results) that cardiac CT provides the largest measurements of the LZs, followed by TEE and fluoroscopy. [6] Saw et al. analyzed 50 patients, 18 of whom were implanted with an Amulet/ACP device. In this series, LZs were measured using fluoroscopy, TEE, and cardiac CT. On cardiac CT, not the mean (computed from the perimeter), but only the maximum diameters were measured. The maximum diameter obtained from CT was 1.8±3.1 mm greater than from TEE and 4.2±3.3 greater than from fluoroscopy. This is in agreement with our findings, despite the absence of the mean diameter on CT analysis. Several reports have documented oval, eccentric, and sometimes irregular LAA orifices and LZs in vast majority of patients. Therefore, it is questionable whether reliance on the maximum orifice diameter (obtained using TEE or fluoroscopy) for device sizing is the best approach. Given the circular nature of the Amulet and the variability of the LAA ostium, a mean orifice diameter might be a much better approach. Compression of the device in the shortest LAA distance can be balanced against its expansion to the widest LAA distance. Parallels can be drawn, in this regard, to experiences with transcatheter aortic replacement, where the mean orifice (derived from multiplanar perimeter measurements) appears to confer more appropriate over the maximum planar diameter, especially if it is eccentric. [9]

Budge et al. compared LZs from measurements obtained from planar and three-dimensional cCT of 53 AF patients. [10] LZs derived from 3D cCT measurements had significantly larger LZs than those derived from planar cCT measurements (by 2.4 mm). Since these patients did not undergo LAAC, the match of cCT measurements with real device implanted could not be done. This data, as well as our own, further supports the potential advantage of incorporating routine multi-planar imaging into the procedural workup. According to the most recent reports, the LAA mean diameter derived from the LAA ostial perimeter from multiplanar measurements on cCTs seems to be the best measure for device selection. It reflects the oval nature of the

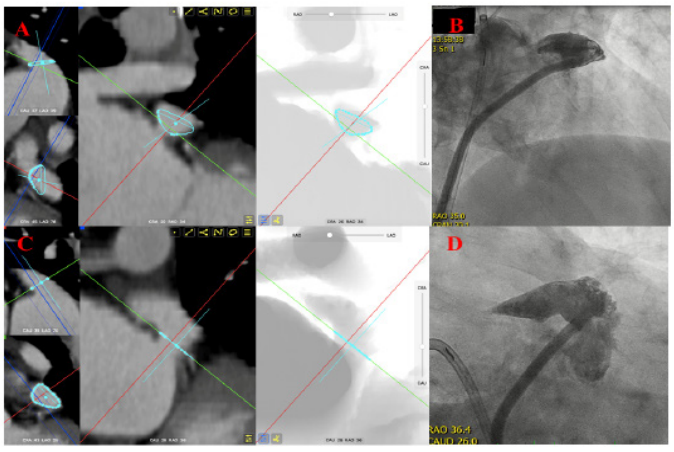

Figure 4: **Examples of the assessment of and the individualized projection angles for a patient with an superiorly-posteriorly (atypically) located LAA**

In a patient with a atypically (posteriorly, or backward orientated, lying on the top of the atrium) appendage, the optimal viewing fluoroscopic angle differed significantly from the projection angles recommended by the manufacturer. In the standard RAO30° - CRA20° projection, only the proximal part of the LAA was visible, creating an image of a "bud" during LAA angiography.
A: cCT reconstruction using Fluoro CT with expected fluoroscopic image at RAO35°-CRA20°, B: real LAA angiography at RAO35°CRA20°
In the personalized RAO36°-CAUD26° view, the whole length of the LAA is visible.
C: cCT reconstruction using Fluoro CT with expected fluoroscopic image at the best view RAO36°-CAUD26° D: real LAA angiography at RAO36°-CAUD26°

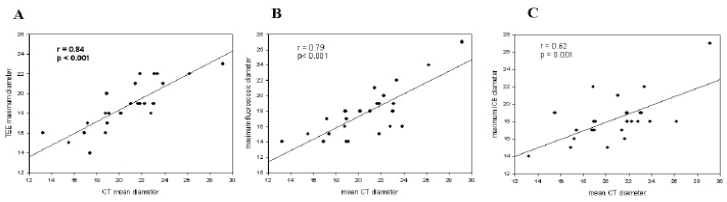

Figure 5: **Correlations of mean CT diameters with maximum TEE (A), maximum fluoroscopy (B), and maximum ICE (C) diameters**

All correlations were analyzed using the Pearson correlation coefficient.

LAA ostium, and device selection based on the maximum diameter of highly elliptical LAAs could lead to significant device oversizing.

Rajwani et al., in a retrospective analysis, compared values obtained from cCT and TEE in patients implanted with a Watchman device using three different imaging modalities. The maximum diameter from 2D TEE was 3.0 mm smaller than the maximum diameter from cardiac CT and 1.1 mm smaller than the mean diameter from cCT (which was derived from perimeter measurements). Although Rajwani et al. compared the LAA parameters used for Watchman implantation (as did the majority of the aforementioned studies), i.e., the LAA ostium was measured to different depths for the LZ compared to Amulet implantation; the results are still in accordance with our findings. Moreover, TEE measurements translated to an altered device selection in more than half of cases, and the median size predicted by cCT was one interval greater than that predicted by TEE. [8] Finally, as was recently reported by Chow et al., using the mean diameter from CT and choosing the next larger-sized LAAC device, the proportion of patients without contrast leakage was significantly higher than if device sizing was based on maximum diameter obtained from 2D-TEE. [11]

In our cohort, if the mean diameter from CT had been used for device sizing, it would have been correct in 92% of cases. However, if only fluoroscopic or only TEE measurements had been used, they would have only been correct in 72% of cases. The standard viewing projection recommended for LAAC, i.e., RAO30° plus mild cranial and caudal views, express the projection in which the minimum diameter of LAA is appreciated. [4] The maximum diameter of the appendage can best be seen in the LAO and CAU projections, which are not used for LAAC. [4] Considering that in most patients, the LAA has an oval shape, this may clearly explain the large differences, especially between the maximum (or mean) parameters measured using CT and fluoroscopy. Importantly, regarding the comparison of cCT with three other modalities, TEE and fluoroscopy constantly undersized the LZ by ~ 2 mm. However, the values obtained from ICE differed inconsistently in comparison to TEE or fluoroscopy, some of them were lower but other higher compared to cCT. It would make the use of ICE very difficult, if used as standard for device sizing.

Personalized fluoroscopic viewing angles for the LAA

The LAA is a finger-like projection that derives from the LA and forms part of the left border of the cardiac silhouette. It lies superior to the left ventricle and inferior to the pulmonary artery. The apex of the LAA can vary in its position, although it usually points anteriorly and superiorly. However, several different variations have been described, e.g., it may point posteriorly backward towards the LA or behind the aorta. [12]

The previously mentioned reports were focused on a comparison of LZ measurements between different imaging modalities. However, optimal LAA visualization during the LAAC procedure is an important issue, and interestingly, it has received far less attention. As noted by Shee et al., personalized viewing projections obtained from a cCT or a 3D printed LA model can improve the accuracy of fluoroscopic measurements of LAA dimensions compared to using standard fluoroscopic angles. [13] Shee et al. analyzed cCT and 3D printed LAA reconstructions from 28 patients prior to Watchman implantation to identify personalized viewing angles in which the LAA maximum landing zone diameter and LAA length were best observed. The LZ and the length of the LAA were measured using standard angles (i.e., RAO30° CAUD20°) as well as using personalized angles for each LAA, which had been obtained from cCT. Maximum measurements obtained from personalized projections were greater than measurements obtained from standard angles and were more consistent with hypothetical device size predictions (since the reference implantation was based on a 3D LAA model and not in vivo measurements). [13] Wang et al. carried out a comprehensive study on cCT morphologies and the location of the LAA (not indicated for LAAC), their relationship to the left pulmonary veins, LAA neck angles and the angle of the first LAA lobe, the distance from the ostium to the first bend, and the angle of the first bend (measured relative to the central axis of the primary lobe). [14] A pronounced bend in the primary lobe was seen in 73.2% of patients; the typical angle of the first bend was around 100°; however, it varied significantly from 40° to 160°. In our cohort, the individualized viewing angles were close to the standard recommended viewing angles (i.e., RAO 30°-CRA 10°–20°, or RAO 30°-CAUD 10°–20°) in the majority of patients. However, in 3 (12%) patients with superiorly and posteriorly oriented appendages (i.e., not oriented towards the left ventricle, but going backward on the left atrium), the optimal viewing fluoroscopy angles differed significantly (i.e., the optimum visualization was present in more caudal views, for example see [Figure 4]). The personalized viewing projections, which we defined as the fluoroscopy projection in which maximum LAA lengths were best observed (which we called as the "banana" view of the LAA), and simultaneously, the device (if optimally implanted) had to be perpendicular to the LAA axis, made the procedure more convenient for the operator. By seeing the whole length of the LAA, the operator can insert the pigtail as distally as possible, can see if the sheath is parallel with the long axis of the LAA, and can confirm the position of the device relative to the LAA axis (i.e., the device should be perpendicular in this view to the LAA axis). This could be even more important for Watchman devices, since the devices are implanted deeper in the LAA, and more distal LAA intubation is needed.

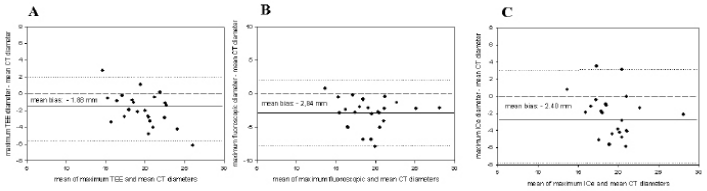

Figure 6: **Bland-Altman plots of mean CT diameters compared to maximum TEE (A), maximum fluoroscopy (B), and maximum ICE diameters (C)**

The mean bias was calculated as the mean of the differences between the values obtained from two measurements. The mean bias, zero, and 2 standard deviation lines are shown.

Limitations

The number of patients was limited, therefore the rate of patients with atypical LAA location could be underestimated. The long-term outcomes of patients were not established.

Conclusions

Our data further support that CT provides the best measurement of the LZ and the best prediction of the optimum fluoroscopy projections for the implantation procedure.

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Diagnostic Utility of Smartwatch Technology for Atrial Fibrillation Detection – A Systematic Analysis

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Abstract

Background: Smartphone technologies have been recently developed to assess heart rate and rhythm, but their role in accurately detecting atrial fibrillation (AF) remains unknown.

Objective: We sought to perform a meta-analysis using prospective studies comparing Smartwatch technology with current monitoring standards for AF detection (ECG, Holter, Patch Monitor, ILR).

Methods: We performed a comprehensive literature search for prospective studies comparing Smartwatch technology simultaneously with current monitoring standards (ECG, Holter, and Patch monitor) for AF detection since inception to November 25th, 2019. The outcome studied was the accuracy of AF detection. Accuracy was determined with concomitant usage of ECG monitoring, Holter monitoring, loop recorder, or patch monitoring.

Results: A total of 9 observational studies were included comparing smartwatch technology, 3 using single-lead ECG monitoring, and six studies using photoplethysmography with routine AF monitoring strategies. A total of 1559 patients were enrolled (mean age 63.5 years, 39.5% had an AF history). The mean monitoring time was 75.6 days. Smartwatch was non-inferior to composite ECG monitoring strategies (OR 1.06, 95% CI 0.93 – 1.21, p=0.37), composite 12 lead ECG/Holter monitoring (OR 0.90, 95% CI 0.62 – 1.30, p=0.57) and patch monitoring (OR 1.28, 95% CI 0.84 - 1.94, p=0.24) for AF detection. The sensitivity and specificity for AF detection using a smartwatch was 95% and 94%, respectively.

Conclusions: Smartwatch based single-lead ECG and photoplethysmography appear to be reasonable alternatives for AF monitoring.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmias affecting over 33.5 million people worldwide, increasing morbidity and mortality [1-3]. AF is frequently subclinical or paroxysmal, which causes a significant barrier to its expedient diagnosis and treatment. Electrocardiogram (ECG) is often normal between the episodes and reflects only single time-point measurements. Other implantable or recording devices are limited by user activation, external factors and are either expensive or invasive. Photoplethysmography was recently developed and implemented in wearable Smartwatches in 2017, providing a cost-effective and non-invasive means for continuous ECG monitoring. Over the past two years, several large-scale prospective trials have compared Smartwatch technology with current monitoring standards for AF detection, such as ECG, Holter Monitor (HM), Implantable Loop Recorder (ILR), and Patch Monitoring (PM). Since initial development, several studies have become available comparing smartwatch technology with the current standards [4-12]. Hence, we performed a meta-analysis comparing the accuracy of Smartwatch-based single-lead ECG and PPG to current monitoring standards for AF detection.

Key Words

Smartwatch, Atrial Fibrillation, Photoplethysmography.

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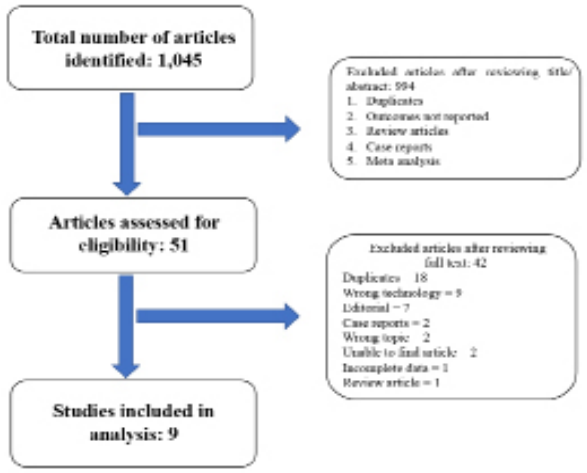

Figure 1: PRISMA flow diagram

Methods

Search Strategy

The initial search strategy was developed by two authors (KA and GM). Systematic search, without language restriction, using PubMed, EMBASE, SCOPUS, Google Scholar, and ClinicalTrials.gov from inception to November 25th, 2019 using the keywords: "smartwatch" OR "watch" AND "atrial fibrillation" or "watch" AND "atrial fibrillation detection."

Study Selection

The eligibility criteria our systematic review and meta-analysis included:

1. All prospective studies reporting clinical outcomes comparing Smartwatch technology simultaneously with current monitoring standards (ECG, Holter, and Patch monitor).

2. Human subjects aged ≥ 18 years

3. Studies in the English language.

Case reports, editorial, and systematic reviews were excluded.

Data Extractions

Two investigators independently performed the literature search and screened all titles and full-text versions of all relevant studies that met the study inclusion criteria.

The references of all identified articles were also reviewed for relevant studies meeting the eligibility criteria. The data from the included studies were extracted using a standardized protocol and a data extraction form. Any discrepancies between the two investigators were resolved with a consultation with the senior investigator (DL). The following data were extracted: title, year of publication, type of study, mean age, sample size, baseline technology used, specific watch used, the specific algorithm used for AF detection, comparator modality, the quantity of ECG leads, and time monitored [Table 1]. Quantitative data on AF detection, including a discrete number of AF events, sensitivity, and specificity, were obtained [Table 2]). The Newcastle Ottawa Scale [Table 3] was used to appraise the quality of the included studies 13. We rated the quality of the studies (good, fair, and poor) by awarding stars in each domain. A "good" quality score required 3 or 4 stars in the selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes. A "fair" quality score required 2 stars in the selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes. A "poor" quality score reflected 0 or 1 star(s) in selection, or 0 stars in comparability, or 0 or 1 star(s) in outcomes.

Outcomes

The primary outcome evaluated in our study was the accuracy of AF detection. Accuracy was determined with concomitant usage of ECG monitoring, Holter monitoring, loop recorder, or patch monitoring.

Table 1: Baseline characteristics of the studies included in our meta-analysis

Study	Perez et al	Bashar et al	Wasserlauf et al	Dorr et al	Tison et al	Bumgarner et al	Faranesh et al	Rajakariar et al	Genicot et al
Year	2019	2019	2019	2019	2018	2018	2019	2019	2018
Type	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective
Mean Age	59	N/A	72.1	76.4	42	68	N/A	67	60
# enrolled	450	37	24	508*, 549†	51	93	96	200	100
Baseline tech used	Plethysmo-graph	Plethysmo-graph	Kardiaband	Plethysmo-graph	Plethysmo-graph	SW single lead ECG (Kardia band)	Plethysmo-graph	SW single lead ECG (iPhone ECG)	Plethysmo-graph
Specific watch used	Apple Watch	Samsung Simband	Apple Watch	Samsung Gear Fit2	Apple Watch	Apple Watch	Fitbit SW	N/A	N/A
Specific algorithm used	PPI on plethysmo-graphy	PPI on plethysmo-graphy	Smart- Rhythm 2.0 (Kardia band)	PPI on plethysmo-graphy	PPI on plethysmo-graphy	Kardiaband	N/A	Kardiaband	PPI on plethysmo-graphy
Comparator	7-day ECG patch - single lead	Holter Monitor	Reveal LINQ	iPhone ECG	Ambulatory ECG post-cardioversion	Ambulatory ECG post-cardioversion	Single lead ECG patch (Cardea SOLO)	12-lead ECG	24-hour Holter Monitor
# of leads in comparator	Single	Multiple	Single	Single	12-lead	12-lead	Single	12-lead	12-lead
Time monitored	117 days	N/A	31,349 hours	1 min each	30 min	30 second strips	7 days	N/A	99 days

* for Plethysmograph SW:Smartwatch †for iPhone ECG PPI: Pulse-pulse intervals

Table 2: Quantitative Evaluation of Atrial Fibrillation Events Detected.

Study	Perez et al	Bashar et al	Wasserlauf et al	Dorr et al	Tison et al	Bumgarner et al	Faranesh et al	Rajakariar et al	Genicot et al
# enrolled	450	37	24	508*,549†	51	93	96	200	100
# with AF	153	10	24	237	51	93	35	38	N/A
% with AF	34	27	100	46.65	100	100	36.46	19	N/A
Sensitivity of SW AF detection	N/A	98.18%	97.70%	93.70%	98%	93%	N/A	89.5%	N/A
Specificity of SW AF detection	N/A	98.07%	98.90%	98.20%	90.20%	84	N/A	94.40%	N/A

* for Plethysmograph AF: Atrial Fibrillation †for iPhone ECG SW: Smartwatch

Statistical Analysis

Statistical analysis for odds ratio (OR) estimates of each study was calculated using Stata (Version 16.1, StataCorp, College Station, TX 77845). Subsequent meta-analysis was performed using Comprehensive Meta-Analysis (CMA) software (version. 3.3.070, Biostat, Englewood, NJ 07631) with a random-effects model. Results were expressed as an OR with a 95% confidence interval (CI). Higgins I-squared (I2) was used to quantify heterogeneity (I2<50% was defined as low) 14. P < 0.05 was considered statistically significant. Sensitivity analyses were performed for outcomes that demonstrated significant heterogeneity (I2 >50%) to assess the individual contribution to the aggregate. Funnel plots were also used in conjunction with sensitivity analysis to assess for publication bias.

Results

Search Results and study characteristics

A total of 1,045 citations were identified [Figure 1] during the initial search. Nine hundred four records were excluded, and a total of 51 relevant articles were identified. After a detailed evaluation, nine articles ultimately met the inclusion criteria enrolling a total of 1,559 patients [Figure 1]. A total of 1559 patients were enrolled (mean age 63.5 years, 39.5% had an AF history). The mean monitoring time was 75.6 days. [Table 1] summarizes the study characteristics of the included trials.

Primary Outcome [Figure 2]

AF Detection

Smartwatch was non-inferior to composite ECG monitoring strategies (OR 1.06, 95% CI 0.93 – 1.21, p = 0.37) [Figure 3A], composite 12 lead ECG/Holter monitoring (OR 0.90, 95% CI 0.62 – 1.30, p = 0.57) [Figure 4A] and patch monitoring (OR 1.28, 95% CI 0.84 - 1.94, p = 0.24) [Figure 5A] for AF detection. Both mean sensitivity and specificity for AF detection using smartwatch was 95% and 94%, respectively. Several studies demonstrated statistically significant differences in AF sensing capability. Perez et al., Faranesh et al., and Tison et al. demonstrated statistically significant oversensing [4,8,10], while Wasserlauf et al. and Genicot et al. demonstrated smartwatch comparative undersensing [6,12].

Sensitivity Analysis

Due to significant heterogeneity observed in the primary outcome, a sensitivity analysis was performed by excluding one study at a time to see if any study had a substantial contribution to observed heterogeneity. The heterogeneity found may be associated with individual study differences, institutional variation, and the difference in evaluation among the included studies.

Sensitivity analysis performed on a composite analysis [Figure 3B] demonstrated no significant heterogeneity changes (I2 = 99.2%). In comparison, the reduction in heterogeneity (from I2 = 75.3% to 0%) was observed with the exclusion of Genicot et al., which had a significant proportion of weight in the study for watch monitoring vs. composite 12 lead and Holter monitoring comparison. This is consistent with the single study outlier noted in the corresponding funnel plot [Figure 4B]. Sensitivity analysis was not performed on watch monitoring vs. patch monitoring comparison as only two studies were included in the subgroup analysis (I2 = 99.1%).

Publication Bias

In addition to sensitivity analysis, publication bias was assessed visually using funnel plots [Figure 3], demonstrating asymmetrical funnel plot figures. Consequently, despite the overall findings of no difference between watch monitoring and routinely practiced wearable/implantable devices, results should be interpreted with caution (given funnel plot asymmetry and high heterogeneity).

Discussion

Our analysis demonstrated no significant difference in AF detection in Smartwatch monitoring compared to composite ECG monitoring, Holter monitoring, loop recorder, and patch monitoring [Figure 2]. There has been a progressive increase in the incidence and prevalence of AF worldwide, with an increased risk of morbidity and mortality. Atrial fibrillation is known to have a significant impact on health care costs,

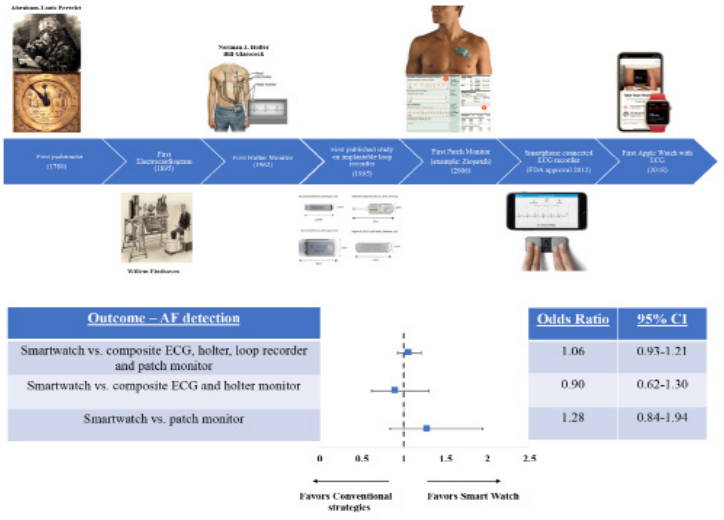

Figure 2: Diagnostic Utility of Smartwatch Technology for Atrial Fibrillation Detection: The Smartwatch-AF Study

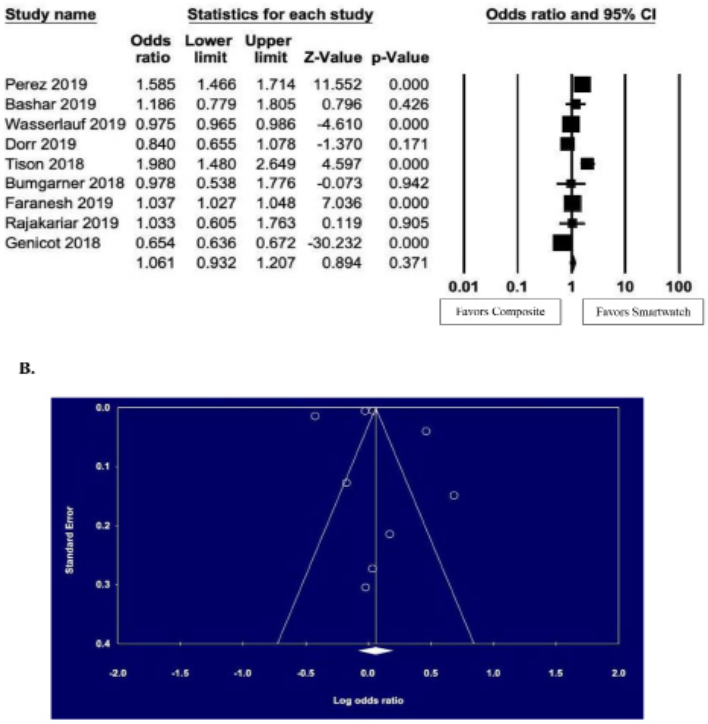

Figure 3: **A. Smartwatch Monitoring vs. Composite ECG, Holter, Loop Recorder and Patch Monitor; B. Funnel plot demonstrating asymmetry suggestive of publication bias.**

with the major cost-drivers being the loss of productivity, stroke, and hospitalizations [1]. Studies have also shown that increased AF burden directly correlates with thromboembolic stroke risk [15-19]. Accordingly, increased awareness of AF symptoms and early clinical diagnosis is imperative to prevent long term morbidity and mortality. Often, given the asymptomatic nature of paroxysmal AF, long term monitoring for detecting these clinically relevant silent AF episodes is essential [4,20]. Although cardiac implantable electronic devices are commonly used for monitoring of silent AF episodes, they are associated with potential disadvantages such as invasiveness of the procedure, procedure-related complications, and long-term patient discomfort [4]. There is a growing need to develop non-invasive and wearable technology to enable continuous monitoring of silent arrhythmias in high-risk patients [21].

Photoplethysmography-based technology included in the smartwatches (Apple or Samsung) is regarded as the most accurate method for diagnosing AF [21-24]. Photoplethysmography based smart devices; mobile health (Mobile Health) in combination with machine learning, has transformed patient care by precisely and accurately diagnosing AF [25-27]. Photoplethysmography in smartwatches consists of an infrared light-emitting diode sensor that detects blood volume changes in the microvasculature [21,28]. The synchronous changes in blood volume in small blood vessels with each heartbeat are transformed into a physiological pulsatile waveform by Photoplethysmography [21,28]. It is regarded as a portable, low-cost, simple, and wearable technology most suitable for monitoring patients in primary care and community-based clinical settings [21]. Furthermore, this technology has been formerly used for measuring oxygen saturation, blood pressure, cardiac output, autonomic changes, and peripheral vascular disease 4; with better reliability than previously used technologies such as pulse palpation, modified sphygmomanometers, and non–12-lead ECG for detection of AF episodes [29-31]. Smartwatch-based arrhythmia detection (with a photoplethysmography-based AF detection) is a simple, non-invasive technique and a safer alternative to the routinely utilized AF detection tools.

Previous studies

Several studies have been conducted to assess the efficacy of photoplethysmography based smartwatch technologies for detecting AF episodes. The overall sensitivity and specificity for detecting AF episodes using smartphone technology is approximately 90-96% and 85-99%, respectively [32-37]. ECG watchband (KardiaBand, AlivaCor, USA), which is connected to the Apple Watch, was first introduced in April 2017 for detecting AF [38]. Kardiaband was based on a proprietary algorithm (rhythm irregularity and absence of P waves) for AF detection 38 and transmitting a 30s segment of single-lead ECG via Bluetooth to the Apple Watch [38]. Similarly, Bumgarner et al. compared the efficacy of the Apple Watch with a standard clinical 12 lead ECG in 100 AF patients and demonstrated that the sensitivity and specificity of the Apple Watch for detecting AF are 93% and 84%, respectively [39]. Several other studies have used AlivaCor Kardia Mobile approaches and demonstrated that sensitivity and specificity were >95% [40-42]. With the help of motion and noise artifacts and premature atrial contraction algorithms, photoplethysmography based smartwatch detected AF with higher sensitivity (98.18%), specificity (97.43%), and accuracy (97.54%) [5]. According to Wasserlauf et al., AF-based smartwatches had higher sensitivity for detecting the AF episodes (episode sensitivity 97.5%) and AF duration (duration sensitivity 97.7%) as compared to implantable cardiac monitor (ICM) [6].

The WATCH-AF trial demonstrated relatively high sensitivity (93.7%), specificity (98.2%), overall accuracy (96.1%), positive predictive value (97.8%), and negative predictive value (94.7%) in diagnosing AF [7], findings that also echoes (comparing simultaneously performed 12-lead ECG) in a recently published study by Rajakariar et al. [43]. Using single-channel electrocardiogram (ECG), multi-wavelength photoplethysmography, tri-axial accelerometry, the accuracy, sensitivity, and specificity of detecting AF episodes with Samsung Simband watch was 95%, 97%, and 94%, respectively [34]. Photoplethysmography based smartwatch technology combined with deep neural network passively predicted AF in patients undergoing cardioversion better than standard 12-lead ECG with higher sensitivity (94%) and specificity (90.2%)

Table 3: **Qualitative Evaluation of Included Studies Using Newcastle-Ottawa Scale**

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcome (max 3 stars)
Perez et al	****	**	***
Bashar et al	***	**	**
Wasserlauf et al	****	**	***
Dorr et al	****	**	***
Tison et al	****	**	**
Bumgarner et al	****	**	***
Faranesh et al	****	**	***
Rajakariar et al	****	**	**
Genicot et al	****	**	***

Table 4: Patient comparison with and without rhythm control intervention within AF-CM group.

Characteristic	No intervention n=132	DCCV n=47	DCCV + ablation n=17	P value
Sex				0.02
Female	57 (43.2%)	12 (25.5%)	3 (17.6%)	
Male	75 (56.8%)	35 (74.5%)	14 (82.4%)	
Age, years	77.61±11.34	66.15±9.34	62.06±7.32	<0.001
Ethnicity				0.78
Hispanic/Latino	1 (0.8%)	0 (0.0%)	0 (0.0%)	
Not Hispanic/Latino	131 (99.2%)	47 (100.0%)	17 (100.0%)	
Tobacco use	78 (59.1%)	30 (63.8%)	11 (64.7%)	0.8
Hypertension	96 (72.7%)	32 (68.1%)	10 (58.8%)	0.46
Diabetes mellitus	44 (33.3%)	12 (25.5%)	3 (17.6%)	0.3
Coronary artery disease	56 (42.4%)	6 (12.8%)	4 (23.5%)	<0.001
Death	53 (40.2%)	8 (17.0%)	1 (5.9%)	<0.001
Baseline LVEF, %	29.62±7.85	29.81±7.54	28.18±6.94	0.74
Follow-up LVEF, %	44.66±12.42	50.46±11.49	56.71±6.89	<0.001

Data presented as n (%) or mean±standard deviation.

in an ambulatory care setting [8]. Furthermore, although both Apple Watch Series 3 and Fitbit were equipped with Photoplethysmography technology, the precision and accuracy for AF detection was higher in Apple Watch Series 3 (75% correlation) as compared to Fitbit (FBT) Charge HR Wireless Activity Wristband (30% correlation) in a phase-II prospective clinical study conducted in Japan [28]. The false-positive rate and accuracy of AF detection in healthy volunteers and AF patients using smartwatches with Photoplethysmography based algorithm was approximately 0.2% and 96%, respectively [44], thus demonstrating the efficacy of photoplethysmography based wearable devices accurately differentiating AF from sinus rhythm in at-risk patients [44].

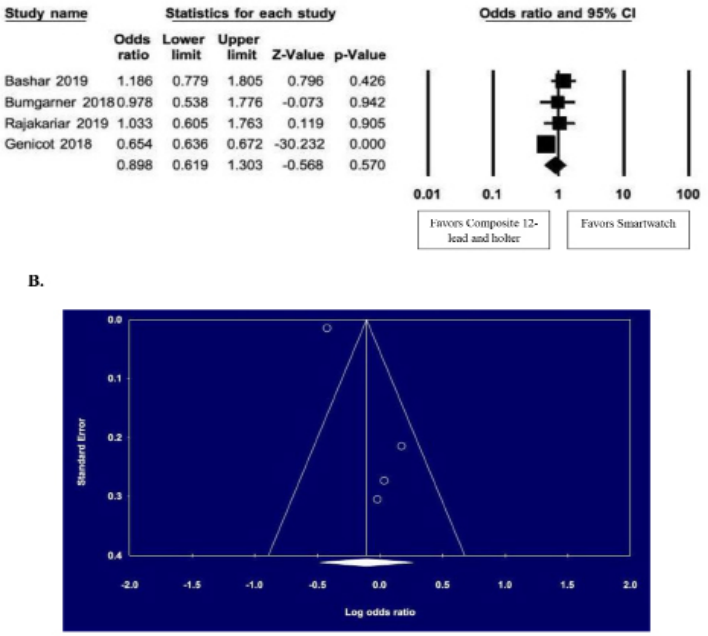

Figure 4: A. Smartwatch Monitoring vs. Composite 12-Lead ECG and Holter Monitoring; B. Funnel plot demonstrating asymmetry suggestive of publication bias.

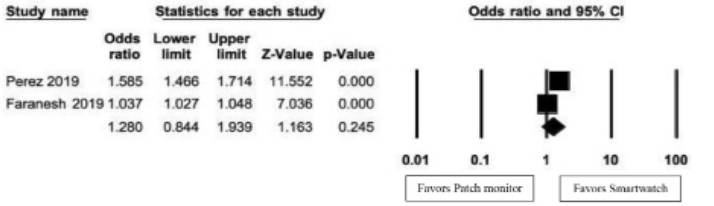

Figure 4: Smartwatch Monitor vs. Patch Monitor

Limitations

There are several limitations to the performed meta-analysis. The limitations did not include a comprehensive text and comparison to literature.

1. Patients with implantable cardiac pacemakers were excluded from the studies.

2. Some studies included patients with prior history of paroxysmal AF, while others excluded these patients, limiting the generalizability of the studies.

3. Study heterogeneity.

4. Variation in algorithms used for different devices.

5. Differences in metrics of assessment among different studies.

Conclusions

While composite 12-lead ECG, Holter monitor, implantable loop recorders, or patch recording are the standards for AF detection, photoplethysmography based smartwatch technology is a simple, efficient, and non-inferior alternative that may expedite detection and treatment of subclinical AF, preventing morbidity and mortality from stroke and cardiovascular disease.

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New-onset Heart Failure With Atrial Fibrillation: A Distinct Type of Cardiomyopathy?

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Abstract

Objective: There is limited research comparing demographic and clinical characteristics between patients who present with atrial fibrillation (AF) and new-onset cardiomyopathy (CM) to patients with new-onset CM without dysrhythmia. We aimed to evaluate clinical characteristics and outcomes in patients with new-onset CM with and without AF and to report their real-world treatment.

Methods and Results: The study population was identified using patient records from our healthcare system from January 1, 2012 to September 30, 2016. Patients with a left ventricular ejection fraction ≤40% without a prior history of CM were divided into two groups: those with an antecedent or concomitant diagnosis of AF (AF-CM group) and those with no history of dysrhythmia (CM group). Patients in the AF-CM group (n=196) were older, more likely to be male, had a higher burden of comorbidities but lower levels of cardiac biomarkers, and had lower voltage on surface electrocardiogram than the CM group (n=197). In AF-CM, symptom onset was insidious, leading to a higher likelihood of outpatient diagnosis; 88.3% of AF-CM patients presented with atypical symptoms of AF. The AF-CM group had higher mortality on follow-up. Only 8.7% of patients in this group underwent an ablation procedure. Women, those with a history of coronary artery disease, and older patients were less likely to receive a cardioversion or ablation procedure.

Conclusions: Patients presenting with new-onset CM associated with AF have a markedly different risk factor and demographic profile, clinical presentation, and outcomes. In real-world practice, a minority of patients undergo a rhythm control strategy.

Introduction

This study evaluates differences between new-onset cardiomyopathy (CM) with and without atrial fibrillation (AF). New-onset CM is defined as a left ventricular ejection fraction (EF) ≤40% with no prior history of CM. The distinction between the two CM groups is whether there is a concomitant or preceding history of AF (AF-CM group) or there is no history of concomitant or antecedent AF (CM group). There has been increasing recognition that AF may present with typical or atypical symptoms and often can be classified as asymptomatic [1-4]. The prevalence of AF with typical or atypical symptoms in this patient population is not known, and we attempt to answer that question. We also report the real-world treatment pattern for these patients in a large healthcare system.

Key Words

Atrial fibrillation, Heart failure, New-onset cardiomyopathy, Ablation.

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Material and Methods

The local institutional review board approved this study, which was conducted in accordance with the Declaration of Helsinki. Informed consent requirement was waived.

Study Population and Data Collection

Through retrospective review of echocardiographic data in patient charts in the Aurora Health Care system's electronic medical records (EPIC, Verona, WI) from January 1, 2012 to September 30, 2016, we identified patients with new-onset CM with a left ventricular EF ≤40% and no prior history of low EF. Initial data were abstracted by Aurora Research Institute's EPIC data retrieval team electronically. Both inpatients and outpatients were included in the study. Each patient was

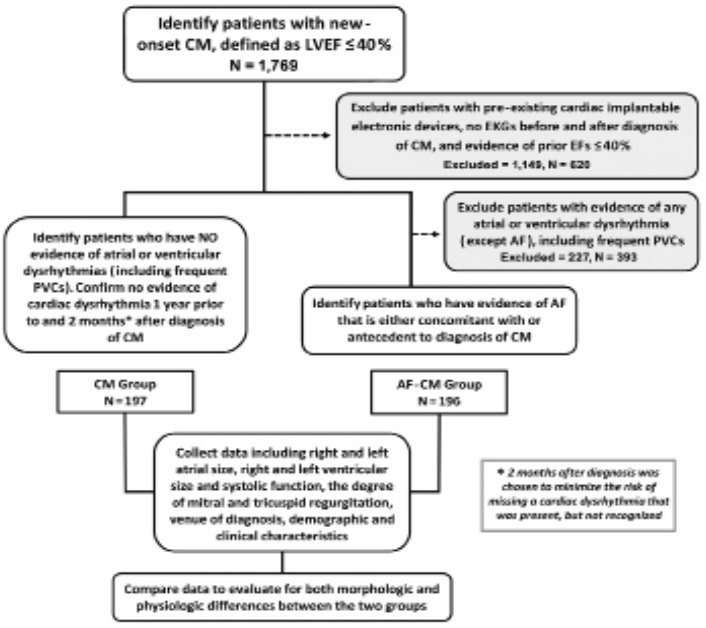

Figure 1: **Study design. AF, atrial fibrillation; CM, cardiomyopathy; EF, ejection fraction; EKG, electrocardiogram; PVC, premature ventricular contraction.**

manually assessed for inclusion and exclusion criteria by the research coordinators under the supervision of the principal investigator. Patients with any pre-existing evidence of CM based on office notes and/or cardiac imaging were excluded. Patient demographic data, medical comorbidities, admission diagnosis, admission laboratory values, peak troponin values, and voltage based on EKG were collected. EKG voltage was measured utilizing the Sokolow criteria [5], measuring the S wave in V1 plus the R wave in V5 or V6 (whichever was largest). Information about the treatment these patients received both as an inpatient and outpatient was collected. Readmission and mortality data were obtained. An almost equal number of patients were included for each 5% difference in left ventricular EF. An equal number of patients were collected for EF <20%.

Patients with a pre-existing cardiovascular implantable electronic device were excluded, as were patients with a history of any other dysrhythmia, including frequent premature ventricular contractions (PVCs; >2 PVCs on surface EKG, ventricular trigeminy, or more on telemetry). Additional exclusion criteria were unreadable or poor-quality echocardiogram, mortality during inpatient admission, and presence of congenital heart disease.

Then, patients were divided into two categories: those with an antecedent or concomitant diagnosis of AF (AF-CM group) and those without a history of any preceding dysrhythmias (CM group). Patients included in the isolated CM group were required to not have had any atrial or ventricular dysrhythmia in the preceding 1 year or the consecutive 2 months after the diagnosis of CM. The consecutive 2 months after the diagnosis of CM was selected as part of this criterion to minimize the likelihood of missing cryptogenic AF or other dysrhythmias in this population. Patients were matched according to left ventricular EF [Figure 1]. All data were stored electronically in a secure and de-identified manner on official Aurora Health Care computer systems.

Statistical Methods

Study subjects were matched for left ventricular EF. Descriptive data are presented in tables as frequencies and percentages and means ± standard deviations. Baseline characteristics were compared among intervention groups by chi-square or Fisher's exact tests and one-way analysis of variance or Kruskal-Wallis test, accordingly. The association between AF-CM or CM alone with the composite outcome of hospital readmission or death was examined using Kaplan-Meier analysis. Linearity and proportional hazards assumptions were assessed and fulfilled. All P values are reported as 2-tailed, with <0.05 considered to be statistically significant. All statistical analysis was performed using SAS 9.4 (SAS Institute, Cary, NC) or Stata version 15 (StataCorp, College Station, TX).

Results

[Figure 2]

Differences in Demographic Characteristics and Comorbidities

Over a 4-year period, 393 patients with new-onset CM were identified: 196 patients were identified in the AF-CM group, and 197 patients in the CM group.

Table 1: **Demographic and clinical characteristics.**

Characteristic	AF-CM group (n=196)	CM group (n=197)	P value
Age, years	73.51±12.14	64.18±15.98	<0.001
Body mass index	31.5±8.2	29.8±7.7	0.04
Sex, male	124 (63.3)	97 (49.2)	0.01
Race			<0.001
White	190 (96.9)	151 (76.7)	
Black/African American	4 (2.0)	39 (19.8)	
Others	2 (1.0)	7 (3.5)	
Tobacco use	119 (60.7)	132 (67.0)	0.19
Alcohol use	24 (12.2)	71 (36.0)	<0.001
Hypertension	138 (70.4)	105 (53.3)	<0.001
History of PCI	36 (18.4)	38 (19.3)	0.82
Hyperlipidemia	115 (58.7)	81 (41.1)	<0.001
Coronary artery disease	66 (33.7)	41 (20.8)	<0.01
Diabetes mellitus	59 (30.1)	57 (28.9)	0.80
History of drug abuse	4 (2.1)	15 (7.6)	0.01
Outpatient diagnosis	70 (35.7)	20 (10.2)	<0.001
Presenting symptoms			<0.001
Congestive heart failure	128 (65.3)	82 (41.6)	
Myocardial infarction	0 (0.0)	46 (23.3)	
Others/unknown	68 (34.7)	69 (35.0)	
Deceased	62 (31.6)	44 (22.3)	0.04
Palpitations on presentation	23 (11.7)	3 (1.5)	<.0.001
LVEF on diagnosis			0.99
36-40%	43 (21.9)	42 (21.3)	
31-35%	40 (20.4)	43 (21.8)	
26-30%	45 (23.0)	43 (21.8)	
21-25%	33 (16.8)	33 (16.8)	
≤20%	35 (17.9)	36 (18.3)	

Data presented as n (%) or mean±standard deviation.

Table 2: Electrocardiography and laboratory characteristics.

Characteristic	AF-CM group (n=196)	CM group(n=197)	P value
Bundle branch block			0.98
None	153 (78.1)	152 (77.2)	
Left	24 (12.2)	25 (12.7)	
Right	19 (9.7)	20 (10.1)	
Ventricular rate	109±26.43	89.7±18.80	<0.001
BPM			
Voltage group			<0.001
Low	79 (39.0)	54 (27.6)	
High	5 (2.5)	24 (12.2)	
Voltage (mV)	1.8±0.85	2.14±1.07	<0.001
Troponin I	0.91±5.72	14.27±63.48	0.01
BNP	771.3 ±809.3	1015.6±1040.2	0.02

Data presented as n (%) or mean±standard deviation.

Patients in the AF-CM group, in comparison to the CM group, were older (73.51 years vs. 64.18 years, respectively; P < 0.001), more likely to be male (63.3% vs. 49.2%, respectively; P=0.005), more likely to have a history of hypertension (70.4% vs 53.3%, respectively; P=0.0005), and more likely to have a history of coronary artery disease (33.7% vs 20.8%, respectively; P=0.0042). They were also likely to have a slightly higher body mass index (31.5 vs. 29.8, respectively; P=0.04) [Table 1].

Differences in Clinical Presentation, Diagnosis Setting, and Myocardial Infarction

A majority of patients in the AF-CM group had an atypical clinical presentation of AF. Only 23 patients (11.7%) had palpitations listed as one of their presenting complaints. A majority (65.3%) of AF-CM patients presented with insidious onset of congestive heart failure (CHF) symptoms. There were no patients in this group who presented with an acute myocardial infarction [Figure 3].

The CM group patients presented more frequently with acute CHF symptoms (41.6%) or acute myocardial infarction (23.3%). Presentation with insidious onset of CHF was less frequent in the CM group.

A significant number of patients in both groups had varied presentations that could not be clearly related to a cardiac etiology, e.g., fall, tiredness, "not feeling right," infection, confusion. They were grouped in the "Others/Unknown" category.

Patients in the AF-CM group were more likely to be diagnosed as outpatients than patients in the CM group (35.7% vs. 10.2%, respectively; P<0.0001); CM group patients were predominantly diagnosed in the hospital setting.

Differences in Laboratory Values and EKG

Patients with AF-CM presented with lower peak troponin values and brain natriuretic peptide (BNP) levels. Low voltage on surface EKG was more prevalent in the AF-CM group than the CM group (39.0% vs. 27.6%, respectively; P=0.0003) [Table 2].

Differences in Outcomes

Hospital readmissions did not differ between patients with AF-CM and CM, though the mortality rate was significantly higher in patients with AF-CM and the survival curves continued to diverge throughout the follow-up data collection period [Figure 4].

Real-world Treatment for AF-CM Group

A large proportion of AF-CM patients (n=107, 54.6%) never saw a cardiac electrophysiologist either as an inpatient or outpatient. A majority of the patients in both groups were evaluated and treated by a cardiologist. Direct current cardioversion (DCCV) was performed only in 47 (24%) patients. Using DCCV as a surrogate for an attempt at rhythm control, only a minority of patients underwent a rhythm control strategy. Interestingly, within the AF-CM group, more patients (79 [40.3%]) underwent a diagnostic cardiac catheterization than a cardioversion procedure (24%), though none had presented with an acute myocardial infarction.

Ablation for AF was performed in a small minority (17/196 [8.7%]) of patients [Table 3]. All patients did undergo pulmonary vein isolation. Additional ablation was at the discretion of the treating electrophysiologist. The small number of patients undergoing an AF ablation procedure is especially relevant as multiple trials have demonstrated a benefit for patients who have a dual diagnosis of AF and heart failure with reduced ejection fraction. Older individuals, women, and those with a history of coronary artery disease were less

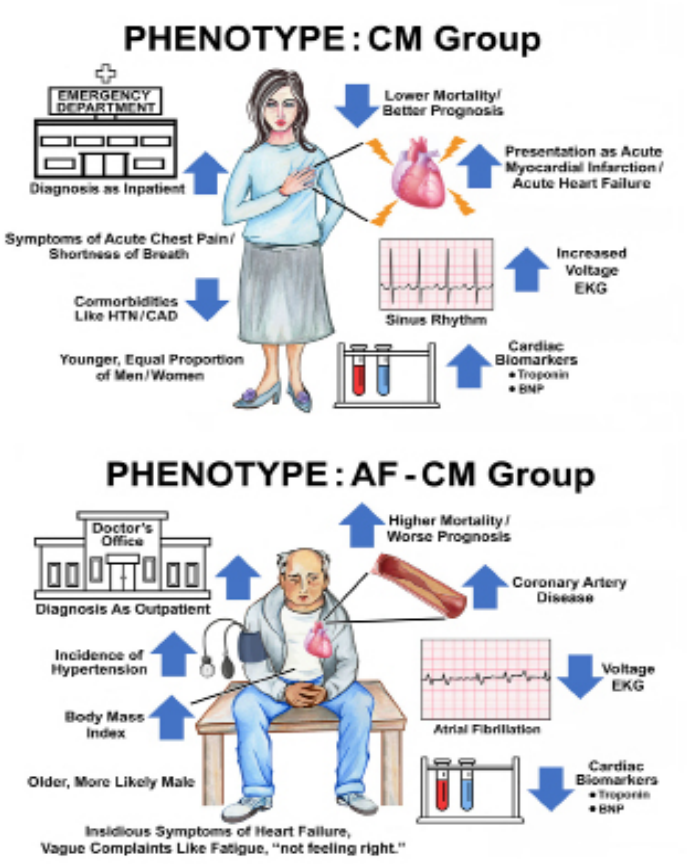

Figure 2: Prototypical patients. The prototypical patients with new-onset heart failure with (AF-CM Phenotype) and without atrial fibrillation (CM Group) are depicted. AF, atrial fibrillation; BNP, brain natriuretic peptide; CAD, coronary artery disease; CM, cardiomyopathy; HTN, hypertension.

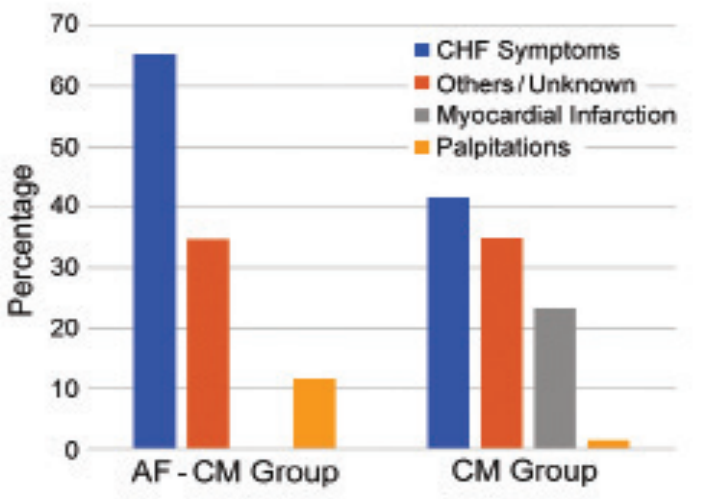

Figure 3: **Presenting symptoms. Patient-reported symptoms at the time of new-onset cardiomyopathy diagnosis. AF-CM Group, group with cardiomyopathy with atrial fibrillation; CHF, congestive heart failure; CM, cardiomyopathy without atrial fibrillation.**

likely to undergo a rhythm control strategy with either cardioversion or an ablation procedure. Those who did undergo cardioversion improved their left ventricular EF more than those who did not, and those who underwent an ablation procedure improved their EF the most. The incidence of mortality on follow-up was extremely high (40.2%) in patients who did not undergo a cardioversion or ablation, significantly lower (17%) in those who underwent a cardioversion, and markedly lower (5.9%) in those who did undergo an AF ablation procedure. This is observational data and should be interpreted with caution as there were significant confounding differences in the treatment groups [Table 4].

Discussion

Inpatient Vs. Outpatient Diagnosis

It appears that AF-CM patients have several distinctive characteristics compared to those with new-onset CM not associated with AF. To the best of our knowledge, these two groups that are commonly encountered in clinical practice have not been compared in the literature. AF-CM patients appear to have a higher likelihood of detection as an outpatient. This may be owing to the slow, insidious progression of vague symptoms like tiredness, fatigue, exertional shortness of breath, and inconspicuous weight gain. As patients in the AF-CM group are older and sicker, their sub-acute CHF or atypical symptoms are more likely to be attributed to old age or other comorbid conditions. Patients in the CM group were much more likely to be diagnosed in the inpatient setting, possibly because their symptoms had a more sudden onset as they had a higher likelihood of presenting with an acute myocardial infarction or acute symptoms of heart failure.

Typical Vs. Atypical Symptoms

A majority of patients with AF-CM did not have typical symptoms of AF (e.g., palpitations). Only 11.7% of patients were listed as having palpitations as one of their complaints. There is some evidence that atypical symptoms of AF (tiredness, fatigue, heart failure) may be associated with a more sinister form of AF [3,4]. Not having the typical symptom of palpitations has also been shown to be associated with a longer duration of preceding AF and with older age [2,6]. In a population-based study, palpitations were reported only by 10.35% of patients >75 years of age [7]. The reason for asymptomatic or atypical symptoms in AF is unknown. There is some evidence that neuronal innervation as evaluated by I-MIBG iodine-123 (meta-iodobenzylguanidine) [8] is decreased in patients with left ventricular systolic dysfunction and may carry a worse prognosis. Furthermore, the perception of typical symptoms of AF is decreased after an AF ablation procedure [9]. Is it possible that damaged or decreased cardio-neural innervation in the AF-CM group leads to a decreased perception of typical symptoms of palpitations while increasing the prevalence of atypical symptoms?

Differences by Sex

Males constituted a higher percentage of the AF-CM group (63.3% men), whereas males and females were almost equally represented in the isolated CM group (49.2% men). Men have been reported to develop AF almost a decade earlier than women [10]. Several studies have also shown that "asymptomatic" AF is more common among males [1-4]. The earlier development of AF with a lack of overt symptoms may predispose men to accrual of subclinical damage over time with eventual presentation as new-onset CM. Further studies are required to investigate this interesting correlation.

Differences on EKG

Voltage on surface EKG was lower in the AF-CM group than the CM group. Low voltage on surface EKG has been associated with a worse prognosis both in patients with left ventricular systolic dysfunction and in patients free of cardiovascular disease [11,12]. In the AF-CM group, lower voltage may be caused by myocardial scar tissue as this group had a higher incidence of coronary artery disease, higher body mass index, or unknown factors.

Differences in Cardiac Biomarkers

Higher troponin levels have been found to be an adverse prognostic marker in heart failure and a wide variety of cardiovascular diseases [13,14]. In our study, peak troponin levels were lower in patients with AF-CM than in patients with isolated CM, but, paradoxically, the mortality for the AF-CM group was higher. One of the reasons for lower levels of troponin in the AF-CM group compared to the CM group may be that the latter more commonly had acute myocardial infarction as the presenting complaint. BNP has also been associated with diagnosis of heart failure [15] and as a prognostic factor, with higher levels portending a worse prognosis [16]. However, BNP levels were also lower in AF-CM patients, despite them presenting more often with CHF symptoms. This may be owing to a slower progression of symptoms in the AF-CM

Table 3: **Real-world treatment characteristics.**

Characteristic	AF-CM group n=196)	CM group (n=197)
Cardiology consult	178 (90.8)	188 (95.4)
Electrophysiology consult	89 (45.4)	63 (32)
Diagnostic cardiac catheterization	79 (40.3)	139 (70.6)
Percutaneous coronary intervention	18 (9.2)	53 (27)
Direct current cardioversion	47 (24)	NA
AF ablation	17 (8.7)	NA

Data presented as n (%).

Table 4: Patient comparison with and without rhythm control intervention within AF-CM group.

Characteristic	No intervention n=132	DCCV n=47	DCCV + ablation n=17	P value
Sex				0.02
Female	57 (43.2%)	12 (25.5%)	3 (17.6%)	
Male	75 (56.8%)	35 (74.5%)	14 (82.4%)	
Age, years	77.61±11.34	66.15±9.34	62.06±7.32	<0.001
Ethnicity				0.78
Hispanic/Latino	1 (0.8%)	0 (0.0%)	0 (0.0%)	
Not Hispanic/Latino	131 (99.2%)	47 (100.0%)	17 (100.0%)	
Tobacco use	78 (59.1%)	30 (63.8%)	11 (64.7%)	0.8
Hypertension	96 (72.7%)	32 (68.1%)	10 (58.8%)	0.46
Diabetes mellitus	44 (33.3%)	12 (25.5%)	3 (17.6%)	0.3
Coronary artery disease	56 (42.4%)	6 (12.8%)	4 (23.5%)	<0.001
Death	53 (40.2%)	8 (17.0%)	1 (5.9%)	<0.001
Baseline LVEF, %	29.62±7.85	29.81±7.54	28.18±6.94	0.74
Follow-up LVEF, %	44.66±12.42	50.46±11.49	56.71±6.89	<0.001

Data presented as n (%) or mean±standard deviation.

group or to a slightly higher body mass index in AF-CM patients as obesity also has been found to attenuate BNP levels [17]. Interestingly, despite lower troponin and BNP levels, which usually confers better prognosis, mortality was significantly higher in the AF-CM group.

Differences in Hospital Readmissions and Mortality

Hospital readmissions were no different between the two groups, though mortality was significantly higher in the AF-CM group. As shown in Figure 4, the mortality curves were still diverging after almost 4 years of follow-up. Our reviewed data revealed low utilization of electrophysiologic expertise, cardioversions, or ablation strategy in the management of patients with AF-CM.

Differences in Patient Management

Some recent studies have found a lower risk of death and other cardiovascular complications associated with specialist care in AF [18,19]. There is also some evidence that heart failure patients treated by cardiologists have better outcomes than patients treated by general practitioners [20,21]. There are limited data about what percentage of patients with AF-CM in the real world are evaluated by a cardiac electrophysiologist or undergo an ablation procedure. This is especially relevant as more evidence is accumulating that an ablation strategy may be beneficial for patients with left ventricular systolic dysfunction and AF [22-25].

Our sample is representative of the practice in the Aurora Health Care system, a large health care system in the Midwest. This may or may not reflect either Midwestern or national patterns. A large proportion of patients in the AF-CM group (n=107 [54.6%]) were never evaluated by a cardiac electrophysiologist, and for most of these patients, no cardioversion or ablation was performed (n=132 [67.3%]). A minority of patients underwent an ablation procedure (17/196 [8.7%]). There appeared to be significant bias in patients who were referred for a rhythm control strategy. Older patients, those with a history of coronary artery disease, and women were less likely to receive either a cardioversion or an ablation procedure. With a history of coronary artery disease, there may be a perception that CM is ischemic and conversion to sinus rhythm would not be helpful. Whether that perception is true is unclear. The lower likelihood of older patients and women receiving these interventions may reflect a systemic bias. These factors need to be evaluated further in larger population studies.

Those who did undergo a rhythm control strategy showed significant improvements in their left ventricular EFs, with the most robust response observed in those undergoing an ablation procedure [Table 4]. Patients who underwent these procedures had markedly low mortality on follow-up compared to the no-intervention cohort, though there were significant confounding factors between these groups that make causal inferences inappropriate.

Limitations

Each patient chart was thoroughly evaluated by a research coordinator to identify a group of new-onset CM patients with a concomitant or antecedent diagnosis of AF (AF-CM group); the CM group patients were also carefully assessed to rule out any contribution of dysrhythmias to CM. Nonetheless, it is possible that some CM group patients had AF that was undiagnosed or not captured in medical documentation or EKG, telemetry, or rhythm strip evaluation. We excluded patients with a cardiovascular implantable electronic device because a significant percentage of them have pre-existing structural heart disease, and also, pacing can confound both patient characteristics and outcomes. Thus, we obtained as uncontaminated a sample as possible so that patients with AF-CM and CM without any dysrhythmias could be compared. But this is a retrospective study with all the limitations inherent in that type of study, including incomplete or inaccurate data and the possibility of selection bias. Echocardiographic reports were utilized for assessing left ventricular EF; sometimes, these can be challenging to read, especially in patients with atrial dysrhythmias. One of the reasons a cut-off of 40% was selected was to minimize the probability of patients with a normal EF being included in the study.

Conclusions

Patients in whom AF either precedes or is concomitant with development of new-onset CM (defined as left ventricular EF ≤40%), appear to have significant differences compared to patients who develop CM without AF. In our study, the AF-CM group was older and more likely to be male; had more comorbidities, lower voltage on surface EKG, and lower cardiac biomarkers; and seemed to have

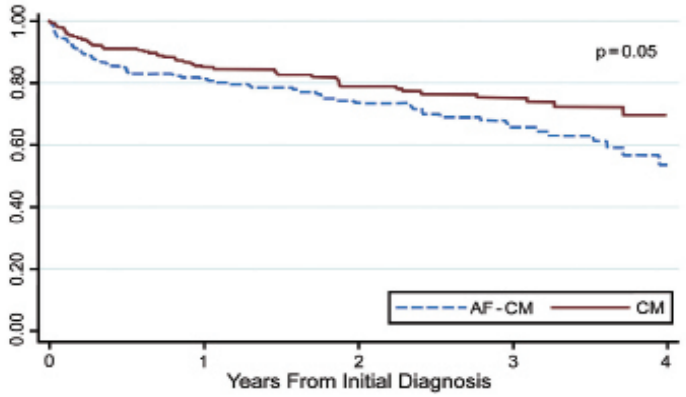

Figure 4: Kaplan-Meier survival estimates. This figure represents survival of patients in cardiomyopathy with atrial fibrillation (AF-CM) and cardiomyopathy without atrial fibrillation (CM) groups.

more insidious onset of symptoms but still a significantly worse prognosis. We hypothesize that AF-CM represents a specific type of cardiomyopathy with a distinctive etiology, presentation, and outcomes. Only a small percentage of patients in the AF-CM group underwent cardioversion and a smaller percentage yet underwent an ablation procedure, but those who did fared remarkably better than those who did not receive these interventions. Women, those with a history of coronary artery disease, and older patients were less likely to undergo these interventions. Whether this reflects a systemic bias in referral and treatment needs to be investigated further with larger, population-based studies.

Acknowledgments

The authors are grateful to the Aurora Research Institute for its support, Jennifer Pfaff and Susan Nord of Aurora Cardiovascular and Thoracic Services for editorial preparation of the manuscript, and Brian Miller and Brian Schurrer of Aurora Cardiovascular and Thoracic Services for assistance with the figures. Special thanks to Dr. Roderick Tung at the University of Chicago for his suggestions and input, and the Aurora BayCare Medical Center research interns for data acquisition.

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Hemodynamic Management of Patients with Ejection Fraction < 50% Undergoing Pulmonary Vein Ablation

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Abstract

There is no consensus regarding optimal methodology for blood pressure monitoring in patients with a depressed ejection fraction undergoing catheter ablation for atrial fibrillation. Our goals were to determine if hemodynamic management differences exist during radiofrequency ablation for atrial fibrillation in patients with and without an ejection fraction< 50%, and whether management was influenced by the utilization of invasive arterial blood pressure monitoring. This single-center trial retrospectively compared blood pressure management during catheterablation of atrial fibrillationin all patients with an ejection fraction< 50% over a 2-year span (n=44), and compared to an age-matched cohort with preserved ejection fraction ablated over the same span in time (n=44). Blood pressure was not significantly managed differently between the groups, and did not appear to be influenced by the use of invasive arterial blood pressure monitoring. Hemodynamic management is similar across the spectrum of ejection fraction, regardless of invasive arterial blood pressure monitoring, which challenges the need for invasive arterial blood pressure monitoring during catheter ablation of atrial fibrillationin left ventricular systolic dysfunction.

Introduction

It has been over 15 years since the early description of catheter ablation (CA) outcomes for atrial fibrillation (AF) in patients with left ventricular systolic dysfunction (LVSD) [1]. Subsequently, the results of multiple studies [2-7], and most recently the Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction (CAMERA-MRI) [8], Catheter Ablation for Atrial Fibrillation with Heart Failure (CASTLE-AF) [9] and Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients with Atrial Fibrillation (CABANA)[10] have suggested efficacy of catheter ablation (CA)for achieving normal sinus rhythm in patients with AF and LVSD. None of these studies, however, described the hemodynamic management during the CA process. Also, current an esthesia recommendations and Heart Rhythm Society guidelines are vagueregarding the subject of optimal methodology for blood pressure monitoring in LVSD during CA for AF[11-13].We sought to determine if significant blood pressure management differences exist between patients with and without significant LVSD undergoing CA of AF, and whether management was influenced by the use of invasive arterial blood pressure monitoring (IABP).

Key Words

Ablation, Atrial fibrillation, Left ventricular systolic dysfunction, Tolerance

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Materials and Methods

All patients with an EF< 50% undergoing CA for AF over a 2-year span were included in the retrospective analysis. An age-matched cohort with preserved EF (> 50%) also having CA for AF during the same timeframe was included for comparison [Table 1].The study was approved by the University of Kentucky institutional review board. Pre-procedure, there was no discontinuation of guideline-directed or advanced medical therapies for heart failure (including continuous milrinone). Cessation of anti-arrhythmic drug therapy 5 days prior occurred at the discretion of the attending electrophysiologist.

All CA procedures were performed after informed consent was obtained, and under general anesthesia. The choice of inhaled anesthetic (desflurane, isoflurane, sevoflurane) and paralytic agent (rocuronium, succinylcholine, etomidate) was determined by the attending anesthesiologist. Otherwise, propofol(150 mg) or dexmedetomidine (1 mcg/kg), lidocaine (50 mg) and fentanyl (100 mcg) single boluses were also dosed at induction. Venous vascular access was obtained at all sites with ultrasound guidance. All patients were also monitored with an indwelling intracardiac echocardiography (ICE) catheter throughout the CA. The method of blood pressure monitoring, invasive arterial blood pressure (IABP) via a radial line versus a non-invasive cuff, was also determined by anesthesia services. Vasopressor (VP) agents were given for a 20% drop in mean arterial pressure (MAP) from baseline, or to maintain MAP > 60 mmHg. VP dosing was charted at time of occurrence. Choice of VP titration, continuous drip (phenylephrine 0.1-0.25 mcg/min or norepinephrine 2-4 mcg/min) and/or bolus (ephedrine 5 mg, phenylephrine 100-200 mcg, and/or vasopressin 1

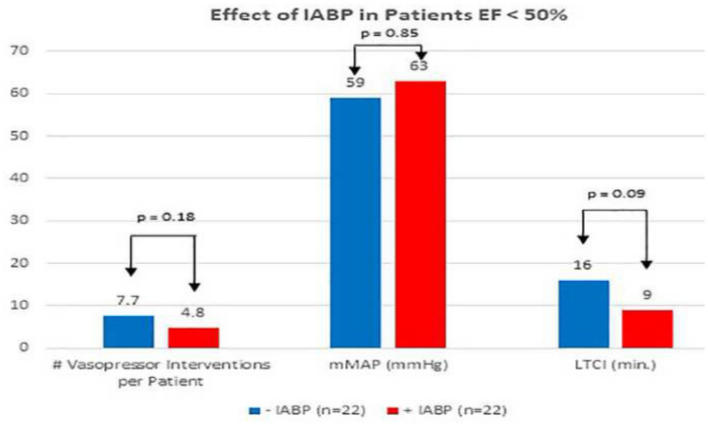

Figure 1: Effect of IABP in patients EF < 50%

unit) was determined by the attending physician/nurse anesthetist as well. Intra-operative up-titration of milrinoneoccurred at the discretion of the attending electrophysiologist. Vital signs were charted at least every 5 minutes. All patients received a Foley catheter to monitor urinary output.

Radiofrequency CA was accomplished with a 3.5 mm irrigated tip catheter. This consisted of a wide circumferential isolation of all pulmonary veins (left veins first followed by the right), then posterior wall isolation for patients with persistent AF only, and ablation of resultant or inducible atrial tachyarrhythmias in all patients. An intra-cardiac echocardiography catheter provided continuous monitoring capabilities to address the presence of a pericardial effusion when needed. An isoproterenol drip at 10 mcg/min was used during the post-ablation induction process. Single doses of protamine 100 mg and furosemide 60 mg were given intravenously once the study was completed. All access sheaths were then removed. Hemostasis was obtained via direct manual compression for an internal jugular venous sheath, and a purse-string stitch with manual compression at both groins. The endo-tracheal tube was removed at study completion in the procedure room. Chest radiography(CXR) was ordered post-procedure by advanced practice providers to rule out pneumothorax, and for other clinical reasons on an individual basis.

Patients were recovered on a telemetry unit with planned discharge home the next day. Near term follow-up consisted of a 1-week post procedure phone call and 1-month office visit.

Data Analysis

Specified data endpoints included procedure duration, percent continuous IABP and VP utilization, number of VP interventions per patient, time of VP intervention, time to first VP intervention, minimum MAP (mMAP), average procedural urinary output > 100 ml/hour, length of stay, 30-day re-hospitalization, and longest time of continuous intervention (LTCI). A VP intervention was an instance of VP bolus in time or initiation/titration up or down of a VP drip. LTCI was defined as the longest time of VP bolus and/or drip titration before a 5 minute charting gap not requiring an intervention was reached. The effect of IABP monitoring presence on number of interventions, mMAP, and LTCI in the EF < 50% groups was also studied.

Statistical Analysis

Statistical analysis included student's t-test for comparison of unpaired means, and Fisher's exact for comparison of continuous categorical variables. A p-value < 0.05 was considered statistically significant.

Results

All patients had successful completion of the intended ablation. There were no incidences of pericardial effusion or complications at the vascular access sites. Additionally, ablation of induced or converted rhythms (atrial flutter, atrial tachycardia, and typical atrio-ventricular nodal reentry tachycardia) occurred and were most common in the EF 7lt; 40% group; 70% (16/23), but not significantly more than the EF 40-49%; 33% (7/21) or EF > 50%; 34% (15/44) groups. [Table 2] displays the results for the specified study endpoints. Other than IABP utilization there were no significant differences among the study groups. The presence of IABP monitoring [Figure 1] also did not significantly influence the number of VP interventions, mMAP, or LTCI. Use of a vasopressor drip [Table 3] was not different amongst all groups. Its use significantly lessened the number of VP interventions only within the EF 40-49% group, and had no significant impact otherwise on mMAP or LTCI.

[Figure 2] shows the number of VP interventions with respect to time during the ablation procedure. There appeared 3 distinct periods of increased VP intervention, 0-95 minutes, 96-125 minutes, and 126-200 minutes. The most interventions in a single patient within a 5-minute charting period was a single instance of 4, followed by 2 instances of 3. These all occurred in patients with EF > 50% and no IABP monitoring. Average hourly urinary output was > 100 ml/hour during the procedure in 95% (42/44) of EF > 50%, 81% (17/21) of EF 40-49%, and 87%

Table 1: Baseline Characteristics at Procedure Initiation

Group	n	% male	Age (y)	% Diuretic	% Anti-HTN	% DM or PN	% NSR	MAP (mmHg)	Mean HR (bpm)
EF ≥ 50%	44	66 (29/44)	62	25 (11/44)	80 (35/44)	25 (11/44)	59 (26/44)	99 +/- 18	82 +/- 25
EF < 50%	44	80 (35/44)	60	64 (28/44)	95 (42/44)	32 (14/44)	45 (20/44)	94 +/- 17	83 +/- 18
EF 40-49%	21	62 (13/21)	63†	33 (7/21)	90 (19/21)	43 (9/21)	38 (8/21)	99 +/- 17	86 +/- 18
EF < 40%	23	96 (22/23)	57†	91 (21/23)	100 (23/23)	22 (5/23)	52 (12/23)	90 +/- 16	80 +/- 19
EF 31-39%	6	100 (6/6)	56	100 (6/6)	100 (6/6)	0 (0/6)	33 (2/6)	85 +/- 12	81 +/- 25
EF 21-30%	10	90 (9/10)	48	80 (8/10)	100 (10/10)	40 (4/10)	70 (7/10)	87 +/- 13	76 +/- 20
EF ≤ 20%	7	100 (7/7)	63	100 (7/7)	100 (7/7)	14 (1/7)	42 (3/7)	100 +/- 16	84 +/- 11

DM = diabetes mellitus, HR = mean heart rate, HTN = hypertension, MAP = mean arterial pressure, NSR = normal sinus rhythm, PN = peripheral neuropathy

Table 2: Specified Procedure Outcomes

Group	Procedure Time (min.)	% IABP	% Needing VP	% VP Drip Use	Total # Interventions (Int. per Patient)	Time to First Int. (min.)	mMAP (mmHg)	Mean LTCI (min.)
EF ≥ 50%	151	2 (1/44)* + †	80 (35/44)	29 (10/35)	221 (5)	34	58	12
EF < 50%	156	50 (22/44)*	95 (42/44)	50 (21/42)	276 (6)	32	61	13
EF 40-49%	157	24 (5/21)+	95 (20/21)	70 (14/20)	165 (8)	27	61	17
EF <40%	156	74 (17/23)†	96(22/23)	32 (7/22)	111 (5)	35	61	9
EF 31-39%	133	67 (4/6)	83 (5/6)	20 (1/5)	41 (7)	31	59	9
EF 21-30%	167	70 (7/10)	100 (10/10)	40 (4/10)	51 (5)	35	61	7
EF ≤ 20%	159	86 (6/7)	100 (7/7)	29 (2/7)	19 (3)	38	62	13

EF = ejection fraction, IABP = invasive arterial blood pressure, Int. = Intervention, LTCI = longest time of continuous intervention, mMAP = minimal mean arterial pressure, VP = vasopressor

(20/23) of EF < 40% groups (p=NS). All patients were extubated and had complete discontinuation of VP drips before leaving the procedure room. All patients except one in the EF 40-49%group (96%) were recovered and monitored on a telemetry unit. The single exception had transient complete heart block post ablation that resolved with cessation of beta blockade by the next morning after intensive care unit observation. Three EF < 40% patients (13%)required post-op intervention for respiratory status before discharge the following day. One was for subjective shortness of breath, mild vascular congestion on CXR, and decreased oxygen saturation.

Management consisted of brief bi-level positive airway pressure and a single intravenous dose of furosemide. Two patients had shortness of breath, mild vascular congestion without edema on CXR, and received a single dose of intravenous furosemide.

Length of stay was 1.3± 1.8 days in the EF > 50% group, 1.1± 0.5 days in the EF 40-49%group and 1 day in the EF < 40% group (p=NS). A single patient with EF > 50% (2%) had a pre-existing pacemaker system issue that required management and a 13-day stay, and one EF 40-49% patient (5%) had nausea and vomiting due to suboxone withdrawal prompting a 3-day stay. Three patients each in the EF >50% (7%) and < 50% (7%) groups were re-hospitalized within 30 days. One in each group was for infection, one also in the EF 40-49% group for astroke event presenting as confusion/dizziness (positive head CT scan), and one in the EF < 40% group for hypokalemia. One patient in the EF < 40% group had abdominal discomfort with shortness of breath and was discharged from the emergency room following a brisk diuresis 4 days after their procedure.

Discussion

In addition to efficacy, understanding safety is critical for wider acceptance of CA for AF in LVSD by the general electrophysiology community. To date, there is no study of CA for AF describing the hemodynamic management and optimal methodology for blood pressure monitoring, particularly in those with significant LVSD. This study showed the hemodynamic management of a radiofrequency CA procedure in a cohort of patents with EF < 50%under general anesthesia to be similar to that of a preserved EF population. There was no significant difference between groups for the specified hemodynamic endpoints. IABP monitoring did not significantly affect the need for VP interventions within EF 40-49% and EF <40% groups and when they were compared to an EF > 50% group. Taken together our data are also suggestive of the safety of non-invasive blood pressure monitoring for VP titration in the LVSD population. This is particularly relevant to the overall safety of the process given that vascular issues are the most frequently reported complication of CA for AF, albeit occurring in only approximately 2% of cases[14]. The rate of major complication from radial artery access is fortunately significantly less [15]. A resultant compartment syndrome, however, can be very devastating. The femoral arterymay be also utilized for IABP monitoring as well for CA of AF, and was not used in this study. Femoral access can contribute to the incidence of pseudoaneurysm and AV fistula[16]. These complications can be eliminated or minimized with use of non-invasive blood pressure cuffs.

Three distinct periods of increased blood pressure intervention were identified during the CA process in this study, each likely with a different physiologic cause. The first period began shortly after anesthesia induction and was likely due to a combination of negative inotropy, attenuated sympathetic reflex, pre-load reduction, and decreased vascular resistance [19-20]. The second occurred when programmed stimulation, linear lines for posterior wall isolation, or rhythm conversion to atrial flutter were most common, likely contributing to transient increased VP needs following pulmonary vein isolation [21-22]. VP interventions were more prominently seen in the EF 40-49% group in this timeframe. Patients with heart failure mid-range EF (HFmrEF) have been shown to have a large prevalence, upwards of 76%, of diastolic dysfunction based on echo cardiographic findings [23]. Our mid-range EF group was not categorized HFmrEF

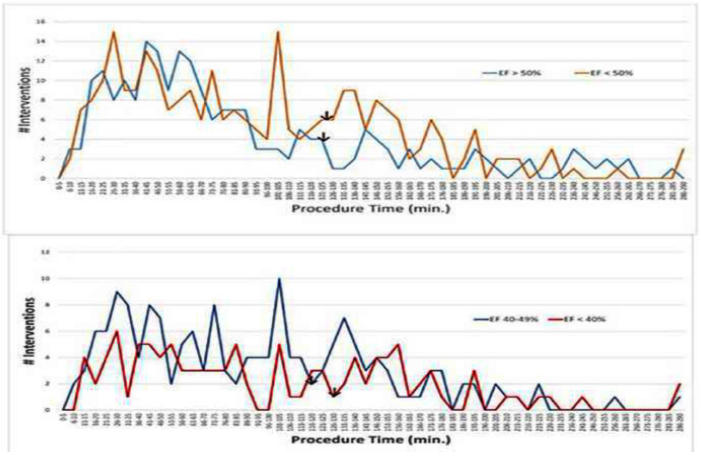

Figure 2: Specified Procedure Outcomes.

EF = ejection fraction, IABP = invasive arterial blood pressure, Int. = Intervention, LTCI = longest time of continuous intervention, mMAP = minimal mean arterial pressure, VP = vasopressor

simply because we did not seek to establish the European Society of Cardiology diagnostic criterion in this group [24]. There does not appear to be a consensus at this point whether this EF range represents a new category of heart failure [25]. However, the authors separately analyzed this group to see if there were any hemodynamic differences detectable in our process. It seems reasonable to assume that our EF 40-49% group may have had some incidence of diastolic dysfunction to explain the hemodynamic reaction during this timeframe. The third period of escalation correlated with initiation of isoproterenol. The vasodilatory effects of its beta-2 receptor actions may outweigh the beta-1 receptor agonist increase in heart rate and contractility, thus causing a drop in blood pressure [26]. Each of the groups showed similar responses during the active isoproterenol infusion and washout phase. Regardless, the physiologic effects and the corrective actions in all 3 time periods, were similarly experienced and efficiently managed in all groups regardless of IABP use.

Overcorrection of hypotension from VP interventions did not appear to be an issue as only one instance of intravenous beta blockade was dosed for this reason in a patient receiving VP boluses in the 88 patient study population. Otherwise, VP drips were titrated down without issue to achieve the desired MAP.

Limitations

This study represents the non-randomized experience at a single facility with modest sample size, using general anesthesia, and radiofrequency energy. There were multiple anesthesia practitioners, who were not dedicated cardiac specialists. As such, this likely provided more variability in management choices, including the use of IABP monitoring. Our results are also not necessarily applicable to an alternate anesthesia strategy. Regardless, the patients were safely attended within this construct resulting in similar management whether or not IABP monitoring occurred.

Time to first VP intervention, number of interventions, mMAP, average hourly urinary output > 100 ml/hr, and LTCI were chosen as measures of hemodynamic tolerance by the investigators, and to our knowledge have not been described before for this purpose. Their validity may be questioned. These data endpoints, however, seemed a reasonable means to describe blood pressure management within our process.

Table 3: Effect of Vasopressor Drip Presence on Intervention Management

Group	# Interventions (Int. per Patient)		p value	Mean LTCI (min.)		p value	mMAP (mmHg)		p value
	- Drip	+ Drip		- Drip	+ Drip		- Drip	+ Drip	
EF > 50% (n=35)	133 (5.3)	88 (8.8)	0.26	11	16	0.20	58	59	0.65
EF < 50% (n=42)	175 (8.3)	101 (4.8)	0.13	12	13	0.64	60	61	0.50
EF 40-49% (n=20)	96 (16)	69 (4.9)	0.03	20	16	0.25	58	61	0.47
EF < 40% (n=22)	79 (15)	32 (4.6)	0.78	10	7	0.26	60	62	0.60

CA = catheter ablation, ICD = implantable cardioverter defibrillator, Q = every

There were no incidences of tamponade and access site bleeding in this study. This was likely due to operator experience, ultrasound guidance and use of ICE for venous and transseptal access. As such it is unclear from our results whether IABP would have been superior to a non-invasive cuff for navigating such adverse events in those not as experienced or utilizing ICE and ultrasound for access.

Conclusions

Hemodynamic management of CA for AF appears similarly experienced in patients across the spectrum of EF. Blood pressure interventions were handled in a timely fashion with and without IABP monitoring. The need for increased VP intervention in the 3 groups in 3 distinct time periods was universal, and not influenced by the presence of IABP monitoring. Based on our findings, vascular complications can be further minimized with use of non-invasive cuffs for blood pressure monitoring without sacrificing safety in the LVSD population in our process. CA for AF, even in patients with Class IV chronic systolic heart failure on ambulatory inotropic therapy, appears to be safe in the hands of experienced practitioners. Further study will be required to further address safety and efficacy in this group.

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Catheter Ablation for Persistent Atrial Fibrillation in Class IV Systolic Heart Failure: A Single-Center Case Series

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Abstract

Questions remain as to how aggressively catheter ablation for atrial fibrillation may be applied to patients with advanced systolic congestive heart failure, owing to a historic under-representation in multicenter clinical ablation trials. We sought to describe the experience of catheter ablation for persistent atrial fibrillation in Class IV systolic heart failure patients at our institution. All Class IV systolic heart failure patients (left ventricular assist device patients excluded) between 2017 and 2020 referred for radiofrequency ablation were included. Out of 10 patients, 7 agreed to proceed, had restoration of normal sinus rhythm upon completion of the catheter ablation procedure, and of which five (71%) remain in normal rhythm at a mean follow-up of 23 months. Catheter ablation for atrial fibrillation in patients with Class IV chronic systolic heart failure, even on advanced heart failure therapies, is feasible, and can improve heart failure status with maintenance of NSR.

Introduction

Despite multiple observational and recent clinical trials supporting the efficacy of catheter ablation (CA) of atrial fibrillation (AF) for restoration of normal sinus rhythm (NSR), patients with Class IV systolic congestive heart failure remain under-represented [1-16]. Questions therefore remain regarding how aggressively ablation may be brought to bear in left ventricular systolic dysfunction (LVSD) and which operators should perform it? Additionally, there has been no prior report in the literature describing ablation in a cohort consisting only of Class IV systolic congestive heart failure (CHF) patients, including those on advanced therapies such as continuous ambulatory milrinone. We sought to address these issues by describing our experience for AF ablation in such patients.

Materials and Methods

We included all patients referred and who agreed to CA of persistent AF with Class IV systolic heart failure at our institution between 2017 and 2020 in this case series. Patients with a left ventricular assist device (LVAD) were excluded. Records were reviewed for history, medication management, electrophysiologic study results, with particular attention to clinical course after CA. [Table 1] summarizes the cohort characteristics and ablations performed. All had failed previous trials of amiodarone and cardioversion for rhythm control, and were on guideline-directed medical therapy (GDMT) for heart failure management. Informed consent was obtained on all patients prior to their CA procedure, and the study was approved by the University of Kentucky institutional review board.

All electrophysiologic studies (EPS) were performed as outpatient under general anesthesia with continuous invasive radial arterial blood pressure monitoring, and no discontinuation of GDMT, amiodarone, or inotropic agents. Procedural expectations were addressed between anesthesia and electrophysiology attendings with the patient in a shared discussion. Vasopressor (VP) agents were directed by anesthesia services, however upward titration of milrinone was done at the discretion of the attending electrophysiologist. Three-dimensional mapping of the left atrium was performed at the beginning of each procedure. Radiofrequency ablation was accomplished with a 3.5 mm irrigated contact force ablation catheter, a double trans-septal technique, and by personnel with a 2000+ experience with CA for AF. An intra-cardiac echocardiography catheter remained deployed throughout. Ablation parameters for WACA and posterior wall isolation (PWI) have previously been described [14]. CA consisted of a step-wise approach:

1) Wide area circumferential ablation (WACA) of the pulmonary veins, carinal lines allowed

2) Posterior wall isolation (PWI) only if remaining in AF after WACA with roof and inferior wall lines

3) Ablation of spontaneously converted rhythms at any step in the process. Increased power titration up to 40 Watts allowed for atrial flutter

Key Words

Atrial Fibrillation, Catheter Ablation, Heart Failure

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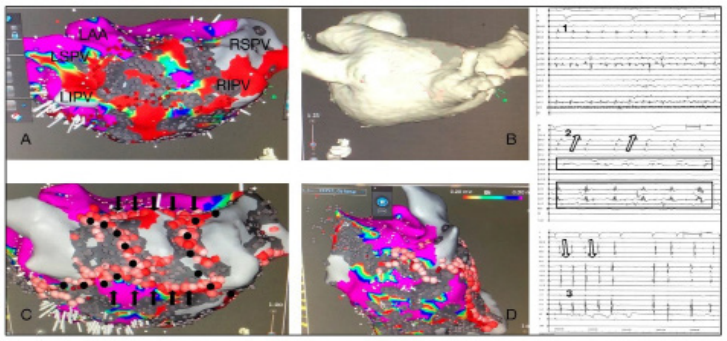

Figure 1 Case 1: **Panel A: The initial bipolar voltage map (posterior left atrium) in atrial fibrillation (AF) demonstrating generous low voltage (threshold 0.2 mV) and scar (threshold 0.03 mV). Panel B: Posterior left atrium CT scan. Panel C: Path of WACA (black dots), and roof/inferior wall ablation (black arrows). Panel D: Caudal left lateral left atrium showing voltage map and posterior mitral line ablation lesion set (circle) consolidating an area of scar and low voltage. Panel 1: Baseline AF, Panel 2: clock-wise peri-mitral flutter during posterior wall isolation; arrow shows distal to proximal coronary sinus activation, and boxes prolonged fractionated signals within the posterior wall measured from a 20-pole circular catheter. Panel 3: Typical counter-clockwise (proximal to distal coronary sinus activation) right atrial flutter terminates with isthmus ablation.**

LAA=left atrial appendage, LIPV=left inferior pulmonary vein, LSPV=left superior pulmonary vein, RIPV=right inferior pulmonary vein, RSPV=right superior pulmonary vein.

4) Cardioversion if remaining in AF after WACA and PWI

5) Ablation of inducible focal or reentrant rhythms post initial ablation both off and on 10 mcg/min isoproterenol infusion with atrial programmed stimulation, and atrial burst pacing from a cycle length of 300 ms down to 200 ms.

All reentrant rhythms were ablated with a combination of activation mapping with entrainment confirmation. In instances of multiple critical isthmus targets being available, the chosen ablation path was individualized after mapping in each patient. Bi-directional block was confirmed with differential pacing across the ablation lines. Each patient received a single bolus of furosemide 60 mg intravenously at study completion. Post-CA plans were for a telemetry unit recovery and discharge the following day. All received amiodarone 200 mg daily on discharge. Electrophysiology (EP) follow-up was coordinated with the heart failure service and consisted of a 1-week phone call, 1-month EP visit, and 3-month EP/heart failure follow-up initially. Further follow-up consisted of every 6-month visits, or phone check allowing for difficulties in distant travel. Adjustment of inotropic therapy or GDMT occurred at the discretion of the heart failure service.

Specified data endpoints included procedure duration, VP utilization, minimum MAP (mMAP), average procedural urinary output > 100 ml/hour, length of stay, 30-day re-hospitalization, and longest time of continuous intervention (LTCI). A VP intervention was an instance of VP bolus in time or initiation/titration up or down of a VP drip. LTCI was defined as the longest time period of VP bolus and/or drip titration before a 5 minute charting gap not requiring an intervention was reached.

Results

Case 1 (May 2017)

A 61-year-old male with prior history of paroxysmal AF, previously enrolled in the DREAM-HF mesenchymal cell study [17] for Class III chronic systolic heart failure, and on chronic daily amiodarone self-referred early to EP clinic with severe fatigue, resting shortness of breath, and increased ankle swelling consistent worsening to Class IV status. Interrogation of his implantable cardiac defibrillator (ICD) showed AF that had been persistent for 3 months. Hypotension did not allow further titration of rate controlling medications, and cardioversion did not maintain NSR. CA for AF was scheduled. Initial left atrial voltage mapping in AF showed diffuse areas of low/absent voltage suggesting scar ([Figure 1], panel A). WACA had no effect on AF. During PWI the AF organized into a clockwise peri-mitral flutter with prolonged conduction into the posterior wall before isolation ([Figure 1], panel 2). A posterior mitral ablation line ([Figure 1], panel D) converted the rhythm to a typical counter-clockwise right atrial flutter. A cavo-tricuspid isthmus (CTI) ablation converted flutter

Table 1: **Patient Characteristics.**

Case	Sex (M/F)	Age (y)	Cardiomyopathy Type/Comorbidities	EF/CO(L/min)/CI(L/min/m²)	LA Volume (ml/m²)	Duration of Continuous AF at Ablation	Pre-procedure advanced CHF Rx	Ablation(s)	Follow-up
1	M	61	Ischemic/DM, HTN, ICD, OSA	10%/NA	68	3 months	GDMT, DREAM HF Study	WACA→PWI→LAF→PML→RAF→CTI→NSR	42 months
2	M	43	Non-ischemic/DM	20%/2.68/1.3	42-48	6 years	GDMT, Milrinone 0.25mcg/kg/min	WACA→PWI→CV→NSR	31 months
3	M	60	Non-ischemic/HTN, ICD	12%/3.62/1.5	35-41	4 months	GDMT, Milrinone 0.25 mcg/kg/min	1) WACA→LAF→PML→RAF→CTI→NSR 2) NSR→Re-isolate RSPV	29 months
4	M	66	Ischemic/DM, HTN, ICD	30%/2.96/1.4	>48	4 months	GDMT, Milrinone 0.125 mcg/kg/min	WACA→LAF1→PWI→LAF2→AML→NSR	5 months (deceased)
5	M	76	Ischemic/HTN, ICD	10%/3.20/1.5	35-41	18 months	GDMT, Milrinone 0.375 mcg/kg/min	WACA→PWI→CV→NSR Inducible AT→NSR	5 months(deceased)
6	F	77	Non-ischemic/DM, HTN, ICD	20%/2.35/1.2	>48	7 years	GDMT, Milrinone 0.25 mcg/kg/min	WACA→PWI→LAF→PML→"slow" AF→CV→NSR	12 months
7	M	60	Ischemic/DM, HTN, ICD	40%/4.66/2.3	<35	4 months	GDMT	WACA→CTI→NSR	5 months

AF=atrial fibrillation, AML= anterior mitral line, AT= atrial tachycardia, CHF=congestive heart failure, CI=cardiac index, CO=cardiac output, CTI=cavo-tricuspid isthmus, CV=cardioversion, DM=diabetes mellitus, EF=ejection fraction, F-female, GDMT=guideline-directed medical therapy, HTN=hypertension, ICD=implantable cardiac defibrillator, LA=left atrium, LAF=left atrial flutter, M=male, NA=not applicable, NSR=normal sinus rhythm, OSA=obstructive sleep apnea, PML=posterior mitral line, PWI=posterior wall isolation, RAF=right atrial flutter, RSPV=right superior pulmonary vein, Rx=prescription, WACA=wide area circumferential ablation

Table 2: Post-Ablation Amiodarone Management and Rhythm Surveillance

Case	Amiodarone Management Post-CA	Rhythm Surveillance
1	Discontinued at 3 months	Q6 month in-person and remote ICD monitoring
2	Continued 200 mg daily indefinitely at patient request	In-person/ambulatory monitoring, telephone follow-up Q6 month
3	Discontinued at 3 months	Q6 month in-person and remote ICD monitoring
4	Continued until expiration at 5 months	In-person and remote ICD monitoring
5	Continued until expiration at 5 months	In-person and remote ICD monitoring
6	Discontinued at 3 months	Q6 month in-person and remote ICD monitoring
7	Discontinued at 3 months	Q6 month in-person and remote ICD monitoring

CA = catheter ablation, ICD = implantable cardioverter defibrillator, Q = every

to NSR ([Figure 1], panel 3). Follow-up at 3 months was notable for resolution of resting symptoms and improvement in objective findings without change in medical therapies, save discontinuation of amiodarone. Interrogation of the ICD has been notable for a rare non-sustained atrial tachycardia of a few seconds duration without use of any anti-arrhythmic agent. Follow-up echocardiographic findings are unknown due to blinding from his heart failure research trial.

Case 2 (April 2018)

A 43-year-old male with at least 6 years of long-standing persistent AF was transferred from out of state for advanced heart failure therapy, including work-up for transplant candidacy. Previously, NSR could not be maintained on amiodarone 200 mg daily following loading and despite "numerous" cardioversions. Milrinone was initiated as well as oral anti-coagulation. He was not a candidate for surgical management of severe mitral regurgitation. Initial EP consult suggested an atrio-ventricular nodal ablation with bi-ventricular ICD for AF with rapid response. A second EP consult offered short-term return for CA of AF after discharge. EP study was initially notable for lack of scar/low voltage in the left atrium. He remained in AF despite WACA and PWI. Cardioversion returned NSR. Follow-up echocardiography 3-months later showed an improvement in ejection fraction (EF) to 45-50% with "trace" mitral regurgitation.Milrinone was discontinued. He remains well in NSR, and reluctant to stop amiodarone >2 years later.

Case 3 (June 2018)

A 60-year-old male was referred by the heart failure service for persistent AF with rapid response management, and agreed to CA. Partial ablation around the left pulmonary veins converted AF to a counter-clockwise peri-mitral flutter. WACA was completed ([Figure 2], panel A), and a posterior mitral ablation line ([Figure 2], panel E) converted the rhythm to a CTI counter-clockwise flutter. CTI ablation converted flutter to NSR. Milrinone and amiodarone were discontinued at 3-month follow-up. The EF improved from baseline, yet was significantly depressed (20-25%). A primary prevention ICD was implanted. Near 1-year follow-up from initial CA he had worsened shortness of breath and fatigue. ICD interrogation showed frequent episodes of AF hours to weeks at a time. Milrinone was restarted. Repeat EP study showed an opening in the ablation line around the right superior pulmonary vein that was easily re-isolated ([Figure 2], panels C+D). Bi-directional block remained across the prior flutter lines ([Figure 2], panel G posterior mitral line). Milrinone was discontinued at follow-up due to absence of AF on ICD interrogation and improvement in hall walk test. Repeat echocardiogram 4 months after repeat ablation demonstrated an ejection fraction improvement to 45%. Remote and in-clinic ICD evaluations show maintenance of NSR > 1 year from second ablation.

Case 4 (July 2019)

A 66-year-old male with persistent AF was referred by the heart failure service for management. CA was agreed to be the next best management option. Diffuse posterior wall scarring was noted with initial mapping ([Figure 3], panel A). During WACA, AF converted to an atypical flutter that utilized the posterior wall ([Figure 3], panel C). PWI converted this to a counter-clockwise peri-mitral flutter, and an anterior mitral line terminated the flutter to NSR ([Figure 3], panel D). The CA was otherwise remarkable for brief hypotension early in the procedure that resolved after up-titration of the milrinone. The milrinone rate was returned to the pre-procedure setting before proceeding to recovery. ICD interrogation at the 3-month follow-up showed no arrhythmia events and he had subjective improvement in symptoms. Milrinone was stopped. Subsequent demand remote monitoring initiated by the patient a few days later showed initiation of atrial flutter starting hours after the 3-month follow-up visit ([Figure 3], panel E). Milrinone was restarted shortly thereafter. Elective plans were made for repeat ablation due to persistence of the atypical flutter, however were cancelled due to a spontaneous intra-cranial hemorrhage while on both apixiban and clopidagrel. He convalesced, and neurology service subsequently approved restarting the apixiban only. The patient was re-admitted shortly after with a second spontaneous intra-cranial hemorrhage and expired.

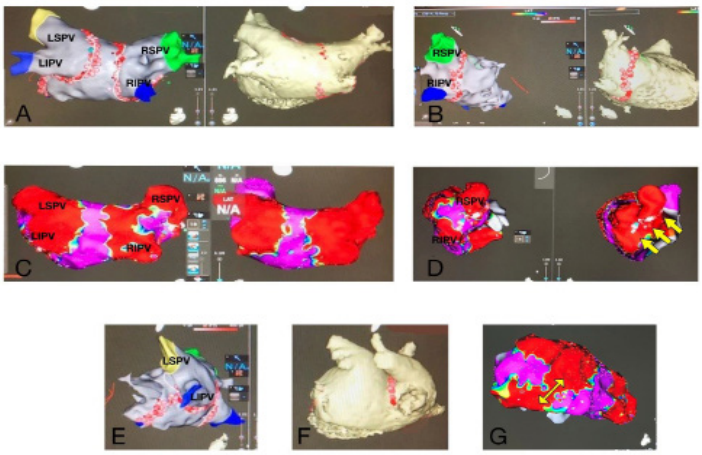

Figure 2 Case 3: Panels: A; Posterior left atrium, B; Right lateral left atrium, E and F; Left lateral left atrium showing ablation and CT anatomy from index procedure. Panels: C; Posterior left atrium and D; Right lateral left atrium showing bipolar voltage maps before (left) and after re-isolation (right). The yellow arrows point to the area of ablation. Panel G: Left lateral voltage map from the repeat ablation displaying the durable posterior mitral ablation line. Note lack of low voltage (threshold 0.2 mV) outside of ablation aspects on all maps.

LIPV=left inferior pulmonary vein, LSPV=left superior pulmonary vein, RIPV=right inferior pulmonary vein, RSPV=right superior pulmonary vein.

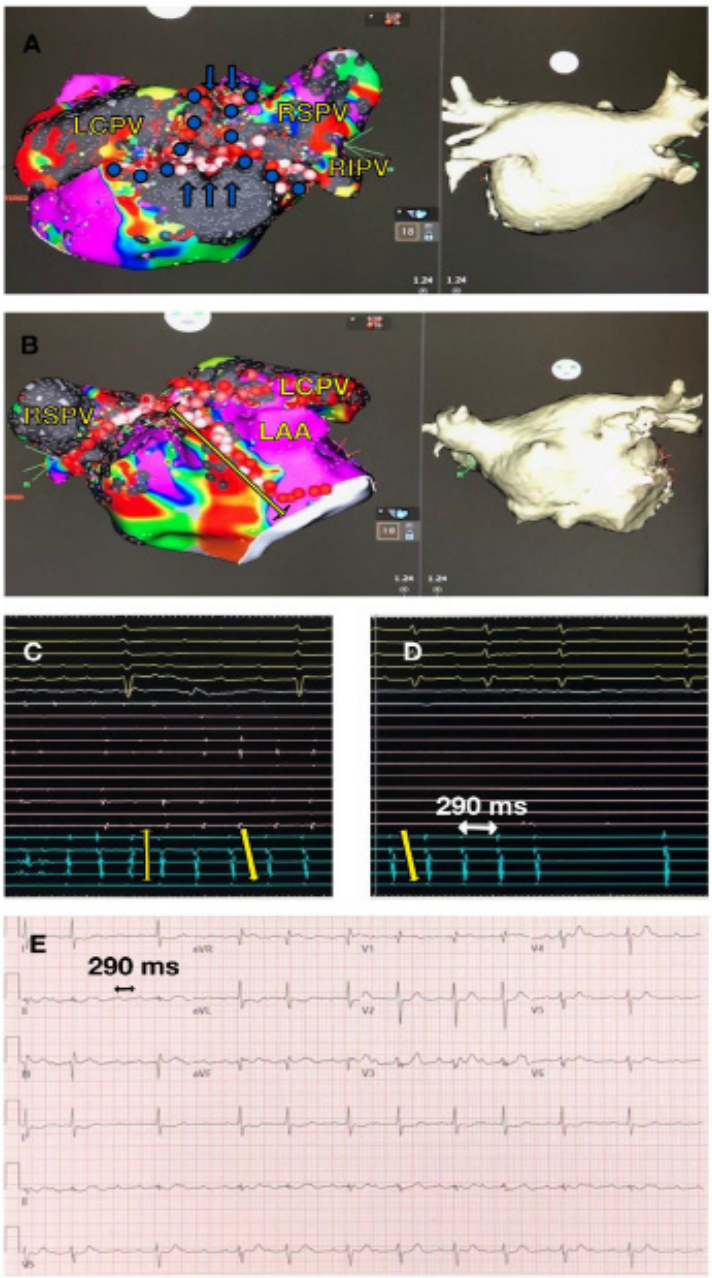

Figure 3 Case 4: **Panel A: Bipolar voltage map and CT scan of posterior left atrium in AF. Highlighted blue dots and arrows represent WACA and roof/inferior wall ablation lines respectively. Note generous dense scar (threshold 0.03 mV) and low voltage (threshold 0.2 mV). Panel B: Bipolar voltage map and anterior mitral ablation line (yellow arrow) with CT anatomy. Panel C: AF converts to organized flutter (vertical and diagonal arrows) that occasionally utilize posterior wall during WACA. Panel D: Counterclockwise peri-mitral flutter only after PWI isolation (pink signals) that terminates to NSR with anterior mitral ablation line. Panel E: 12-lead ECG 4 months post-CA with atypical flutter at same cycle length as peri-mitral flutter at ablation**

LAA=left atrial appendage, LCPV=left common pulmonary vein, RIPV=right inferior pulmonary vein, RSPV=right superior pulmonary vein.

Case 5 (October 2019)

A 76-year-old male with rate-controlled long-standing persistent AF presented to EP clinic with a remarkable interval history of milrinone initiation from the heart failure service. His condition had not improved despite up-titration of the milrinone. Given prior failure to maintain NSR on amiodarone, CA was scheduled after an extensive discussion of the risks and perceived potential benefits. He remained in AF following WACA and PWI. Cardioversion returned NSR. He had a sustained right atrial tachycardia induced that was terminated with ablation at the coronary sinus ostium. Amiodarone was continued post-ablation. At 1-month follow-up his condition had not changed and ICD interrogation showed recurrence of AF 3-weeks after CA. He was successfully cardioverted. Four months later he returned for admission due to a hip fracture following a fall. He appeared in AF with bi-ventricular pacing at lower rate on the 12-lead ECG. He became hypoxic while undergoing hip repair, and was resuscitated from a pulseless electrical arrest. However, he developed persistent cardiogenic shock, was made do-not-resuscitate, and expired after withdrawal of care.

Case 6 (January 2020)

A 77-year-old female with non-ischemic cardiomyopathy and 7 years of long-standing persistent rate-controlled AF was referred by the heart failure service to re-establish ICD management. A detailed rhythm history revealed an EF of 40% at initial discovery of AF, a subsequent pacemaker insertion with atrioventricular nodal ablation, upgrade to a bi-ventricular ICD, and optimization of ICD programming. Worsened symptoms and cardiac function (EF 25%) had prompted ambulatory milrinone. Amiodarone given at initial discovery of the AF did not maintain NSR despite cardioversion. The patient was enthusiastic to proceed with CA given her limited quality of life. Following WACA, PWI converted the AF to a counter-clockwise peri-mitral flutter ([Figure 4], panel D). A posterior-inferior mitral ablation line converted flutter to "slow" AF ([Figure 4], panel E). AF was cardioverted to NSR. The biventricular ICD was reprogrammed for AV optimization ([Figure 4], panel F) based on the near and far-field signals on the diagnostic coronary sinus catheter. A small right groin hematoma was noted at CA completion. It remained stable, and she was observed in the intensive care unit overnight. She was managed with an intravenous saline bolus for a brief drop in blood pressure. Discharge to home occurred later the next day with a stable blood count (Hct 31.3), renal function comparable to baseline (1.97 mg/dL versus 1.86 mg/dL), blood pressure 99/58 (111/50 pre-op) and serial hallway ambulation at baseline. Call-back 5 days later found her to be feeling "good". She was readmitted 2 weeks after ablation with generalized fatigue, "hypotension" (105/61 mm Hg), and an elevated white blood cell count [15]. Hematocrit was 33.5, creatinine 2.87 mg/dL, NT-proBNP level 1619 pg/mL (normal 0-1700 pg/mL) and urinalysis positive for bacteria. 12-lead ECG showed AV sequential pacing and capture ([Figure 4], panel G). There was no pericardial effusion or access site bleeding. Conservative management with intravenous fluids and antibiotics improved her symptoms. Creatinine dropped to 1.67 mg/dL and she was discharged after 3 days. Four months post ablation the milrinone was discontinued after having been on it for 26 months. Seven months from ablation she remained in normal rhythm with 0% AF burden on ICD interrogation. Subjectively she feels "like a new person". Her EF improved to 29%.

Case 7 (July 2020)

A 60 year-old male with chronic ICM, and aortic valve replacement X 2 had EF improved to 40% following insertion of a biventricular ICD in 2019. Over 9 weeks time beginning in April 2020 he was

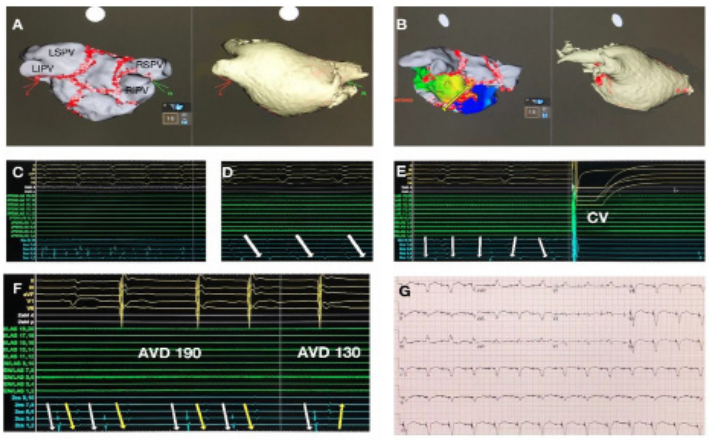

Figure 4 Case 6: **Panel A: Posterior left atrium; 3-dimensional map and CT scan with WACA, PWI, mitral lesion sets. Panel B: Postero-lateral left atrium with activation during counter-clockwise peri-mitral flutter. The yellow arrow shows the chosen ablation path through an area of "early-meets-late" slowed conduction. Panel C: AF remains after WACA (green 20-pole circular catheter signals in left pulmonary veins, blue signals decapolar coronary sinus catheter). Panel D: Counter-clockwise peri-mitral flutter with proximal-to-distal coronary sinus activation following PWI. Panel E: "Slow" AF after mitral ablation line cardioverts to NSR. Panel F: Post cardioversion DDDR 80 bpm sensed AV delay 190 ms. There is insufficient ventricular paced pre-excitation (proximal-to-distal far-field left ventricular signals on coronary sinus catheter, yellow arrows) initially, remedied with shortening the sensed AV delay (distal-to-proximal far-field left ventricular signals on coronary sinus catheter). White arrows represent near-field atrial activity. Panel G: 12-lead ECG at 2 weeks follow-up showing AV sequential capture.**

AVD=atrio-ventricular delay, CV=cardioversion, LIPV=left inferior pulmonary vein, LSPV=left superior pulmonary vein, RIPV=right inferior pulmonary vein, RSPV=right superior pulmonary vein

admitted five times for heart failure in the setting of rate controlled persistent AF and typical atrial flutter that had begun in March. He could not maintain NSR despite amiodarone and cardioversion. Right heart catheterization did not support the initiation of ambulatory inotropic therapy. Renal function was notable for a creatinine of 1.14 mg/dL at the beginning of April 2020 that worsened to 3.35 mg/dL by the end of June. Electrophysiology service was agreeable to urgent ablation. WACA and then CTI ablation returned NSR. He remained hospitalized for 8 days to manage pre-procedure fluid overload. Over the course of admission renal function did not worsen and creatinine improved to 2.95 mg/dL by discharge. He has remained arrhythmia free, off amiodarone, to date and has not required titration of GDMT or been re-admitted.

Cohort Case Summary

Mean duration of persistent AF entering the CA procedure was 27 ± 35 months. NSR was returned spontaneously with ablation in 4/7 (57%) of the patients. All pulmonary veins were successfully isolated. Bi-directional block was achieved at initial ablation in all atrial flutter instances with endocardial ablation only. Mean procedure time for initial ablations was 175 ± 24 minutes. Six out of 7 patients (86%) required a VP during CA. Case 5 required no VP support. The procedure mMAP was 62 ± 8 mmHg, LTCI 9 ± 2 minutes, and average number of VP interventions per patient 4 ± 2. VP agents were discontinued before leaving the procedure room for all patients. Urinary output average > 100ml/hour was present in each case. Serum creatinine was 1.75 ± 0.80 mg/dL pre-procedure versus 1.77 ± 0.84 md/dL post-procedure (p=NS). Six out of 7 (86%) recovered on the telemetry unit, and all but Case 7 were discharged home the next day. None of the patients required bi-level positive airway pressure during their recovery on the telemetry unit. Follow-up has been 23 ± 15 months for the surviving patients.

[Table II] summarizes the management of amiodarone and rhythm surveillance post-CA.

Three patients did not to proceed with CA. One 25-year-old with persistent AF and non-ischemic cardiomyopathy wished to continue milrinone and no other intervention. A 45-year-old with chronic non-ischemic cardiomyopathy and 5 years of long-standing persistent AF on milrinone, desired advancement to a left ventricular assist device as a bridge to possible cardiac transplantation. The third, a 63-year-old male with chronic non-ischemic cardiomyopathy, 7 years of long-standing persistent AF and left bundle branch block, was hospitalized for LVAD and transplant work-up. A cardioversion returned NSR, however the heart failure service did not accept electrophysiology recommendation for a staged intervention of biventricular ICD and then ablation. He received an LVAD.

Discussion

This case series provides insight to questions regarding CA for AF in LVSD that have not previously been answered. CA appeared safe in this cohort. All patients had successful completion of the CA without any apparent difficulty with operative hemodynamic status. All patients except Case 5 required vasopressor support during the ablation. This is consistent with the hemodynamic management during AF CA for any patient at our institution regardless of heart function status (unpublished data). Case 4 had transient up-titration of milrinone to compensate for the presumed negative inotropic effects from the inhaled anesthetic. The infusion drip rate was returned to baseline at procedure's end. No patient needed any post-ablation blood pressure or respiratory support. There were no significant procedural vascular or bleeding complications despite uninterrupted oral anti-coagulation. The use of ultrasound to assist in procedural vascular access likely contributed to this. All patients remained on anti-coagulation post-CA except for Case 4 due to intracranial hemorrhage. There did not appear to be any significant exacerbation of heart failure status from exposure to the CA process. Only in Case 7 was a patient not discharged home the day after the CA. They did not appear euvolemic pre-procedure, and stayed longer post-ablation at the operator's discretion to achieve improved volume status in the face of already tenuous renal function.

Procedure times were significantly greater than that of LVSD EF < 40% contemporaries for our institution, 175 ± 24 min. vs. 153 ± 33 min. (p=0.009) (unpublished data), likely driven by the additional need for PWI, typical and atypical arrhythmia ablation. Case 6 was observed in the ICU transiently after CA, treated with an intravenous fluid bolus for brief hypotension, and discharged later the next day after serial re-evaluations. It was successfully managed conservatively with return to baseline status.

The death in Case 5 occurred after a sequence of events prompting an urgent orthopedic procedure that was not tolerated. By contrast the elective CA for which he did not require any VP support at all, had no complications. The death in Case 4 occurred with concomitant dual direct oral anti-coagulation (DOAC) and monotherapy platelet inhibition use. The deaths were not related to the CA, and serve to emphasize the increased mortality of this at-risk population. While many studies for CA in AF and heart failure have included Class IV patients [2,6,14,15], none have provided a focused report for us to provide safety comparisons. One suspects limited numbers, such as at our institution, to be the reason.

Does the procedure actually do what it purports? More specifically, is it efficacious for maintaining NSR, and does it result in improved heart failure status? Overarching conclusions cannot be drawn from our limited experience regarding long-term AF burden reduction. It has been shown that duration of AF before CA is predictive of freedom from AF following CA in larger groups [18-20]. Our cohort is heterogeneous as regards duration of AF before CA (3-months to 7-years) and underlying cardiac substrate. We did not exclude anyone for CA consideration based on duration of AF or left atrial size, but did for presence of a LVAD. The likely atypical flutter recurrence in Case 4 may have been managed successfully with a repeat procedure had intra-cranial bleeding not intervened. We chose our step-wise approach for the CA process as an attempt to limit the amount of ablation, given prior trial experience showing potential for worsened outcomes [21]. PWI following WACA was chosen as the second step, absent conversion of AF, given multiple studies suggesting added benefit to pulmonary vein isolation, despite understanding the difficulties with durability [22-24] and energy limitations on the posterior wall. Subsequent to initiating our CA process, recent findings have suggested that adjunctive PWI may not have added benefit in a broader group of persistent AF [25]. The potential need for repeat ablation should be expected.

No study to date has reported the concomitant application of CA for AF in patients with continuous ambulatory milrinone infusion. Milrinone is a phosphodiesterase III inhibitor which increases cyclic adenosine monophosphate and intra-cellular calcium. Myocardial contractility is enhanced and systemic vascular resistance decreased as a result, without the expense of increased myocardial oxygen consumption [26]. Thus, milrinone is an attractive management strategy in severe forms of heart failure. However, calcium also plays a promotional role in AF [27]. Clinical data regarding milrinone use has shown an increased incidence of AF in post-cardiac surgery [28,29] and with a short-term use inpatient heart failure study [30]. Ours is the first to report the use in patients undergoing CA for AF. All patients achieved NSR with their procedure and remained arrhythmia-free during their brief hospital stay. Four out of 5 patients maintained NSR following CA up to the 3-month follow-up mark, in spite of milrinone use over that time. As such, milrinone use does not appear to be an impediment to maintaining NSR following CA in this limited experience, despite its pro-arrhythmia propensity. Conversely, CA appears to enhance the likelihood of discontinuing milrinone due to improved subjective symptomatology and 6-minute hall walk evaluations.

Limitations

Minnesota living with heart failure questionnaires were not applied to our group pre- and post-ablation. Long-term follow-up echocardiographic data would be informative as well, and has been limited by study blinding in 1 patient and death in 2 patients. Conclusions applying broadly to Class IV heart failure patients for CA of AF improving heart failure status cannot be drawn based on our smaller case load. Multiple studies have reported improved heart failure status with successful CA for AF in Class II and III patients [2,5,7,9-11], so it does not seem unreasonable to believe the same may not ultimately prove true in Class IV.

Who should be performing CA of AF in LVSD? Our experience is certainly not the basis with which to solely answer this question. The Heart Rhythm Society admits that exact numerical skills for CA in AF in general are hard to determine [31]. What is evident regarding success of CA for AF is that higher volume centers fare better [32,33].

Other Limitations This study represents a single-center, single-operator experience that prevents generalizability to the EP community as a whole. As mentioned above, limited numbers and follow-up do not allow firm conclusions to be drawn. Referral bias cannot be excluded, and might ultimately affect the true safety and success in this population. As a pilot "exercise" in this selected group of patients, though, the results are encouraging, and don't preclude further pursuit.

Conclusions

CA for persistent AF in Class IV chronic systolic heart failure even on advanced therapies is feasible. Milrinone does not appear to impede the ability to attain and maintain NSR in short-term follow-up from CA. Heart failure status and EF may be improved on an individual basis. The possibility of needing repeat ablation should be expected. Enhanced experience of CA will be required from a multi-center approach, including measurement of consistent endpoints across the entire cohort, before conclusions may be more broadly applied to this severe form of LVSD.

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Case Report

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Localization of Right Ventricular Outflow Tract Premature Ventricular Complexes Using a Novel Mapping System

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Abstract

Premature ventricular complexes (PVCs) are common in the general population, usually a symptomatic, and deemed to be benign in structurally normal hearts. The spectrum of "benign" outflow tract PVCs ranges from single PVCs to recurrent non-sustained ventricular tachycardia (NSVT). Short-coupled right ventricular outflow tract (RVOT) PVCs may trigger polymorphic ventricular tachycardia (VT) in some patients and can be high risk. In many patients, PVCs can be more frequent and cause symptoms of palpitations, shortness of breath, dizziness, and heart failure.In the presence of underlying heart disease, they may indicate an increase drisk of adverse cardiovascular outcomes. A high PVC burden may lead to ventricular dysfunction and worsen underlying cardiomyopathy.PVCs may also be a marker of underlying pathophysiologic processes such as myocarditis and other acquired and inherited infiltrative cardiomyopathies. In this unique case report, we describe the use of a novel non-contact mapping array for mapping RVOT PVCs.

Introduction

Premature ventricular complexes (PVCs) are common in the general population, usually asymptomatic, and deemed to be benign in structurally normal hearts [1]. The spectrum of "benign" outflow tract PVCs ranges from single PVCs to recurrent non-sustained ventricular tachycardia (NSVT). Short-coupled right ventricular outflow tract (RVOT) PVCs may trigger polymorphic ventricular tachycardia (VT) in some patients and can be high risk [2]. In many patients, PVCs can be more frequent and cause symptoms of palpitations, shortness of breath, dizziness, and heart failure. In the presence of underlying heart disease, they may indicate an increased risk of adverse cardiovascular outcomes. A high PVC burden may lead to ventricular dysfunction and worsen underlying cardiomyopathy. PVCs may also be a marker of underlying pathophysiologic processes such as myocarditis and other acquired and inherited infiltrative cardiomyopathies [1,3]. In this unique case report, we describe the use of a novel non-contact mapping array for mapping RVOT PVCs.

Case Report

The patient is a 61-year-old male with known recurrent frequent PVCs. His medical history includes non-obstructive coronary artery disease, hypertension, hyperlipidemia, and peripheral artery disease. He underwent heart catheterization in June 2020 which demonstrated a 50% left anterior descending lesion but no significant obstruction. He underwent cardiac positron emission tomography which demonstrated an ejection fraction (EF) of 60% with no myocardial inflammation. The patient was evaluated with thoracic echocardiography before the procedure, left ventricular EF was 60% and the right ventricle cavity, wall thickness, and systolic functions were all normal. An implantable loop recorder (ILR) was placed in August 2020. ILR interrogation demonstrated a high PVC burden (16.9%). A 12-lead ECG suggested probable RVOT PVC origin. Then we decided to perform a PVC ablation procedure. The patient underwent monitored anesthesia care with the anesthesia. Right and left femoral venous access was obtained using vascular ultrasound guidance. Arterial hemodynamic monitoring was provided through the catheter. An intracardiac echo catheter was advanced via an 11-French sheath into the left femoral vein and positioned in the right atrium. A comprehensive EP study was performed with coronary sinus catheter placement and right ventricular ablation catheter. The non-contact mapping catheter was inserted into the RV and shown with Fluoroscopy ([Figure 1A] and Intracardiac Echocardiography [Figure 1B]. AcQMap (Acutus Medical, CA, USA) and EnSite Precision (Abbott, St Paul, MN, USA) mapping systems were used for 3-D mapping of the ventricular arrhythmia. Based on previous 12-lead ECG and implantable loop recorder monitoring, we anticipated the PVCs to be originating from the RVOT. We correlated the PVC site of origin using the Precision mapping system. Then non-contact mapping catheter was successfully passed through the tricuspid valve because it is handling, and deliverability is easy. We mapped the RV and outflow tract using the AcQMap non-contact mapping system [Figure 2A] and were able to successfully identify

Key Words

Premature ventricular complex, Non-contact mapping system, Radiofrequency catheter ablation, Right ventricular outflow tract, New mapping system, Contact mapping system

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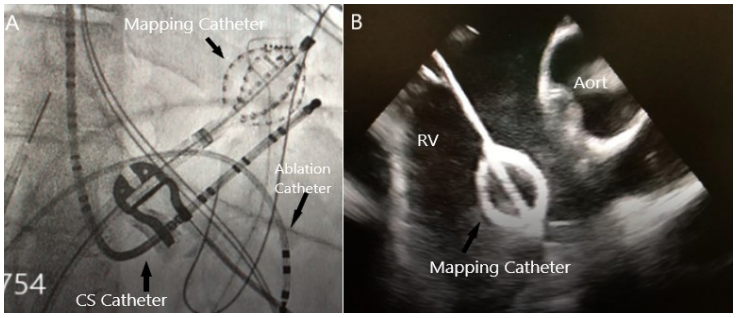

Figure 1: **The Mapping Catheter is shown with Fluoroscopy (A) and Intracardiac Echocardiography (B) in the RV ventricle. The noncontact mapping catheter was positioned generally in the center of the chamber when performing the electrical mapping. In doing so, the majority of endocardial aspects of the RV will likely be within the optimal range.**

and tag the origins of the PVCs. The mapping time at the RV was 180 seconds using the AcQMap non-contact mapping system. Whereas the conventional 3D mapping using the Precision system took close to 14 minutes for the mapping. There were 2 PVCs, one from the RVOT free wall, as well as the second PVC from the RVOT upper septum. We then introduced a contact mapping catheter (HD Grid catheter) [Figure 2B] and similarly mapped the right ventricle and outflow tract localizing the PVCs to the same locations previously identified by the AcQMap system. The earliest local activation timing on the bipolar signal from the tip electrode was provided [Figure 2C]. Both PVCs were successfully mapped using the 3-D map and successfully ablated with a TactiCath Catheter at 40W. Total RF delivery time was for 256 seconds (Abbott, St Paul, MN, USA). At this point, isoproterenol was started with adequate heart rate response. Then a post-procedural programmed stimulation was conducted this did not induce any arrhythmias. Post-ablation intracardiac echo showed no pericardial effusion and RV ejection fraction was unchanged. At this time, we decided to conclude the procedure. The patient's 8 months post-ablation PVC burden was <0.1% (rare).

Non-contact mapping system was used in this case due to rare PVCs and we thought it would be fast, not taking a long time over the conventional mapping.

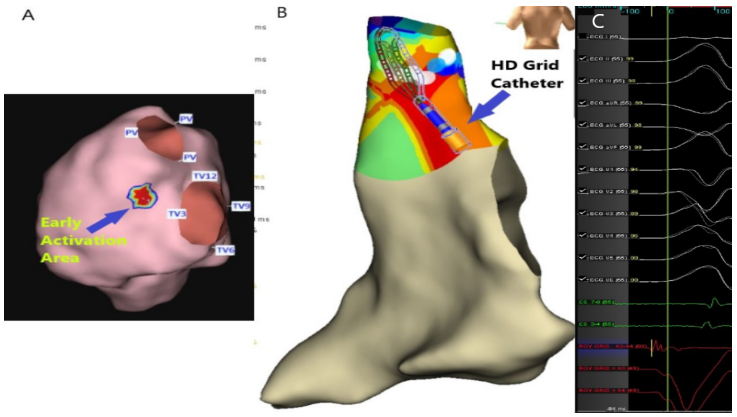

Figure 2: **A: The AcQMap imaging and mapping system demonstrate the three-dimensional right ventricular anatomy and PVC localization (blue arrow). 2B:The Precision Mapping System demonstrates three-dimensional RV and RVOT anatomy with the HD Grid catheter, 2C:Shows PVC and the earliest activation on intracardiac ECG at the bottom (green arrows).**

Discussion

We present the first case of mapping and treatment of PVCs originating from the RVOT using the AcQMap mapping system and AcQMap catheter. The mapping catheter combines 48 ultrasound transducers responsible for reconstructing the chamber anatomy and 48 engineered electrodes which enable charge-density-based activation patterns to be displayed along the endocardial surface of the heart [4]. It is the only integrated high-resolution ultrasound-based imaging and non-contact mapping catheter capable of capturing cardiac imaging information in addition to cardiac activation mapping. When combined with the AcQMap mapping system, the catheter also provides maps of most arrhythmias in under 3 minutes, enabling a map to ablate—remap strategy to evaluate therapy effectiveness [5]. To map PVCs and VTs, the arrhythmia must occur naturally or be induced during the procedure. Patients can become hemodynamically unstable and rapidly decompensate. Currently marketed contact-based mapping systems require contact with the tissue which can be proarrhythmic. Similarly, there exists a likelihood of missing the arrhythmia due to lack of contact at the activation site. Non-contact mapping is ideally suited to map both PVCs and VTs as it allows for global visualization. One is able to identify and target the origin of the arrhythmia with a single beat and achieve it without disturbing the tissue. However, this mapping system was evaluated in the ventricle in an animal study [6] but has not been reported in human ventricle arrhythmias yet. Although the AcQMap catheter is designed and has regulatory approval for use in the left and right atria to map complex atrial arrhythmias, we elected to use it to map PVCs originating from the RVOT.

Conclusions

This case report suggests that patients presenting with PVCs originating in the RVOT can be quickly and easily mapped using a novel non-contact mapping system to identify the target area to be treated by radiofrequency catheter ablation. With appropriate clinical care, this example demonstrates the potential for safe and effective use of the system, not only in the left and right atria, but also to identify the ventricular origins of PVCs, particularly those with RVOT origin.

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Reversible Mechanical Atrioventricular Block Caused by A Steerable Introducer Sheath During Transseptal Catheterization

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*Drs. Siroky and Bisht contributed equally to this manuscript.

Abstract

A 62-year-old woman presents for pulmonary vein isolation (PVI) for paroxysmal atrial fibrillation. During transseptal catheterization (TSC) the patient sustained mechanical injury to the atrioventricular node (AVN) with consequent complete heart block (CHB). Injury to the AVN and CHB recovered after approximately forty minutes. The patient subsequently underwent a successful PVI with the remainder of the hospital stay uneventful. We present a case of reversible injury to the AVN caused by a steerable introducer sheath during TSC and discuss the mechanisms of injury as well as potential measures to avoid such a complication in the future.

Introduction

Peri-procedural atrioventricular block (AVB) is hypothesized to be caused by trauma or inflammation of the tissue surrounding the AVN.[1,2] It may be caused after aortic valve intervention, alcohol septal ablation, ischemic injury during coronary intervention, ablation near the AV node, or during placement of catheters that mechanically interfere with one fascicle when conduction is already impaired in the remaining conduction system. AVB during transseptal catheterization is an uncommon complication which is hypothesized to be caused by mechanical collision of the sheath with the AVN. Two types of sheaths, fixed curve and steerable, are used for transseptal catheterization depending on availability and the operator's preference. Steerable sheaths are relatively stiff and exert greater force on underlying cardiac structures compared to a fixed curve sheath. Being a subendocardial structure, the AVN may be susceptible to mechanical trauma as a result of catheter placement on or near the area, however, the occurrence of reversible AVB caused by a steerable sheath is rare and likely underreported. We present a case of reversible AVB secondary to sheath-induced trauma to the AVN during TSC.

Case

A 62-year-old woman presents for pulmonary vein isolation (PVI) in treatment of symptomatic paroxysmal atrial fibrillation (PAF). A pre-ablation cardiac computed tomography (CT) scan showed a common left sided pulmonary vein (PV), normal PV anatomy on the right side, and a dilated main pulmonary artery suggestive of pulmonary hypertension. Electrocardiography (EKG) showed sinus bradycardia with normal QRS duration [Figure 1A]. The echocardiogram showed left ventricular hypertrophy (LVH) and mild left ventricular systolic dysfunction.

Right and left femoral venous access was obtained to advance a diagnostic decapolar catheter and an intracardiac echo (ICE) catheter to the coronary sinus (CS) and mid right atrium (RA), respectively. In anticipation of transseptal catheterization (TSC) the ICE catheter was positioned to visualize the interatrial septum (IAS). A 0.032-inch J-tip guidewire was advanced under fluoroscopic guidance from the right femoral vein to the superior vena cava (SVC). Keeping the same fluoroscopic and ICE projections, an 8.5F steerable introducer sheath (Agilis NXT, 16.8 mm St Jude Medical, MN, USA) was advanced over the guidewire to the SVC. Once the sheath was 3 to 4 cm superior to the cavoatrial junction, the wire was removed, keeping the tip of the sheath facing leftward in an AP view. The Brockenbrough TSC needle with stylet was advanced to within 3 cm of the sheath tip. The stylet was removed and the needle and the sheath were gradually pulled down with the Brockenbrough needle arrow maintained at a 5 o'clock position. During the descent of the sheath and needle assembly, the IAS was monitored for tenting using the ICE catheter. The Agilis sheath was felt to be too anterior in the fossa ovalis and this was confirmed by ICE and fluoroscopy in a right anterior oblique (RAO) view. When clockwise torque was applied to the Agilis sheath to direct the tip more posteriorly, the patient developed complete AVB [Figure 1B]. The decapolar (CS) catheter was immediately advanced to the right ventricular apex to provide ventricular pacing.

After an almost forty-minute waiting period, during which the patient was hemodynamically stable, AV nodal conduction returned [Figure 1C]. Following resolution of CHB, TSC was performed uneventfully with a standard, fixed curve Swartz braided SL-1 transseptal (TS)

Key Words

Transseptal Puncture, Mechanical Atriventricular Block, Steerable Sheath

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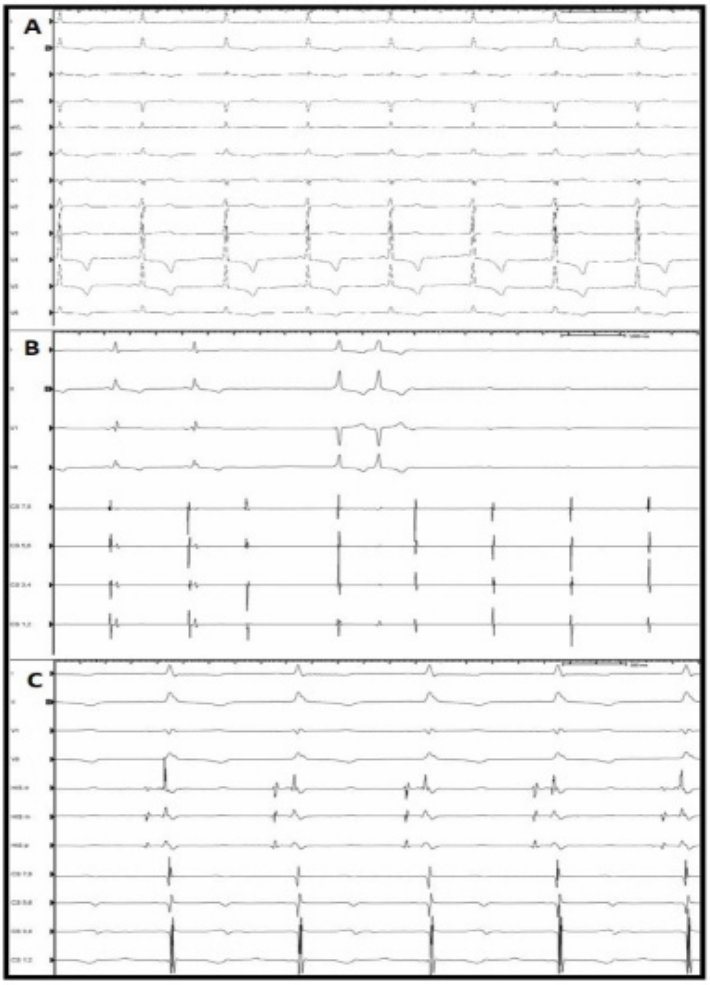

Figure 1: (A) Pre-procedure electrocardiogram showing sinus bradycardia and left ventricular hypertrophy with strain pattern. (B) Intra-procedural development of complete heart block. (C) Resolution of AV block and resumption of normal conduction with normal HV interval.

sheath (St. Jude Medical, MN, USA), Brockenbrough TS needle, and Safesept wire (Cardio medical products, INC, USA) using fluoroscopic and ICE guidance. The SL-1 sheath was exchanged for the Agilis sheath using an Amplatz exchange wire. PVI was performed without incident and the rest of the hospital stay was uneventful.

Discussion

Atrioventricular conduction disturbance during AF ablation is a rare complication and has been reported during cryoablation.[4,5] It has been described that during cryoablation, mechanical bumping of the AVN during cryo-energy delivery around the right inferior pulmonary vein as well as vagally mediated reactions are potential mechanisms for transient AV block.

In our patient, AVB likely occurred due to mechanical, traumatic injury to the AVN during manipulation of the steerable, Agilis sheath, despite fluoroscopic and intracardiac echocardiographic guidance. Clockwise torque applied to direct the sheath posteriorly across the mid part of septum likely traumatized the AVN resulting in conduction block. The degree of AV block was determined to be at the level of the AVN as there was no evidence of distal conduction disease once normal conduction resumed [Figure 1C].

While in our case, AV block lasted for about 40 minutes, Schweiss et al. reported a case of transient heart block which lasted for a total of 3 days.[6] In addition, it was the only reported case found in the literature of traumatic injury to the AV node leading to prolonged CHB during TSC. The authors initially believed that the heart block occurred after ablation of a left lateral accessory pathway as a result of damage to the left lateral extension of the AV node, however, after close inspection of the electrograms, they determined that injury occurred to the AV node during TSC. The only piece of information lacking from their case report was the type of sheath used during the TSC.

Steerable sheaths are being increasingly used for PVI which allows better catheter stability in addition to achieving target contact forces of 10-40gms for ablation lesions.[7] As shown by Reddy et al. in the TOCCASTAR study, there was a higher median contact force when using a steerable sheath (Agilis) versus a fixed curved sheath (23.3grams vs. 14.6grams).[8] While contact force is not directly monitored during TSC, it can be extrapolated to our case that a steerable sheath can be more prone to cause mechanical damage to the compact AV node compared to a fixed curve sheath.

In addition, a basic knowledge and understanding of the cardiac anatomy is required for a safe and successful TSC [Figure 2]. The initial positioning of our sheath prior to TSC was likely too anterior, near the region of the compact AVN, and with clockwise torque to position the sheath more posteriorly, the tip of the sheath mechanically injured the AVN leading to complete heart block.

Based on the above and the development of AVB during this case we propose that TSC be performed with a standard fixed curve sheath (e.g. Swartz braided SL-1 transeptal sheath), which can then be exchanged over a wire for a steerable sheath (e.g. Agilis NXT, 16.8 mm St Jude Medical, MN, USA). Alternatively, TSC can be performed with the VersaCross® system (Baylis Medical, Montreal, QC, Canada) which is

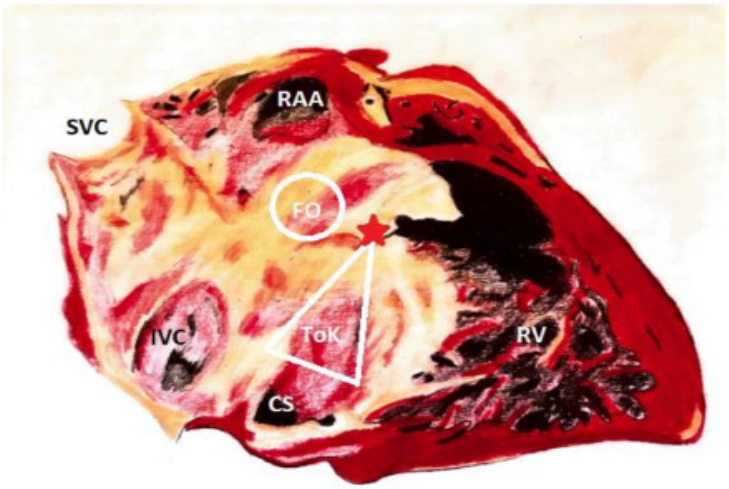

Figure 2: Right anterior oblique view of the right sided cardiac anatomy demonstrating proximity of the compact AV node (red star) to the fossa ovalis (FO). SVC = superior vena cava; IVC = inferior vena cava; CS = coronary sinus; ToK = triangle of Koch; RV = right ventricle; RAA = right atrial appendage. (Illustrated by Shawn Lee, MD and adapted from Alkhouli et al. J Am CollCardiolIntv. 2016;9(24):2465-80)[9]

a needleless apparatus utilizing a stiff radiofrequency-powered pigtail wire advanced through a softer guiding sheath. Once through the atrial septum, the stiff pigtail wire provides adequate support for an exchange to a stiffer steerable sheath. In addition, in this era of routine ICE use for TSC we must still use the RAO projection to ensure that we are not starting too anterior with the transseptal assembly.

Conclusions

We present a rare case of reversible AVB caused by mechanical injury to the AV node during transseptal catheterization by a steerable introducer sheath. This case highlights the critical role of imaging and hardware selection during transseptal catheterization. The approach we suggest of using a fixed curve sheath for initial transseptal access may avoid this complication and allow for safer TSC.

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Safety of Atrial Fibrillation Ablation in the Young – A Real World Analysis

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Letters to Editor

Atrial fibrillation (AF) is the most frequently encountered cardiac arrhythmia seen in clinical practice, with an prevalence expected to increase to an estimated 12.1 million by the year 2030.[1] While most frequently encountered in the elderly, a significant proportion of younger adults are diagnosed with AF as well. It is estimated that 1% of patients with AF are less than 60 years of age.[1] Young patients with earlier onset of AF are exposed to a life time risk of recurrences, tachycardia-mediated cardiomyopathy, heart failure and stroke. In addition, long term adverse effects of anti-arrhythmic therapy and anticoagulation can be additive.[3] To avoid risks from long-term medical therapy, it could be hypothesized that an early catheter ablation approach would be reasonable in younger patients who present with AF. However, safety data of AF ablation in this cohort is limited. We sought to examine the utilization and complications of AF ablation in younger patients (≤50 years) and compare with complication rates in older patients (> 50 years).

We identified all patients that underwent AF ablation using data from the National Inpatient Sample (NIS) from 2005 to 2014. Trends in utilization of AF ablation in the two age groups (<50 and >50 years) was computed. Rates of in-hospital procedural complications were analyzed and compared between the two groups. All statistical analysis was conducted using SPSS (IBM SPSS, Version 27.0. Armonk, NY).

A total of 112,998 AF ablations were identified within the NIS between the years 2005 to 2014, and were included in our analysis, which was weighted in order to represent the general U.S. population. Majority of the ablations occurred in the older patient group with about one-sixth of ablations performed in patients >50 years of age (n = 15,832). Trends in utilization of AF ablations stratified by age group is shown in the [Figure]. Mean age was 43.18±6.6 years in the younger age group. There was a significantly higher proportion of African Americans (6% vs. 3%) and Hispanics (6.2% vs. 2.9%) in the younger cohort compared to those >50 years. Prevalence of comorbidities such as diabetes, hypertension, peripheral vascular disease and obesity ($p < 0.0001$ for all) were also significantly lower in the younger cohort. A large majority (81.1%) of younger patients were privately insured while about half (52%) of patients >50 years of age had Medicare as the primary payer. Rate of in-hospital complications were significantly lower in the younger age group than in the older age group [Table]. Younger patients had significantly lower rates of vascular complications requiring surgery, cardiac tamponade, pneumothorax, need for pericardiocentesis, post-operative stroke/TIA, as well as AV fistula formation ($p < 0.002$ for all). Mean length of stay for those <50 years was 1.97 days compared to 2.38 days for those >50 years.

Our analysis suggests that younger patients <50 years of age comprise about one-sixth of all AF ablation procedures performed in the United States. Young patients have shorter lengths of stay and significantly lower in-hospital complication rates compared to those >50 years of age. These findings are similar to other smaller single center studies that have been reported previously which demonstrated safety and efficacy of AF ablation in younger patients with excellent rates of arrhythmia free survival.[3-5] In these prior studies, ablation was offered as second-line therapy to patients with drug-refractory AF. This practice is in accordance with current AHA/ACC guidelines for management of AF, with first-line catheter ablation for AF is listed as a class IIB recommendation[1]. However, our analysis suggests that a lower threshold to offer ablation to younger patients with AF as first line therapy may be reasonable given its efficacy and safety, and merits further study. Lower rates of overall complications should also be utilized during shared decision making while discussing AF ablation with younger patients.

Key Words
Atrial Fibrillation; Complications; Safety; Young.

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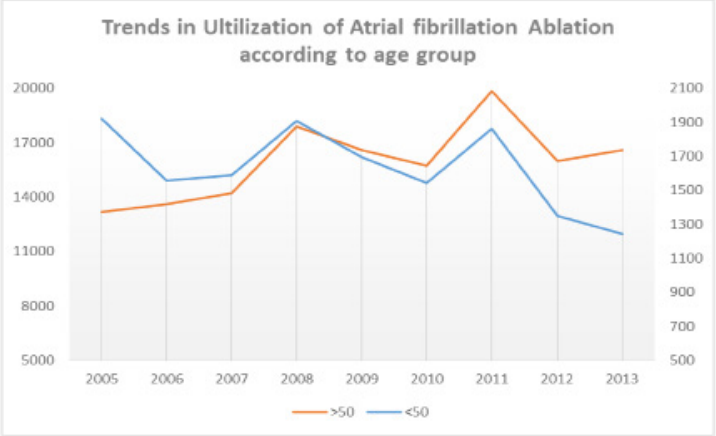

Figure 1: Trends in utilization of AF ablation stratified by age group. Primary Y axis on left depicting utilization of AF ablation in patients >50 years. Secondary Y axis on right depicting AF ablation utilization in patients >50 years

Table 1: Comparison of In-hospital Complications of Atrial fibrillation ablation in young (<50 years) patients with those >50 years old

	Age ≤ 50(n = 15, 832)	Age > 50(n = 97,165)	Total(n=112998)	P-value
Vascular Complications requiring Surgery (%)	0.06	0.22	0.2	<0.0001
AV fistula (%)	0.03	0.12	0.11	0.0016
Hemopericardium (%)	0.29	0.36	0.35	0.1719
Cardiac Tamponade (%)	0.58	1.03	0.97	<0.0001
Pericardiocentesis (%)	1.15	1.79	1.7	<0.0001
Stroke/TIA (%)	0.46	0.85	0.79	<0.0001

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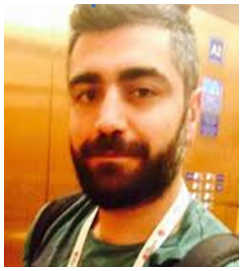

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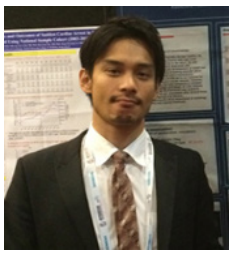
Dr. George Louridas, MD

Emeritus Professor of Cardiology, Aristotle University, Thessaloniki Greece, Director of Cardiac Catheterization Laboratory, AHEPA Hospital (1983-2006), Director of Department of Cardiology, AHEPA Hospital (1996-2006).



Dr. Kyoichiro Yazaki, MD

Affiliation: Ogikubo Hospital, Department of Cardiology,Cardiovascular Center, Tokyo, Japan.
Clinical research of electrophysiology, catheter ablation, and Device therapy are of my interests

Dr. Ashraf Alqaqa, MD, FACC

Dr. Farhad Farokhi received his medical degree from the Kansas City University of Medicine & Biosciences. He finished his internal medicine residency at the Grandview Hospital in Dayton, OH. He currently holds board certification in Cardiovascular Disease and Clinical Cardiac Electrophysiology from the American Osteopathic Board of Internal Medicine, Internal Medicine from the American Osteopathic Board of Internal Medicine, and Echocardiography from the American Society of Echocardiography. Dr. Farokhi's clinical interests include Atrial Fibrillation, Catheter Ablation, Ventricular Arrhythmia, and Left Atrial Appendage Closure (LARIAT).

Dr. Hickey

Dr. Hickey is an Associate Professor of Nursing at Columbia University Medical Center and holds a joint appointment in the Division of Cardiology (electrophysiology) as both a family and adult nurse practitioner. Her interdisciplinary research, clinical practice and scholarship is focused in the areas of cardiac genetics, the clinical care of those with chronic cardiac conditions and arrhythmias, and the prevention of sudden cardiac death. Her current grant awards include a R01 from the National Institute of Nursing Research (iHEART) focusing on arrhythmia telehealth monitoring in those with atrial fibrillation, her newly awarded (multiple-PI) P30 award with Dr. Suzanne Bakken is focusing on improving symptom self-management for underserved populations with or at risk for chronic health conditions.

Dr. Andres Enriquez, MD

Dr. Enriquez received his medical degree from the Universidad de Concepcion, in Chile. He specialized in Internal Medicine, Cardiology and Cardiac Electrophysiology at Pontificia Universidad Catolica de Chile in Santiago.

Between 2013 and 2015 he moved to Canada to continue his electrophysiology training at Queen's University, Kingston, Ontario.

He currently resides in Philadelphia with her wife Karen and is a second-year fellow in the Advanced Clinical Electrophysiology program at the Hospital of the University of Pennsylvania, under the mentorship of Dr. Francis Marchlinski.

Dr. Enriquez interests include electrocardiology, clinical electorphysiology catheter ablation and cardiac devices.

Dr. Ryan Dean White. MD

Dr. Ryan Dean White, MD, medical degree from the University of Missouri and currently training in internal medicine at Indiana University School of Medicine in Indianapolis, Indiana.

Dr. James R Edgerton, MD, FACC, FACS, FHRS

The Heart Hospital

Dr. Jackson J. Liang, MD

Clinical Cardiac Electrophysiology Fellow
Hospital of the University of Pennsylvania

Dr. Gianluca Rigatelli, MD, PhD, EBIR, FACP, FACC, FESC, FSCAI, Vice-Director

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