JAFIB
Original Research
Journal of Atrial Fibrillation

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The Rate Of Complications Associated With Concomitant Use Of Dabigatran With Cryoballoon Ablation For Atrial Fibrillation

Valay Parikh, MD, Vratika Agarwal, MBBS, Jharendra Rijal, MBBS , Vinod Chainani, MD , Soad Bekheit, MD, PhD, FHRS, Marcin Kowalski, MD, FACC, FHRS

Department of Electrophysiology, Staten Island University Hospital, NY .

Abstract

Introduction: Catheter ablation is an evolving therapeutic strategy for the management of atrial fibrillation (AF). It is associated with a risk of thromboembolic events. The peri-procedural anticoagulation management with warfarin has been successful in mitigating this risk. However, introduction of novel oral anticoagulants like dabigatran offers more flexibility in anticoagulation approaches. Previous studies had evaluated the safety and efficacy of dabigatran in the radiofrequency ablation, but data related to cryoballoon ablation is lacking.

Methods and Results: We performed a retrospective observational study involving patients who underwent cryoballoon ablation for drug-refractory, symptomatic AF while on dabigatran in periprocedural period. Thromboembolic, hemorrhagic or other complications occurring within the first 30 days after the ablation procedure were analyzed.

Our study population comprised of 50 patients with mean age of 58.96 ± 3.54 years with 76% (n=38) being male. We found 3 (6%) minor complications in peri-procedural period including 2 groin hematomas and 1 trace asymptomatic pericardial effusion. There were no major intraprocedural or post procedural hemorrhagic or thromboembolic events. None of patients with the minor complications required significant additional workup or extended hospital stay. All the patients were able to continue dabigatran for 30 days without any additional side effects or complications.

Conclusion: Dabigatran is a safe and efficacious agent in patients undergoing cryoballoon AF ablation.

Introduction

Catheter ablation is an evolving therapeutic strategy for the management of atrial fibrillation (AF). A thromboembolic event is recognized as one of the serious complications associated with AF ablation with reported rates varying from 0.4 to 2.1%.[1-4] Prevention of such a devastating complication requires meticulous attention to anticoagulation before, during and after the ablation. Conversely, anticoagulation can contribute to the more common complications associated with the procedure such as cardiac tamponade, hematomas and vascular complications. The peri-procedural anticoagulation management with warfarin has evolved over time to increase the success rate of the procedure and to minimize these complications.[5,6] The introduction of dabigatran, a new oral direct thrombin inhibitor, offered alternative anticoagulation strategies. Previous studies had evaluated the safety and efficacy of dabigatran in the periprocedural period of AF ablation performed with variable results. However, majority of the studies only included patients undergoing ablation with Radiofrequency energy.[7-11] RF ablation and cryoballoon ablation methods are procedurally different and carry different peri-procedural complication risks. So we condcuted this study to investigate the safety and efficacy of peri-procedural dabigatran in patients undergoing cryoballoon ablation.

Key Words:

Atrial Fibrillation, Cryoballoon Ablation, Dabigatran.

Disclosures:
None

Corresponding Author:
Marcin Kowalski, MD FHRS
Director, Department of Cardiac Electrophysiology
Associate Director, Cardiology Fellowship
Staten Island University Hospital,
475 Seaview Ave, Staten Island, NY-10305

Methods

We performed a retrospective observational study involving of 50 patients who underwent cryoballoon ablation for drug-refractory, symptomatic AF at our electrophysiology laboratory between February 2011 and February 2013.

Peri-Procedural Anticoagulation

All patients received anticoagulation therapy with 150 mg Dabigatran exetilate twice daily for at least 30 days before and 30 days after the AF ablation. Each patient was instructed to hold 2 doses (morning and night prior) to procedure. The sheaths were pulled when ACT was below 200 s. Dabigatran was resumed four hours after hemostasis was achieved.

Ablation Procedure

One right femoral vein access was obtained using the modified Seldinger technique and an 11F sheath was advanced into the vein after venous access was confirmed. The left femoral vein was accessed twice using modified Seldinger technique and a 7F and 11F sheaths were advanced into the vein. Also left femoral artery was

accessed once using the modified Seldinger technique and 4F sheath was advanced into the artery. Under intracardiac echocardiography (SoundStar ACUNAV Ultrasound Catheter, Siemens, Washington, D.C.) guidance, one transseptal access was obtained using standard needles and 8F SL1 sheaths (St. Jude Medical Inc., Secaucus, NJ) inserted through the right sided 11Fr sheath. A bolus of 100 U/kg of unfractionated heparin (UFH) was given before the transseptal puncture. The activated clotting time (ACT) was checked after the bolus and every 15 minutes thereafter. Further weight-adjusted UFH boluses were given to maintain an ACT of 300 to 350 s while catheters remained in the left atrium. The 8 F SL1 sheath and the 11F short sheath were exchanged over the wire under the guidance of fluoroscopy for a 12 F French sheath (FlexCath Cryocath, Medtronic Inc., MN) with a 15F outer diameter which was used to guide the ArcticFront cryoballoon (Medtronic Inc., MN). A circular mapping catheter (Achieve, Medtronic, MN) was used for mapping the pulmonary veins and stability of the cryoballoon. A 28 mm cryoballoon was inflated and positioned at the ostium of each pulmonary vein. Remaining of the ablation procedure was carried out in a standard fashion as previously described.[12,13]

Data Collection

Demographic, procedural, and complication data was obtained from the electronic medical records. Events occurring within the first 30 days after the ablation procedure were included in this current analysis. The study protocol was approved by local institutional review board.

Safety Endpoints

Hematomas and new post procedural pericardial effusions were considered as bleeding complications. Cerebrovascular accidents and transient ischemic attacks were considered as thromboembolic complications after ruling out intracranial hemorrhage. Any bleeding requiring blood transfusion, hematomas requiring surgical intervention, and pericardial effusions requiring drainage (tamponade) were considered as major bleeding complications. Minor bleeding complications included small hematomas, re-bleeding and pericardial effusions not requiring an intervention (non-tamponade). Late pericardial tamponades were those occurring more than 48 h after the procedure. The primary safety outcome measured was a composite of bleeding and thromboembolic complications. Miscellaneous non-anticoagulation related events were also recorded.

Results

Our study population comprised of 50 patients. Their mean age was 58.96 ± 3.54 years with 76% (n=38) being male. The baseline characteristics are shown in table 1. We found 3 (6%) minor complications in patients with dabigatran anticoagulation before and after AF ablation (Fig 1). There were no major intraprocedural or post procedural hemorrhagic or thromboembolic events. No intracranial hemorrhage or deaths occurred in the study population. Two (4%) patients had groin hematomas occurred in the left groin where the 4F atrial sheath and the 11F and 7F venous sheaths were inserted. There was no hematoma found in the right groin where the 12 F Flexcath was inserted. None of the hematomas required further intervention. Both hematomas resolved prior to 30 day follow up. One patient (2%) found to have a trace asymptomatic pericardial effusion after the ablation compared to echocardiogram performed immediately prior to the ablation. The pericardial effusion was observed post ablation and its size was not significant enough to require drainage. Repeat echocardiogram the following day did not show any change in the size of the pericardial effusion. None of the patients with the minor complications required additional workup or extended hospital stay. Further characteristics of the three patients with complications are shown in Table 2. All the patients were able to continue dabigatran for 30 days without any additional side effects or complications.

Table 1: Baseline Patient Characteristics:

Characteristics	Dabigatran(n= 50)
Age (yrs.)	58.96 ± 3.54
Age >75	2 (4%)
Gender (Male)	38 (76%)
BMI	30.47 ± 1.48
Hypertension	34 (68%)
Diabetes	5 (10%)
Stroke/TIA	2 (4%)
Heart Failure	3 (6%)
COPD	6 (12%)
OSA	8 (16%)
Paroxysmal AF	27 (54%)
Non-Paroxysmal AF	23 (46%)
$CHADS_2 = 0$	14 (28%)
$CHADS_2 = 1$	27 (54%)
$CHADS_2 = 2$	9 (18%)
CHA_2DS_2-VASC	1.82 ± 1.41
GFR (ml/min/1.73 m2)	81 ± 8.49
Antiplatelets	24 (48%)
Amiodarone	7 (14%)

Discussion

In this study, we reported our experience of peri-procedural anticoagulation regimen involving dabigatran in patients undergoing cryoballoon ablation for AF. To our knowledge, this is the first study primarily focused on this issue in cryoballoon ablation. We found that the use of dabigatran periprocedurally for cryoballoon AF ablation was not associated with any major bleeding or thromboembolic complications. However, it was accompanied by 6% of minor bleeding complications, which is comparable to previously mentioned studies focused on RF ablation.

FDA approved dabigatran for nonvalvular AF in Oct 2010. Since then, multiple regimens have been studied to explore the role of dabigatran in peri-ablation period. Our electrophysiology lab started using dabigatran since Feb 2011. As per our protocol, dabigatran is stopped a day (2 doses) prior to the procedure and is restarted 4 hours after the sheaths are pulled. This approach is different from other approaches studied previously. Our regimen is in accordance to pharmacokinetics of dabigatran. Dabigatran has a half-life of 12-14 hrs.[14] By discontinuing dabigatran a day prior to the procedure, we expected that the medication effect would be negligible, thus avoiding overlapping of effects of dabigatran and heparin. Our speculation was that it will reduce bleeding complication in peri-procedural period while providing maximum protection against thromboembolic events. Quick onset of action makes it easy to restart dabigatran on the same day without increasing any thromboembolic complication in post-procedural period.

Current evidence related to use of dabigatran in AF ablation is

conflicting. Multicenter randomized study done by Lakireddy et al showed significantly increased bleeding complications composed mostly of pericardial effusion with tamponade in dabigatran arm.[7] Dabigatran was stopped in the morning of the procedure and restarted in 3 hours post procedure. This regimen was almost indistinguishable to performing procedure while on dabigatran. Other study done by Kaseno et al used a different protocol with no increased risk of bleeding or thromboembolic complication as compared to warfarin[11] The study excluded patients older than 75 years; had higher number of patients with $CHADS_2$ score of 0 (61%) and paroxysmal AF (83%) and used the 110 mg dose of dabigatran as compared to 150 mg. These details may partly explain less bleeding in dabigatran arm. The study done by Winkle et al was the most favorable study for use of dabigatran in peri-ablation period.[10] Nonetheless, they used the most conservative anticoagulation regimen. Dabigatran was held 36-60 hours prior to the procedure depending upon the renal function. In addition, their target ACT was low as 250ms.This may have resulted in less bleeding complication as compared to above mentioned studies. A recent retrospective study discussing post ablation bleeding complications showed no difference in bleeding rate between warfarin and dabigatran arm. However, it failed to suggest any particular regimen for dabigatran use in peri-ablation period.[8] In an another recent single center randomized trial done by Nin et al, dabigatran was held a day prior and restarted 4 hours after ablation. Dabigatran arm has less bleeding complication as compared to warfarin arm. However, their absolute re-bleeding rate was as high as 20%.[7] Two recently published meta-analyses had consensus on bleeding events, but had conflicting results on thromboembolic events.Dabigatran had similar hemorrhagic complications as warfarin in these analyses. However, one of these meta-analyses found out higher thromboembolic events with dabigatran use.[15, 16] We held dabigatran 24 hours prior to the procedure and achieved target ACT of 350 ms during procedure. Despite of it, our bleeding complication rate was comparable to most and even better to some studies. We did not encounter any major bleeding complications or thromboembolic events. Our minor bleeding complication rate was also extremely low as compared to most of the studies. This supports the notion that more aggressive regimen can be used with similar efficacy and safety.

Table 2: Baseline Characteristics of Patients with Complications:

	Pericardial Effusion	Groin Hematoma #1	Groin Hematoma #2
Age	63	41	48
Gender	M	M	M
$CHADS_2$	1	0	1
Antiplatelets	Yes	No	No
Cr (GFR)	1.0 (75)	1. 05 (78)	0.94 (84)
BMI	27	32	33

Our study is also the first study to focus on use of dabigatran in cryoballoon ablation. Venous sheaths used in cryoballoon ablation have an outer diameter of 15 Fr, which is appreciably larger than sheaths used in radiofrequency ablation (8 Fr). As a result, there is a fear that use of dabigatran with cryoballoon ablation may result in excessive local vascular complications.

Despite of our aggressive anticoagulation strategy, our study had just 2 minor hematomas occurring on the contralateral side of the 15 Fr sheath.

Limitations

The limitations of our analysis relate to the fact that it is a retrospective, non-randomized review with a relatively small sample size. As is true for all retrospective trials, our study is susceptive to a selection bias. In addition, our study did not compare the rate of complications between dabigatran and warfarin as there is no data available at this time with warfarin. So far majority of studies were focused on RF, which makes direct comparison with other studies difficult. However, a low complication rate with our strategy makes it a reasonable strategy to pursue. We also didn't investigate patients for asymptomatic thromboembolic events. Nevertheless with our aggressive approach, we expect fewer asymptomatic thromboembolic events as compared to other lenient regimens. In addition, we focused on only one regimen. It will be interesting to conduct a randomized

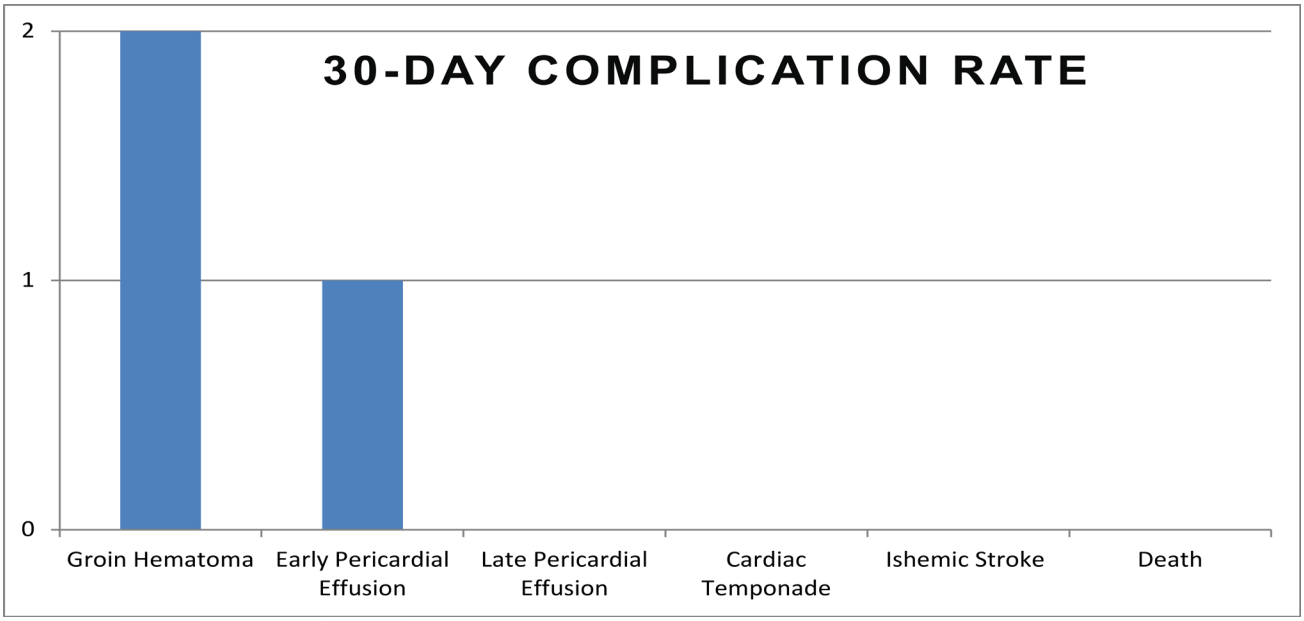

Figure 1: Graph showing 30-days complication rate with use of dabigatran in peri-procedural period with Cryoablation for atrial fibrillation.

trial comparing different regimens to find out the best optimal strategy.

Conclusion:

Currently, there are no established guidelines or data suggesting optimal anticoagulation regimen involving dabigatran in peri-ablation period especially in patients undergoing cryoballoon ablation. Our study provides a potentially safe and efficacious regimen involving dabigatran in patients undergoing cryoballoon ablation for AF, which further needs to be investigated in rigorous clinical trial settings with larger population.

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