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Dear colleagues

Welcome to the April edition of JAFIB. 2015 brings in new challenges and new hopes in advancing the frontiers in Atrial Fibrillation. In the current issue we have many interesting and intriguing manuscripts on predictors and different management and care strategies for AFIB.

ACC 2015 successfully wrapped up in San Diego, CA earlier this month. The FDA's approval of the much awaited Watchman device was a great curtain raiser to the conference. This will really provide great therapeutic solutions for thousands of patients who live with AF. This is great news for the entire field of LAA. This will open up several important clinical studies that have been on hold can now be systematically done comparing to an approved LAA device.

Selcen Tuluce has reviewed the predictors of AF development in Hypertrophic Cardiomyopathy patients, which can cause AF and related embolic complications. The integrated chronic Atrial Fibrillation Management approach described by Hubertus Vrijhoef highlights the importance of integrated care and chronic care model in a patient centered approach. In another nice article by Hui-Nam Pak various ablation strategies for persistent AF cases and the step wise approach, which could achieve better long-term clinical outcome in these patients. He has reviewed the various substrate modification techniques which could help prevent clinical recurrences.

Philipp Sommer and group have an interesting case report on successful ablation on a patient with single reentrant tachycardia arising from a peri-aortic scar and apparently normal heart. Gaita and his group have re-emphasized the biological effects of radiation and discussed the role of newer technologies like using the 3D mapping system for catheter ablation procedures.

Other important articles include a brief review of the management strategies in asymptomatic AF patients, a subgroup study from ASSERT and AFFIRM trials, which showed increased incidence of cerebrovascular events in this subgroup. Seasonal variations in paroxysmal AF, which showed increased rate of AF in winter than summer months. Temperature, duration of daylight and barometric pressure has shown to influence these seasonal variations in the onset of AF. A single center experience of traditional PVI ablation and Cryoballoon ablation for AF has been described in a short original article by Jain etal.

Hope you had a great spring break. At least here in North America we have been eagerly awaiting for this long drawn out winter to end at some point. We wish you happy time with your family and loved ones. Looking forward to see you all at Heart Rhythm Society Annual Sessions in May in Boston.

Sincerely
Dhanunjaya Lakkireddy
Andrea Natale
Abstract

Study Method: The objective of this study was to evaluate the long term efficacy and safety of the atrial fibrillation program at Unity Point Health Methodist in Peoria.

Methods: A retrospective analysis was performed on patients who had atrial fibrillation procedures at Unity Point Methodist from February 19th 2010 to September 26th 2014. Patients were enrolled and information obtained through the patient’s medical records.

Results: The study consisted of 53 patients, 65 percent of patients were paroxysmal, and 35 percent had chronic or persistent atrial fibrillation. The mean age was 66 +/- 23 (45 to 89 years). The average CHADS-Vasc Score is 2.13. Baseline co-morbidities included 34 individuals with HTN, 10 with Diabetes, and 4 with coronary artery disease. The average EF was 55% +/-25 (30% to 70%) and the average LA diameter 41 +/-15 mm (25-56). The average number of antiarrhythmic was 1.5 prior to ablation.

After a mean follow-up of 28 ± 29 months (range, 3 to 57 months), freedom from AF was 94% overall (51 of 53 patients, including 52 were on antiarrhythmic drugs), 94% for paroxysmal AF (34 of 36 patients, including 24 of whom discontinued their antiarrhythmic drugs), and 94% for persistent AF (16 of 17 patients, including 9 no longer on antiarrhythmic drugs). 76 percent experienced a decrease in their antiarrhythmic medications of which 60 percent discontinued antiarrhythmic altogether.

Out of the 53 patients, there were three major but completely reversible transient complications. Two of the complications were related to pericardial effusion that was successfully drained with no recurrence. The last complication was phrenic nerve injury in a patient who showed complete recovery 4 month after the procedure.

Conclusions: Long-term results of atrial fibrillation ablation at Unity Point Health Methodist showed safety and efficacy of the program in the treatment of symptomatic atrial fibrillation in both paroxysmal and persistent groups.

Introduction

Catheter ablation of atrial fibrillation (AF) has become an established therapeutic modality for the treatment of patients with symptomatic AF. Studies reporting outcomes of AF ablation have predominantly limited follow-up to 1 to 2 years after the index ablation procedure.

Until recently, few series have presented the long-term outcomes of AF ablation at ≥3 years of follow-up. In the current study, we evaluated the long-term single- and multiple-procedure efficacy of AF ablation done at a single center (Unity Point Health Methodist in Peoria).

Our atrial fibrillation program started in January 2010, and along with electrophysiologist Dr. Adel Mina, it is supported by 6 cardiologists from Methodist Medical, 2 cardiovascular surgeons, 5 EP lab staff personnel, and 2 supportive advanced practitioner personnel with strong collaborations with anesthesia, nursing and administrative staff.

Atrial fibrillation is a burden not only economically but quite burdensome to the patient’s quality of life. To date approximately 16.6% of strokes are originating from atrial fibrillation due to embolic phenomena. Adjusted mortality based on Framingham Heart Study is increased in patients who had atrial fibrillation. Furthermore, symptoms of atrial fibrillation along with side effects from rate control and antiarrhythmic medication often negatively affect the quality of life of patient.

Unity Point Health Methodist Medical Center is the first center in Peoria to start atrial fibrillation ablation program. Initiation of program required special consideration in terms of staff training, equipment update, other logistics in terms of implementing protocols and strict patient follow up for such detailed procedures.

Methods

Patients who had atrial fibrillation ablation between February 19th 2010 to September 26th 2014 were analyzed via chart reviews. Statistical analysis was performed. Also Ablation protocol is mentioned.

Atrial Fibrillation Ablation Procedure

Standard venous access using three 8 French sheaths were inserted into the right common femoral vein using ultrasound guidance.
Two transseptal punctures were done using Across system. This was done under intracardiac echo as well as fluoroscopy guidance. This was also continued to be monitored with hemodynamic guidance. SafeSept wire was used to avoid through and through punctures.

A spiral catheter was used to obtain electroanatomical mapping of the left atrium which was later merged with CT imaging anatomy.

Esophageal temperature probe was advanced into the esophagus and intermittently repositioned in close proximity to the ablating catheter. This was important to evaluate change in temperature during ablation. Any significant rise of more than 0.5°C was enough to consider lowering the wattage output, as well as moving to another area. Power was titrated at 20 watts with an irrigation catheter in areas close to the esophagus.

All patients had pulmonary vein antral isolation, care was taken to insure entrance and exit block from the pulmonary veins, later during the last year care was also given to achieve delayed signal into the veins prior to complete isolation. Multiple substrate modifications including left atrial roof line, mitral annular line and cavotricuspid isthmus line, other lines and complex fractionated atrial electrograms were also targeted in patients with persistent or long lasting persistent atrial fibrillation.

Anticoagulation was done with heparin bolus, as well as drip to maintain ACT more than 350 and less than 400, frequent ACTs were checked every 15 minutes, and heparin readjusted until ACTs remained stable.

Left atrial pressure, as well as patient’s inputs and outputs were continuously monitored throughout the procedure. Ablation done using saline irrigation catheters with power of 35 watts except for areas close to the esophagus or inside the veins it was titrated to 20 watts. Care was done to avoid ablation inside veins and rather to isolate veins just outside the os.

After ablation, if the patient continued to have atrial fibrillation, DC cardioversion was done.

Isuprel started in all patients with decremental atrial pacing down to cycle length of 200. Patients with inducible atrial fibrillation or

Likewise, a 9 French sheath into the left common femoral vein and a 7 French sheath into the right internal jugular vein.

Transesophageal echocardiogram had been done prior to the procedure as well as a 64 slice CAT scan. Anatomy obtained from both modalities was integrated with electroanatomical mapping anatomy obtained from EnSite Velocity System.

Anticoagulation was done by keeping patients on Coumadin. Target INR between 2 and 3 before the procedure, as well as after the procedure for at least 3 months. Periodic INRs were done before and after the procedure.

General anesthesia with hemodynamic monitoring was done in all patients with the anesthesia team. Arterial lines were inserted through the femoral arteries to confirm hemodynamic stability.

AcuNav intracardiac echocardiogram 8 French was inserted into the left common femoral vein and placed into the right atrium, it was used to monitor transeptal puncture as well as confirming catheter stability and position, it was also used to evaluate contact of catheter during ablation and to provide safety guards for early detection of complications.

Duodecapolar catheters were inserted through the right internal jugular vein into the coronary sinus with the proximal poles in the high right atrium. Right ventricular quadripolar catheter inserted into the right ventricle.

Table 1: Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Total Number of Patients</th>
<th>53</th>
</tr>
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<tbody>
<tr>
<td>Mean AGE</td>
<td>66.22+/- 10.8</td>
</tr>
<tr>
<td>MALE</td>
<td>33</td>
</tr>
<tr>
<td>FEMALE</td>
<td>20</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10</td>
</tr>
<tr>
<td>CAD</td>
<td>4</td>
</tr>
<tr>
<td>Left Atria AP diameter (mm)</td>
<td>41 +/-5</td>
</tr>
<tr>
<td>LVEF %</td>
<td>55%+/-8</td>
</tr>
<tr>
<td>CHADS2/VASC Score</td>
<td>2.13</td>
</tr>
<tr>
<td>Number of Prior Drugs Failed</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Failure more than 1 Antiarrhythmic</td>
<td>14</td>
</tr>
<tr>
<td>Efficacy Failed AF drugs</td>
<td></td>
</tr>
<tr>
<td>Flecainide</td>
<td>5</td>
</tr>
<tr>
<td>Propafenone</td>
<td>2</td>
</tr>
<tr>
<td>Sotalol</td>
<td>36</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>1</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>23</td>
</tr>
<tr>
<td>Multaq</td>
<td>9</td>
</tr>
<tr>
<td>Anticoagulation &gt;3 months Post Procedure</td>
<td></td>
</tr>
<tr>
<td>Coumadin</td>
<td>25</td>
</tr>
<tr>
<td>ASA</td>
<td>17</td>
</tr>
<tr>
<td>Pradaxa</td>
<td>6</td>
</tr>
<tr>
<td>Eliquis</td>
<td>3</td>
</tr>
<tr>
<td>Xarelto</td>
<td>4</td>
</tr>
</tbody>
</table>

Figure 1: Freedom from AF for both paroxysmal and persistent groups after single and multiple procedures

Percent Freedom from AF post ablation

<table>
<thead>
<tr>
<th></th>
<th>1=PAF single procedure success rate</th>
<th>2= PAF multiple procedures success rate</th>
<th>3=Persistent AF single procedure success rate</th>
<th>4=Persistent AF multiple procedures success rate</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>80.6</td>
<td>91.4</td>
<td>76.5</td>
<td>96.1</td>
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Table 2: Adverse Events

<table>
<thead>
<tr>
<th>Procedure Adverse Events</th>
<th>N=53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>0</td>
</tr>
<tr>
<td>TIA</td>
<td>0</td>
</tr>
<tr>
<td>Tamponade</td>
<td>2</td>
</tr>
<tr>
<td>MI</td>
<td>0</td>
</tr>
<tr>
<td>Hemorrhage Requiring transfusion</td>
<td>0</td>
</tr>
<tr>
<td>New Atrial Flutter</td>
<td>0</td>
</tr>
<tr>
<td>Esophageal Fistula</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
</tr>
<tr>
<td>Phrenic Nerve Injury</td>
<td>1</td>
</tr>
<tr>
<td>Ateriovenous Fistula</td>
<td>0</td>
</tr>
<tr>
<td>Pseudoaneurysm</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary Vein Stenosis</td>
<td>0</td>
</tr>
</tbody>
</table>

Adverse Events 77 out of 66 in multiple procedure 43 out of 40 in single procedure.

Multiple Procedure 0.00028 of 0.05 was considered significant. NS= Not-significant

Table 3: Clinical Outcome in correlation with baseline characteristics

<table>
<thead>
<tr>
<th>Clinical Variables</th>
<th>Paroxysmal AF(36 patients)</th>
<th>Persistent AF (17 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Recurrence</td>
<td>Single Procedure Recurrence</td>
</tr>
<tr>
<td>Number of Patients</td>
<td>29</td>
<td>7</td>
</tr>
<tr>
<td>Mean Age</td>
<td>68</td>
<td>63</td>
</tr>
<tr>
<td>Left Atrial AP</td>
<td>40</td>
<td>44</td>
</tr>
<tr>
<td>Diameter(mm)</td>
<td>57</td>
<td>51</td>
</tr>
</tbody>
</table>

P = P value comparing patients with no recurrence to single procedure recurrence in both paroxysmal and persistent groups. P<0.05 was considered significant. NS= Not-significant.

The present study confirmed the high success rate (94%) of circumferential PV ablation in a small cohort of patients with paroxysmal AF. It also confirmed a high success rate (94%) of circumferential PV ablation followed by multiple substrate modifications with persistent AF. Although most patients were free from structural heart disease we were able to still achieve good results in patients who are elderly and has multiple comorbidities.
Left atrial size did not seem to influence the outcome in paroxysmal AF patients or persistent AF patients may be related to small sample size and patient selection as most patients had no significant left atrial enlargement. Patient with lower ejection fraction were more likely to have recurrence in the paroxysmal group.

There were no significant difference in atrial size, age or ejection fraction between patients with paroxysmal and persistent atrial fibrillation. Patients with persistent AF were more likely to go for a second ablation than patients with paroxysmal AF, most of them related to atypical flutters that needed further substrate modifications.

Compared with other studies, the patients done at Unity Point Health Methodist were a somewhat older population. Despite the age difference, late outcome was highly favorable. Our long term success rate with single and multiple procedures in both paroxysmal and persistent AF patients are better than those reported in other long term follow up studies. This could be related to better patient selection, better technique, or smaller population sample.

Also our number of procedures per patient is 1.32 lower compared with 1.51 or 1.75 averages in other centers. Our fluoroscopy use is below other reported studies. We also had five patients who had their ablation procedure performed without use of any fluoroscopy.

Compared with our early outcome for atrial fibrillation ablation we noticed decrease in fluoroscopy time, improved success and lower rate of complications. These findings strengthen the development for new organized, well-structured atrial fibrillation ablation programs in underserved areas. Continued assessment and evaluation of the program will be essential to have continued success of maintaining the best outcome.

Limitations

There are some limitations of this study including, it is a single center experience with limited number of patients. There was potential for atrial fibrillation recurrence to be missed as the tools available to monitor the patient (Holters and event monitors) only allow for short windows of monitoring.

Conclusion

The data presented in this study showed encouraging rates of success at long-term follow-up with catheter ablation of AF. Long-term freedom from atrial arrhythmia was achievable in the majority of patients in our center.

Atrial fibrillation ablation program at Unity Point Health Methodist in Peoria is safe and effective for treatment of symptomatic atrial fibrillation. Our outcomes are favorable and comparable with other centers of excellence for AF ablation.

References

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Seasonal Variation in Paroxysmal Atrial Fibrillation: A Systematic Review

Rohit S. Loomba MD

Children's Hospital of Wisconsin/Medical College of Wisconsin, Milwaukee, WI.

Abstract

Introduction: A variety of cardiovascular diseases have been demonstrated to have seasonal variations with peaks in the winter and troughs in the summer. Studies regarding atrial fibrillation (AF) have had varying results and this review describes the current data regarding the seasonal variation of AF and mechanisms mediating this seasonal fluctuation.

Methods: A systematic review was conducted of PubMed, EBSCO and OVID for manuscripts describing the association between seasonal variation and the occurrence of AF. Studies meeting eligibility criteria were assessed for quality and reporting bias. Data was extracted in regards to the following associations: seasonal variation and AF paroxysms, temperature and AF paroxysms, duration of daylight and AF paroxysms, barometric pressure and AF paroxysms, alcohol and AF paroxysms, as well as seasonal variation and AF related stroke.

Results: A total of 15 studies were identified for inclusion. Of these, 11 studies assessed seasonal variation and the remaining 4 studies assessed seasonal variation in AF related stroke. AF paroxysms peaked in winter with a trough in summer. There was an inverse correlation between temperatures as well barometric pressure and the occurrence of AF paroxysms and a positive correlation with duration of daylight.

Conclusions: The rate of occurrence of paroxysmal AF varies by seasons and is greatest during winter and least in summer.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is responsible for a majority of arrhythmia-related hospitalizations. As the prevalence of AF continues to rise so does the number of related hospitalizations, morbidity, and mortality. AF mechanisms include atrial ectopy, single localized reentry circuits, or multiple microreentrant circuits, all of which can be influenced by genotype, ischemic heart disease and inflammation. Other risk factors include hyperthyroidism, obstructive sleep apnea and congenital heart disease. As the burden of AF begins to increase it is of utmost importance to identify all potential risk factors.

Multiple studies have demonstrated an association between seasonal variation and a variety of cardiac and non-cardiac disorders such as deep venous thrombosis, pulmonary embolism, aortic dissection, stroke, hypertension, congestive heart failure, angina, ventricular arrhythmias, myocardial infarction, and sudden cardiac arrest. Many of these diseases have been found to be more frequent in winter, with inverse correlations to outdoor temperature. Similar associations have been proposed for AF as well as AF related stroke.

The primary purpose of this review is to summarize data regarding the association between seasonal variation and occurrence of AF paroxysms. Secondary aims of this review were to summarize data regarding additional associations to further investigate the primary association:

1) outdoor temperature and occurrence of AF paroxysms.
2) duration of daylight and occurrence of AF paroxysms.
3) barometric pressure and occurrence of AF paroxysms.
4) alcohol consumption and occurrence of AF.
5) seasonal variation and the occurrence of AF related stroke.

Methods

A systematic review of the literature was performed to identify manuscripts studying the association between various seasons and AF. This included the occurrence of AF paroxysms, AF related stroke, and AF related mortality. The overall association of AF with the seasons, any particular month, temperature, amount of daylight, and barometric pressure were all studied. The review was conducted using the PRISMA checklist.

Manuscript Search And Identification Strategy

Electronic databases including PubMed, EMBASE, and Ovid were queried using the following search terms: "atrial fibrillation" in conjunction with one of the following “season”, “summer” or “winter”.

Disclosures:

None.

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9000 Wisconsin Avenue,
Milwaukee, WI, 53226.

Key Words:
Atrial Fibrillation, Season, Summer, Winter, Stroke, Death.
Table 1: Study characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Design</th>
<th>N</th>
<th>Endpoint</th>
<th>Parameters studied</th>
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<tbody>
<tr>
<td>Kupari et al</td>
<td>1990</td>
<td>Cohort, unclear if retrospective or prospective</td>
<td>286 patients</td>
<td>AF</td>
<td>Season, temperature, alcohol</td>
</tr>
<tr>
<td>Gluszak et al</td>
<td>2008</td>
<td>Cohort, unclear if retrospective or prospective</td>
<td>739 patients</td>
<td>AF</td>
<td>Season, barometric pressure</td>
</tr>
<tr>
<td>Watanabe et al</td>
<td>2007</td>
<td>Cohort, unclear if retrospective or prospective</td>
<td>237 patients</td>
<td>AF</td>
<td>Season, temperature, daylight</td>
</tr>
<tr>
<td>Gluszak et al</td>
<td>2009</td>
<td>Cohort, unclear if retrospective or prospective</td>
<td>1,475 patients</td>
<td>AF</td>
<td>Season, daylight</td>
</tr>
<tr>
<td>Kountouris et al</td>
<td>2005</td>
<td>Prospective cohort</td>
<td>342 patients</td>
<td>AF</td>
<td>Season, daylight</td>
</tr>
<tr>
<td>Frost et al</td>
<td>2002</td>
<td>Retrospective cohort</td>
<td>32,992 patients</td>
<td>AF</td>
<td>Season, temperature</td>
</tr>
<tr>
<td>Deshmukh et al</td>
<td>2013</td>
<td>Retrospective cohort</td>
<td>2,909,423 hospitalizations</td>
<td>AF</td>
<td>Season</td>
</tr>
<tr>
<td>Kiu et al</td>
<td>2004</td>
<td>Retrospective cohort</td>
<td>24 patients</td>
<td>AF</td>
<td>Season</td>
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<tr>
<td>Upshur et al</td>
<td>2004</td>
<td>Retrospective cohort</td>
<td>90,200 hospitalizations</td>
<td>AF</td>
<td>Season</td>
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<tr>
<td>Fustinoni et al</td>
<td>2013</td>
<td>Retrospective cohort</td>
<td>899 patients</td>
<td>AF</td>
<td>Season, temperature</td>
</tr>
<tr>
<td>Murphy et al</td>
<td>2004</td>
<td>Retrospective cohort</td>
<td>68,045 hospitalizations</td>
<td>AF</td>
<td>Season, temperature</td>
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<tr>
<td>Christensen et al</td>
<td>2012</td>
<td>Retrospective cohort</td>
<td>39,632 patients</td>
<td>Stroke in AF</td>
<td>Season</td>
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<tr>
<td>Christensen et al</td>
<td>2012</td>
<td>Retrospective cohort</td>
<td>36,088 patients</td>
<td>Stroke in AF</td>
<td>Season</td>
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<tr>
<td>Frost et al</td>
<td>2006</td>
<td>Retrospective cohort</td>
<td>24,470 patients</td>
<td>Stroke in AF</td>
<td>Season</td>
</tr>
<tr>
<td>Spengos et al</td>
<td>2003</td>
<td>Retrospective cohort</td>
<td>315 patients</td>
<td>Stroke in AF</td>
<td>Season</td>
</tr>
</tbody>
</table>

No specific restriction on year of publication was used. Two reviewers (RL and SA) screened the resulting studies by title and abstract. Full text of the selected studies meeting eligibility criteria was then retrieved in their entirety. Further, references of these studies were hand searched for additional relevant manuscripts. Studies in a language other than English were excluded.

Published manuscripts available in full text were included in this review if they presented data from retrospective or prospective cohort studies or randomized controlled trials investigating the occurrence of AF paroxysms, AF related stroke, and AF related death and their association with season, calendar month, temperature, amount of daylight, and barometric pressure. Studies were included in this analysis if they included at least one of the factors identified above.

Authors RL and SA then reviewed these full text manuscripts for quality. Any disparities in scoring of manuscripts were then independently reviewed by another author. The Newcastle-Ottawa scale and Critical Appraisal Skills Programme (CASP) checklist were used to assess the quality of cohort studies.

Data Extraction

Data regarding baseline patient characteristics and outcomes were extracted from the manuscripts identified for inclusion. Study level data were independently collected with use of a data collection tool. The data extraction was then reviewed to ensure integrity of the resulting data. If no information was available about particular outcomes this was designated separately. Authors of included studies were not contacted for additional data.

Bias Analysis

Bias was assessed concurrently with quality assessment of studies using the Newcastle-Ottawa scale and CASP checklist for cohort studies as described above.

Data analysis

No quantitative data analysis was performed.

Results

Study Identification

Using the search terms as described above 96 unique manuscripts were identified. Of these papers, 12 focused on stroke in AF and 84 of these were not related to stroke in AF. Ultimately, quantitative data were extracted from 15 studies after inclusion of only cohort studies and randomized trials, 4 of which focused on stroke in AF and 11 of which were not related to stroke in AF (Figure 1).21

Study Characteristics

All 15 studies from which quantitative data were extracted from were cohort studies. Of these studies, 8 were retrospective and 1 was prospective. For the 6 remaining studies it was unclear whether these were retrospective or prospective. Of the 11 non-stroke related AF studies, 5 were retrospective, 1 prospective, and 5 unknown. Of the 4 stroke related studies, all were retrospective (Table 1).

The 11 non stroke related AF studies consisted of 36,994 patients. Two studies did not report patient number but rather hospitalizations, which consisted of 3,067,668 hospitalizations. Three of these studies were registry based studies while the remainder were retrospective or prospective.

No specific restriction on year of publication was used. Two reviewers (RL and SA) screened the resulting studies by title and abstract. Full text of the selected studies meeting eligibility criteria was then retrieved in their entirety. Further, references of these studies were hand searched for additional relevant manuscripts. Studies in a language other than English were excluded.

Published manuscripts available in full text were included in this review if they presented data from retrospective or prospective cohort studies or randomized controlled trials investigating the occurrence of AF paroxysms, AF related stroke, and AF related death and their association with season, calendar month, temperature, amount of daylight, and barometric pressure. Studies were included in this analysis if they included at least one of the factors identified above.

Authors RL and SA then reviewed these full text manuscripts for quality. Any disparities in scoring of manuscripts were then independently reviewed by another author. The Newcastle-Ottawa scale and Critical Appraisal Skills Programme (CASP) checklist were used to assess the quality of cohort studies.

Data Extraction

Data regarding baseline patient characteristics and outcomes were extracted from the manuscripts identified for inclusion. Study level data were independently collected with use of a data collection tool. The data extraction was then reviewed to ensure integrity of the resulting data. If no information was available about particular outcomes this was designated separately. Authors of included studies were not contacted for additional data.
prospective cohort studies. Two of these studies reported incidence rate only, 1 study reported prevalence rate only and 8 studies reported both incidence and prevalence rates.7-17

The 4 stroke related AF studies consisted of 100,505 patients. All 4 of these studies were registry based studies. All 4 of these studies reported incidence rates.18-21

Association Data
Data regarding particular associations were extracted from the following number of studies: seasonal variation and occurrence of AF paroxysms from 11 studies, outdoor temperature and occurrence of AF paroxysms from 6 studies, duration of daylight and occurrence of AF paroxysms from 2 studies, barometric pressure and occurrence of AF paroxysms from 1 study, duration of alcohol and occurrence of AF paroxysms from 1 study, and seasonal variation and occurrence of AF related stroke from 4 studies.

Bias and Quality
Subjective analysis of bias with respect to patient selection, patient allocation, blinding, and outcome reporting showed minimal overall bias amongst the included studies. Quality assessment is outlined in Table 2.

Seasonal Variation And The Occurrence Of AF Paroxysms
Of the studies that analyzed the association between seasonal variation and the occurrence of AF paroxysms, 10 (91%) demonstrated an association between the seasons and AF paroxysms. All 10 of these studies demonstrated peak occurrence of AF paroxysms in winter with a nadir in summer with a 20% to 300% increase in the rate of AF paroxysms during the winter peak when compared to the summer nadir. February and April were both identified by 33% of studies as the peak months while July was identified by 42% of studies as the nadir month.7,15,17 Murphy et al. also demonstrated a 15% to 26% increased risk of AF related mortality during winter.15 (Table 3).

Outdoor Temperature And The Occurrence Of AF Paroxysms
Of the studies that analyzed the association between outdoor temperature and the occurrence of AF, 3 (50%) of these studies demonstrated an association between outdoor temperature and AF paroxysms.8,13,15,16 The studies that demonstrated an association found an inverse correlation between temperature and AF paroxysms.8,12,15 Again, the study by Murphy et al. demonstrated a 5% increased risk of inpatient mortality but no increase in outpatient mortality.13 (Table 3).

Duration Of Daylight And The Occurrence Of AF Paroxysms
Two studies investigated the association between duration of daylight and the occurrence of AF paroxysms. Watanabe et al. demonstrated a strong inverse correlation while Gluszak et al. noted such an inverse correlation in women but not in men.11,17 (Table 3).

Barometric Pressure and the Occurrence of AF Paroxysms
A single study investigated the association between barometric pressure and the occurrence of AF paroxysms and noted that the risk of AF paroxysms was greatest 24 to 48 hours before the arrival of a low pressure front.7 (Table 3). Further details were not provided.

Alcohol And The Occurrence Of AF Paroxysms
Kupari et al. demonstrated a positive correlation between alcohol sales and the occurrence of AF paroxysms, with both being highest in April.12 (Table 3). Further details were not provided.

Seasonal Variation And AF Related Stroke
All the studies that investigated the association between seasonal variation and AF related stroke demonstrated highest risk in winter with the lowest risk in summer. There was a 22% to 200% increase in the risk of AF related stroke in the winter compared to summer.18-21 There was no association between seasonal variation and mortality after AF related stroke.20 (Table 3).

Discussion
In our analysis, a majority of studies demonstrated an association between seasonal variation and the occurrence of AF paroxysms. AF paroxysms were most frequent during winter and early spring and least frequent in the summer with peak months being February and April. The nadir of AF paroxysms was observed to be in the month of July. It is reasonable to imagine that stroke, a complication of AF,

### Table 2: Study quality and bias evaluation

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline patient characteristics described</th>
<th>Patient selection</th>
<th>Allocation Concealment</th>
<th>Blinding</th>
<th>Incomplete Outcome Data</th>
<th>Free of Selective Outcome Reporting</th>
<th>Other Bias</th>
<th>Newcastle-Ottawa Score</th>
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<tbody>
<tr>
<td>Kupari et al</td>
<td>yes</td>
<td>moderate</td>
<td>n/a</td>
<td>n/a</td>
<td>low</td>
<td>low</td>
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<tr>
<td>Gluszak et al (2008)</td>
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<td>moderate</td>
<td>n/a</td>
<td>n/a</td>
<td>low</td>
<td>low</td>
<td>low</td>
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<tr>
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<td>low</td>
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<td>n/a</td>
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<td>low</td>
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<tr>
<td>Gluszak et al (2009)</td>
<td>yes</td>
<td>moderate</td>
<td>n/a</td>
<td>n/a</td>
<td>low</td>
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<td>low</td>
<td>8</td>
</tr>
<tr>
<td>Kountouris et al</td>
<td>yes</td>
<td>moderate</td>
<td>n/a</td>
<td>n/a</td>
<td>low</td>
<td>low</td>
<td>low</td>
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<tr>
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<td>moderate</td>
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<td>n/a</td>
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</tr>
<tr>
<td>Deshmukh et al</td>
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<td>moderate</td>
<td>n/a</td>
<td>n/a</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>7</td>
</tr>
<tr>
<td>Kiu et al</td>
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<td>moderate</td>
<td>n/a</td>
<td>n/a</td>
<td>low</td>
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<tr>
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<td>moderate</td>
<td>n/a</td>
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<tr>
<td>Murphy et al</td>
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<td>n/a</td>
<td>n/a</td>
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<td>n/a</td>
<td>low</td>
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<td>8</td>
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<tr>
<td>Christensen et al (2012)</td>
<td>yes</td>
<td>moderate</td>
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<td>n/a</td>
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<td>n/a</td>
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<td>Spengos et al</td>
<td>no</td>
<td>moderate</td>
<td>n/a</td>
<td>n/a</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>8</td>
</tr>
</tbody>
</table>

*Must have described at least gender and age
would be more frequent at times of greatest AF burden and thus studies investigating seasonal variation and AF related stroke were also reviewed which demonstrated highest frequency of AF related stroke during the winter and the lowest during summer. Mortality during AF hospitalizations also appears to be greatest in winter while inpatient mortality during AF related stroke hospitalizations does not appear to be affected by seasonal variation.\(^7\,15,17,20\)

Several mechanisms have been proposed to explain the increased risk of AF paroxysms in winter with lower temperatures being the common denominator. Lower temperatures have been demonstrated to enhance sympathetic function by activation of central angiotensin or hypothalamic mineralocorticoid receptors, which can increase the risk of AF.\(^22-25\) Blood pressure can also increase due to lower temperatures, which can ultimately lead to increased atrial pressure with subsequent atrial dilatation and pulmonary vein stretch leading to initiation and propagation of AF.\(^26-28\) Endothelin I, renin, and angiotensin II levels may increase due to lower temperatures, which can also enhance arrhythmogenesis.\(^29-32\) Cold temperatures may worsen atrial ischemia and promote glucose intolerance, both of which may increase the risk of AF paroxysms.\(^33\) Our review demonstrates equivocal results regarding the association between temperature and the occurrence of AF paroxysms.

Duration of daylight has also been proposed as a mechanism to explain the increased risk of AF paroxysms in winter. Yamashita et al. have demonstrated circadian variation in the expression of potassium channels, particularly that decreased exposure to sunlight can lead to alterations in cardiac ion channels such that action potentials shorten, increasing the risk of reentrant arrhythmias such as AF.\(^34\) The role of Vitamin D, a vitamin whose synthesis is dependent upon exposure to sunlight, in the setting of this particular association has also been investigated and it appears that Vitamin D does not mediate this phenomenon. Vitamin D does not appear to have a role in this interaction.\(^35\)

Barometric pressure may be another factor mediating the effects of seasonal variation on the occurrence of AF paroxysms. Gluszak et al. demonstrated that barometric pressure, specifically low pressure fronts, increases the risk of AF paroxysms. Interestingly, risk was greatest 24 to 48 hours before the actual change in barometric pressure.\(^7\) This temporal finding was consistent with previously reported findings from a study by Delyukov et al. that demonstrated negative effects of changes in barometric pressure on cardiovascular function preceding arrival of the atmospheric front by 3 to 24 hours.\(^34\) The timing of the effects of low pressure fronts on physiologic changes may be due to alterations in the electrical field that occur before arrival of the atmospheric front.

Alcohol consumption may also play a part in the increased occurrence of AF paroxysms in the winter. Kupari et al. investigated and found a positive correlation between alcohol sales and the occurrence of AF paroxysms. Actual alcohol consumption, however, was not directly assessed in this study and alcohol sales were used as a surrogate.\(^12\) This association remains unclear.

Other factors that may contribute to the association between seasonal variation and the occurrence of AF paroxysms include the increased burden of respiratory infections and chronic obstructive pulmonary disease in the winter, which can trigger AF. These factors, although possible AF triggers, may also confound the association between seasonal variation and occurrence of AF paroxysms as asymptomatic AF may be detected more frequently in the winter due to an increased number of hospitalizations for these other reasons. Additionally, heart failure and sepsis, which are also more frequent in winter, may attribute to the greater risk of AF in winter.\(^6\)

The risk of AF-related stroke peaks during winter season and nadirs in summer. This is likely due to previously documented seasonal variations in fibrin, fibrinogen, and factor VII.\(^35,36\) Additionally, cold temperatures increase erythrocyte and platelet count, increasing blood viscosity and subsequent risk of thrombus formation.\(^37\) Whether prescription of therapy or compliance rates with treatment have any role remains unclear. This association is important to note as care providers should stress the importance of monitoring and controlling blood pressure, activity level, and avoiding infections

### Table 3: Study results

<table>
<thead>
<tr>
<th>Study</th>
<th>Seasonal association</th>
<th>Peak season</th>
<th>Trough season</th>
<th>Peak month</th>
<th>Trough month</th>
<th>Temperature association</th>
<th>Daylight association</th>
<th>Pressure association</th>
<th>Alcohol association</th>
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<td>Late spring and summer</td>
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<td>July</td>
<td>Yes</td>
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<td>--</td>
<td>Yes</td>
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<tr>
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<td>Yes</td>
<td>Winter</td>
<td>Summer</td>
<td>February</td>
<td>July</td>
<td>Yes</td>
<td>No</td>
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<td>Fall</td>
<td>Summer</td>
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<td>Summer</td>
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<td>No</td>
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<tr>
<td>Frost et al (2002)</td>
<td>Yes</td>
<td>Winter</td>
<td>Summer</td>
<td>February</td>
<td>July</td>
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<tr>
<td>Deshmukh et al</td>
<td>Yes</td>
<td>Winter</td>
<td>Summer</td>
<td>February</td>
<td>July</td>
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<tr>
<td>Kiu et al</td>
<td>Yes</td>
<td>Winter</td>
<td>Summer</td>
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<tr>
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<td>Yes</td>
<td>Spring</td>
<td>Summer</td>
<td>April</td>
<td>August</td>
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<tr>
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<td>Fall and winter</td>
<td>Spring and summer</td>
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<td>Murphy et al</td>
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<td>Winter</td>
<td>Summer</td>
<td>December</td>
<td>July</td>
<td>No</td>
<td>--</td>
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<td>--</td>
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<tr>
<td>Christensen et al (2012)</td>
<td>Yes</td>
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<td>Summer</td>
<td>February</td>
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<td>Yes</td>
<td>Winter</td>
<td>Summer</td>
<td>December and january</td>
<td>August</td>
<td>--</td>
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in those with already known AF as the winter season approaches. Those with hypertension should be advised to ensure compliance with current therapy and blood pressure should be closely monitored. All patients should be encouraged to maintain appropriate activity levels and exercise during the winter, a season often associated with decrease in activity. Those with AF should be particularly encouraged to obtain the influenza vaccination during winter as this has been demonstrated to reduce cardiovascular and all-cause mortality and may help prevent infection induced AF.

Notwithstanding, patients with AF need to be counseled on the fore-mentioned things all-round the year but especially in winter season.

The strengths of reviewed studies include the large sample size of some of these studies, particularly those based on registry data. Some of the included studies also studied not only the seasonal variation and occurrence of AF paroxysms but also investigated potential factors mediating this association such as temperature, duration of daylight, and barometric pressure. Limitations of reviewed studies include that all but 1 study captured only those hospitalized for AF or those who had AF while hospitalized for other reasons. This allows for missing “milder” or asymptomatic cases. Additionally, some studies were not able to distinguish between incident and prevalent cases. Some reviewed studies also only included AF that was coded as the primary diagnosis and may have ignored cases with AF coded as the secondary or tertiary diagnosis. The use of discharge records also brings into question the reliability of discharge diagnosis, which may not always be accurate. Caution should also be exercised in determining causality due to the retrospective nature of majority of these studies.

Our study has the inherent limitations of a systematic review. We did not have access to patient level data, hence some important endpoints like medication adherence and other comorbidities could not be assessed. Due to lack of similar definitions across studies, quantitative analysis could not be performed. We are unable to make firm conclusions on most endpoints due to very low number of studies for those endpoints. Large prospective studies are needed to further clarify this potential association.

**Conclusions:**

There is an association between seasonal variation and the occurrence of AF paroxysms with the greatest risk being during winter and early spring and the nadir being in summer. Temperature, duration of daylight, and barometric pressure are thought to mediate this seasonal fluctuation in AF occurrence.

**References**


10. Upshur RE, Moineddin R, Crighton EJ, Mandani M. Is there a clinically significant seasonal component to hospital admissions for atrial fibrillation? BMC health services research 2004;4:5.


Improved Resource Utilization With Similar Efficacy During Early Adoption of Cryoballoon Pulmonary Vein Isolation as Compared to Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

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Hospital and Academic Affiliations: Center for Atrial Fibrillation, Heart and Vascular Institute, University of Pittsburgh Medical Center, Pittsburgh, PA.

Abstract

Background: Cryoballoon pulmonary vein isolation (PVI) is an alternative to radiofrequency (RF) PVI for the treatment of paroxysmal atrial fibrillation (AF). Treatment effect, complication rates, and hospital length of stay are not well established with early use of cryoballoon PVI as compared to more experienced performance of RF PVI.

Methods: We reviewed the early experience of cryoballoon PVIs for paroxysmal AF performed by 3 operators at our institution compared to their most recent RF PVIs. All repeat procedures were excluded. Patients were assessed for recurrence of AF at 6 months after the procedure, including a 3-month blanking period. Complications, procedure time, and hospital length of stay were recorded.

Results: Final analysis included 50 cryoballoon PVIs and 50 RF PVIs. There was no significant difference in baseline characteristics or percentage of patients wearing a home monitor (80% for cryoballoon vs 80% for RF). Symptomatic improvement was experienced by 96% of cryoballoon PVI as compared to 86% of RF PVI patients (p=0.08). Freedom from AF at 6 months was similar between the two groups (70% for cryoballoon and 70% for RF, p=1). Complications were seen in 6% of cryoballoon procedures as compared to 10% of RF procedures (p=0.46). Hospital length of stay was significantly shorter in the cryoballoon group (1.6 vs 3.4 nights, p=0.003).

Conclusions: At the time of its adoption, cryoballoon PVI is associated with shorter procedure times and hospital length of stay as compared to RF PVI in experienced operators while maintaining similar efficacy outcomes and complication rates.

Introduction

It has been previously shown by Haisseguerre et al that the main trigger for paroxysmal atrial fibrillation (PAF) is ectopy arising from within the pulmonary veins. Ablation therapy for PAF has therefore focused on the electrical isolation of the pulmonary veins. This has traditionally been performed using radiofrequency (RF) catheter ablation with a point-by-point technique. Cryoballoon ablation has more recently become available as a method to achieve pulmonary vein isolation (PVI) en bloc. The potential advantages of cryoballoon PVI include shorter procedure times and quicker learning curve, however the published experience is limited in this regard and it is not entirely clear if these potential gains are at the cost of efficacy. We therefore examined the comparative efficacy, complications, procedure time, and hospital length of stay of RF and cryoballoon for PVI during its initial adoption at our center.

Material and Methods

Consecutive patients undergoing cryoballoon PVI procedures for symptomatic PAF by three operators at the University of Pittsburgh Medical Center were identified from August 2011 to March 2013 including the first cases in the learning curve of this procedure. As a comparison group, consecutive RF PVI procedures by the same operators were selected from June 2009 to August 2011. All patients had symptomatic PAF, which was defined as self-terminating atrial fibrillation lasting no longer than 7 days, and not having previously required cardioversion. Patients with persistent or permanent atrial fibrillation were excluded. Patients were also excluded with insufficient follow-up or if they had previously undergone pulmonary vein isolation by any technique. Patient follow-up was as per standard protocol with outpatient visits at 6 weeks, 3 months and 6 months post-ablation. Retrospective chart review was performed to assess clinical outcomes through 6 months post-procedure. Recurrence was defined as an episode of an atrial arrhythmia (atrial fibrillation, atrial tachycardia, atrial flutter) lasting > 30 seconds on event monitoring or a recurrence of typical symptoms, if not captured on monitoring. Persistent phrenic nerve injury (PNI) was defined as still present at the end of the procedure. Hospital length of stay (LOS) was defined as the number of nights the patient was hospitalized after...
All patients underwent cardiac CT to assess the pulmonary vein anatomy as well as transeosophageal echocardiogram to exclude the presence of left atrial thrombus either the day before or the morning of the procedure. Most patients underwent a follow-up transthoracic echocardiogram on the evening of the procedure or the next day. Periprocedural anticoagulation was managed as per physician discretion.

All ablation procedures were performed under general anesthesia and paralytics were avoided post induction during cryoballoon ablations to allow monitoring of phrenic nerve function. The cryoballoon pulmonary vein isolation procedure has been previously described in detail,4,5,6 but will be briefly reviewed here. All cases were performed using the Arctic Front cryoballoon (Medtronic, Inc, Minneapolis, Minnesota). Single and double transseptal punctures were performed but after initial learning curve, most cryoballoon cases were performed with a single transseptal approach. For most cases, after occlusive venogram, two 240 second lesions were applied in each pulmonary vein and additional cryoballoon or RF lesions were applied if conduction persisted until isolation was confirmed by elimination or dissociation of pulmonary vein potentials and high output pacing within the pulmonary veins. For the right-sided pulmonary veins, high-output pacing was performed from the superior vena cava to monitor phrenic nerve function and ablation was immediately terminated with any decreased diaphragmatic excursion.

The radiofrequency pulmonary vein isolation has also been described previously in detail,7,8 but the technique utilized is briefly summarized here. All procedures were performed utilizing jet ventilation. Double transseptal puncture was performed and a 3.5mm open irrigation ablation catheter (NaviStar Thermocool Irrigated Tip Catheter; Biosense Webster, Inc, Diamond Bar, California) was utilized with 3D electroanatomic mapping with the Carto system (Biosense Webster). A 9MHz intracardiac echocardiography catheter was placed in the left atrium through the second transseptal site to allow continuous visualization of the ablation catheter position and tissue contact. RF energy was delivered at a maximum of 30W, and limited to 25W during applications in the posterior left atrial wall. Two encircling ablation lesion sets were created to isolate the left and right pulmonary venous vestibules, respectively. Electrical isolation was confirmed by high output pacing within the pulmonary veins. No additional left atrial lines or complex fractionated electrograms were targeted.

All continuous variables were reported as mean +/- standard deviation. Statistically significant differences between the two groups were defined as a p-value < 0.05. P-values for continuous variables were determined by the Student’s t-test. For discrete variables, p-values were calculated using chi-square. Multivariate analysis using binary logistic regression was performed in the analysis of hospital length of stay. The primary endpoint of the study was occurrence of atrial fibrillation at 6 months post-procedure. The secondary endpoints were procedural complications, procedure time, fluoroscopy time, and hospital length of stay.

### Results

Patients were selected from a pool of 77 consecutive cryoballoon PVIs and 62 RF PVIs for PAF. Eight redo PVIs were excluded from each group, as well as those with insufficient follow-up (N=19 cryoballoon PVIs, 4 RF PVIs), leading to 50 patients in each group. The baseline characteristics of the two groups are shown in Table 1.

CT revealed conventional pulmonary vein anatomy in 39/50 (78%) cryoballoon cases and 36/49 (73%) RF PVI cases. CT scan was not available in one RF PVI patient. A common left pulmonary vein trunk was found in 7 cryoballoon and 7 RF PVI cases. An accessory right pulmonary vein os was found in 3 cryoballoon and 3 RF PVI patients. One cryoballoon and 3 RF PVI patients had both a common left pulmonary vein trunk and an accessory right pulmonary vein os.

The first generation balloon was used in 66% of cryoballoon cases, while the remaining 34% of cases used the second generation balloon. Touch-up RFA was utilized in 6/33 (18%) cases with the first generation balloon and 2/17 (12%) cases with the second generation balloon. Cavo-tricuspid isthmus ablation for right atrial flutter was performed in 2 cases.

Pulmonary vein isolation was confirmed in 49 of 50 cryoballoon cases (98%). In the unconfirmed case, isolation was confirmed in all veins except the right inferior pulmonary vein. In this vein, transseptal access was lost after one 4-minute freeze cycle, and was not reestablished. PVI was confirmed in 48 of 50 RF cases (96%). In one case, isolation was confirmed in the left veins, however the patient developed tamponade, and the case was ended before any ablation of the right veins. In the other case, isolation was confirmed in the left veins, however there were significant technical challenges during ablation of the right veins, and the case was terminated after transseptal access was lost for a third time.

Procedural results are summarized in Table 2. Procedure time was available for 31/50 (62%) cryoballoon procedures and 32/50 (64%) RF procedures. Mean procedure time was 2.7 hours for cryoballoon PVI compared to 4.8 hours for RF PVI (p<0.001). The fluoroscopy time was available for 49/50 (98%) cryoballoon procedures and 49/50

---

### Table 1: Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cryo</th>
<th>RF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58±10</td>
<td>55±11</td>
<td>0.24</td>
</tr>
<tr>
<td>Male</td>
<td>39 (78%)</td>
<td>34 (68%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Hypertension</td>
<td>31 (62%)</td>
<td>26 (52%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>4 (8%)</td>
<td>0 (0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10 (20%)</td>
<td>4 (8%)</td>
<td>0.08</td>
</tr>
<tr>
<td>CHADS2</td>
<td>1.0±0.9</td>
<td>0.6±0.7</td>
<td>0.02</td>
</tr>
<tr>
<td>CHADS2-VASc</td>
<td>1.6±1.3</td>
<td>1.3±1.2</td>
<td>0.29</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>59±2.8</td>
<td>58±2.5</td>
<td>0.38</td>
</tr>
<tr>
<td>Left atrial size (cm)</td>
<td>4.1±0.6</td>
<td>4.0±0.7</td>
<td>0.52</td>
</tr>
<tr>
<td>AF duration (months)</td>
<td>38±45</td>
<td>56±78</td>
<td>0.16</td>
</tr>
<tr>
<td># previous AADs</td>
<td>1.3±0.7</td>
<td>1.4±1.1</td>
<td>0.41</td>
</tr>
<tr>
<td>Prior AAD use</td>
<td>45 (90%)</td>
<td>45 (90%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Prior amiodarone use</td>
<td>5 (10%)</td>
<td>6 (12%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Warfarin use</td>
<td>17 (34%)</td>
<td>36 (72%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
The mean fluoroscopy time was 46 minutes for cryoballoon PVI and 45 minutes for RF PVI (p=0.84). Contrast usage was available for 31/50 (62%) cryoballoon procedures, and an average of 49cc of contrast was used during cryoballoon PVI, while no contrast was used for RF PVI.

During the follow-up period, home monitors were worn by 40/50 (80%) patients after cryoballoon ablation, and 40/50 (80%) patients after radiofrequency ablation, including one patient in each group with a permanent pacemaker. An additional 3 patients in each group did not wear a monitor due to documented recurrence of AF on EKG. Therefore, 7 patients in each group (14%) did not wear a monitor to document the absence of recurrent AF. The patients wore the monitors for an average of 21 days in the cryoballoon group and 18 days in the RF group (p=0.3). The monitors were placed an average of 165 days after cryoballoon PVI and 168 days after RF PVI (p=0.7).

Freedom from atrial fibrillation at 6 months was achieved in 35/50 (70%) patients after cryoballoon PVI and 35/50 (70%) patients after RF PVI after a 3-month blanking period. Patient-reported symptomatic benefit was observed in 48/50 (96%) cryoballoon patients and 43/50 (86%) RF patients (p=0.08). Patients undergoing cryoballoon PVI using the first generation cryoballoon had AF recurrence in 12/33 (36%) as compared to 3/17 (18%) for the second generation balloon (p=0.17).

Following the procedure, 17/50 (34%) cryoballoon PVI and 10/50 (20%) RF PVI patients were not on antiarrhythmic medications (AADs) at any point during the follow-up period (p=0.11). Patients were on AADs for an average of 9.4 weeks after cryoballoon PVI and 11.7 weeks after RF PVI (p=0.2). At 6 months, 13/50 (26%) cryoballoon and 15/50 (30%) RF PVI patients were on AADs (p=0.7). Amongst the patients who did not have any recurrence of AF, 6/35 (17%) cryoballoon and 6/35 (17%) RF PVI patients were on AADs at 6 months.

There were 3 (6%) complications in the cryoballoon group (one groin bleed and 2 persistent PNIs) and 5 (10%) complications in the RF group (right buttock hematoma, prolonged respiratory failure, femoral pseudoaneurysm, cardiac tamponade, and persistent PNI). There was no significant difference in the complication rate between the 2 procedures (p=0.46). The two persistent PNIs following cryoballoon PVI resolved within two months after the procedure, although the one PNI after RF PVI persisted through the follow-up period.

The average LOS following cryoballoon PVI was 1.6 nights as compared to 3.4 nights after RF PVI (p=0.003). Removing one outlier from the RF group (LOS = 29 days), the mean LOS after RF PVI decreases to 2.9 nights, which remained significantly greater than for cryoballoon PVI (p<0.001). Four out of 50 (8%) cryoballoon PVI patients spent more than 2 nights in the hospital post-procedure as compared to 24/50 (48%) RF PVI patients (p<0.001). Fewer cryoballoon than RF PVI patients were anticoagulated with warfarin (34% vs 72%, p<0.001). Using binary logistic regression, cryoballoon PVI was an independent predictor of having LOS < 2 nights, even after correcting for the difference in warfarin use between the groups (HR=0.01, 95% CI 0.03–0.33, p<0.001).

Discussion

There remains no consensus on the optimal method of ablation to treat patients with paroxysmal atrial fibrillation. While RF is the most widely utilized technique, cryoballoon is increasing in popularity at our institution. In this retrospective review, there was no significant difference in baseline characteristics between the cryoballoon and RF patients. Despite inclusion of initial “learning curve” cases with the cryoballoon amongst 3 RF PVI experienced operators, no significant difference in 6-month efficacy was seen.

One of the most appealing features of cryoballoon PVI as compared to RF PVI is the possibility of shorter procedure times and decreased complexity. The idea of shorter procedure times was supported by some smaller studies, although a recent German registry showed no difference in procedure time, and actually suggested longer fluoroscopy times and ablation time with the cryoballoon technique. In our patient population, there was a significantly shorter procedure time for cryoballoon as compared to RF PVI procedures, while fluoroscopy times were similar. These results were also demonstrated in a recent multicenter European study.

Our study demonstrated shorter hospital LOS following cryoballoon PVI as compared to RF PVI. As the RF PVI were performed before the cryoballoon cases, there was more warfarin use in the RF patients. However, even after accounting for this difference, there was a significantly shorter hospital stay following the cryoballoon procedure. The shorter procedure times for the cryoballoon cases may have helped these patients recover faster. It is also possible that the use of JET ventilation for the RF cases contributed to a longer hospital length of stay. The combination of shorter procedure time and decreased hospital length of stay with the cryoballoon procedure could have significant health care utilization implications.

The recent COR trial compared a reduced-complexity version of the cryoballoon PVI where 2 freeze cycles were utilized, but no further ablation was used to ensure PV isolation. This method proved to be less efficacious than RF PVI, which was performed until PV isolation was confirmed. In our study, we used the most common cryoballoon strategy, which involved cryoballoon ablation until PV isolation is confirmed, with the use of RF for touch-up if needed. Although this added step increases the procedural complexity, the majority of cases were able to achieve acute PV without the use of RF. Most of the cases requiring touch-up RF were early in the learning curve, and with the use of the first generation balloon. Furthermore, those cases that utilized adjunctive touch-up RF in addition to the cryoballoon were no more or less likely to have freedom from AF at 6 months.

The primary endpoint of this study was freedom from AF at 6 months. Both cryoballoon and RF had a 70% freedom from AF at 6 months. This is in line with previously published data for these techniques separately, when a single procedure is used for paroxysmal atrial fibrillation. It is also important to note that this is...
the initial experience with cryoballoon ablation in these operators as compared to the RF procedures in those same operators, who are experienced in RF PVI. This would imply that either the success rate with cryoballoon would increase with experience, perhaps to surpass RF, or there is no significant learning curve for the cryoballoon procedure.

The complication rates for both the cryoballoon and RF PVI procedures were similar and in line with previously published series.9,11,12,14,16 For the cryoballoon cases, there were two cases of PNI that persisted at the end of the case. Both cases of PNI occurred in the operator’s first 7 cases, and resolved within 2 months after the procedure. However, if recent techniques such as compound motor action potentials17 gain widespread acceptance, the incidence of PNI is likely to be further reduced in cryoballoon procedures. It was also noted that the complication rate with the cryoballoon procedure was low and comparable to the RF cases. Moreover, there were no life-threatening complications with the cryoballoon procedure, even during initial adoption of the procedure.

There are some notable limitations to this study. First, patients were not continuously monitored for recurrence of atrial fibrillation, although 80% of patients wore a monitor during the follow-up period. Although it is possible that continuous monitoring may have revealed additional AF recurrences, the significance of the additional asymptomatic cases is uncertain. Additionally, data for procedure times was limited to ~60% in each group, although subsequent evaluation of our own database confirms the trend seen in this study.

As was mentioned previously, the cryoballoon cases represent the initial operator experiences. It is unknown if the results would be different if compared to more experienced use of the technique. During the time under consideration, the Arctic Front cryoballoon transitioned from a first to a second generation device, and some evidence does suggest that the second generation device may have greater ablation efficacy.18 Our study showed a trend toward superiority of the second generation cryoballoon, although this did not reach statistical significance. However, in light of the results of other reports,19,20 our findings would only underestimate the efficacy of cryoballoon given the widespread adoption of the second generation balloon.

In regards to the RF procedure, newer catheters which measure contact force and may impact procedural efficacy21 were not in use during the time of this study. As the RF cases were performed before the adoption of cryoballoon, it is unknown if the difference in hospital length of stay would remain significant when comparing cases performed during the same time period. This was a retrospective study involving only 100 patients for a short follow-up such that the data cannot be utilized to make conclusions regarding long-term efficacy. Larger and randomized trials are ongoing which should provide more data as to confirm or refute these findings. Lastly, this study represents the results from 3 operators within one university-based health system, and it is uncertain how well this data can be generalized to other practices.

Conclusion
In operators who are experienced in RF PVI, the cryoballoon cases immediately after the adoption of the technique were performed with a shorter procedure time and were associated with a shorter hospital length of stay. These advantages came while maintaining similar procedural efficacy, and without increased complication rates. Our results suggest cryoballoon ablation is a viable alternative to RF ablation for paroxysmal atrial fibrillation ablation patients and has important implications regarding resource utilization.

References


The Atrial Fibrillation Therapies after ER visit: Outpatient Care for Patients with Acute AF - The AFTER 3 Study

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Abstract
Background: Visits to the emergency room (ER) for atrial fibrillation/flutter (AF) are common, but follow-up care is rarely systematically organized and is often delayed.

Purpose: We conducted a pilot program to develop a systematic, protocol-based system of care for patients presenting to the ER with a primary diagnosis of AF.

Methods: Consecutive patients presenting to the ER with ECG-documented AF at an urban teaching hospital were treated according to a guideline-based care protocol, including a patient toolkit at ER discharge, and systematic referral to a rapid access AF clinic. Consenting patients received questionnaires on AF knowledge, patient satisfaction, and the AFEQT questionnaire at first visit and three-month follow-up.

Results: Of the 321 patients with AF, 244 (76%) were discharged from the ER and 166 (68%) were referred to the AF clinic for urgent follow-up. Among 166 referred, 144 (87%) were seen, within a median 10.5 days (IQR 6-16.5 days); 128 (89%) patients agreed to participate in the study and 81% received a toolkit in the ER. The mean age of patients seen in AF clinic was 63.6±13.2 years and 59% were male. Eighty-seven percent were aware of their diagnosis, stroke risk (82%), possible complications (90%), treatment options (86%) and benefits of adherence (86%). Severity of Atrial Fibrillation class was > 2 in 51% at baseline; AFEQT scores increased from baseline (56.4±25.5) to three months post-ER visit (76.4±20.0), a moderately large improvement in QOL (p<0.0001). Seventy eight percent of patients with CHA2DS2-VASc score > 1 were treated with an oral anticoagulant.

Conclusions: A systematic program to improve patient transition of care from the ER to community clinic was associated with prompt, guideline-based care, and high levels of patient disease awareness. Quality of life scores improved substantially between the index ER visit and 3 months post-visit.

Introduction
Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide and is associated with considerable morbidity and mortality.1,2 The main cause of increased mortality associated with AF is the risk for thromboembolic stroke, which can be substantially reduced by appropriate stroke prevention therapy with systemic anticoagulation.3,4

Patients with AF are diagnosed in many clinical situations, ranging from asymptomatic AF discovered during a routine clinical evaluation, to symptomatic AF presenting at an outpatient facility or an emergency room (ER). The ER is a common place to present, making the ER a prime location to focus efforts that can intervene in the course of illness. According to Canadian and International Guidelines, among patients for whom AF is the primary reason for the ER visit, the majority do not require hospital admission, and can safely be discharged from the ER to their place of residence.5-7 Recent studies indicate that 70-85% of such patients can be safely discharged, however discharge rates vary widely.8 In the province of Ontario (population of 13 million),9 between 2002 and 2010 there were approximately 20,000 visits per year to an ER with a primary diagnosis of AF, representing almost 16,000 individual patients. The province-wide discharge rate was approximately 60%.10

Some studies suggest that these patients may receive incomplete, inconsistent, or fragmented care in follow-up, and that the proportion of these patients receiving evidence-based stroke prevention treatment on discharge from the ER is undesirably low.11 Furthermore, there are rarely standardized transition of care systems that ensure timely and appropriate follow-up care following ER discharge, as well as
standardized patient information and instructions.

The main purpose of the AFTER3 Study was to evaluate and verify feasibility of a comprehensive program of outpatient care for patients with AF as their primary ER diagnosis, consisting of a care pathway and patient toolkit. Secondary outcomes include guideline-indicated oral anticoagulant use and quality of life measures at AF clinic follow-up and at 3 months. We hypothesize that this comprehensive program will be feasible and provide optimal outpatient care for patients with AF identified in the ER.

Material And Methods

Patient Eligibility

All study participants over the age of 18 years with atrial fibrillation or atrial flutter (AF) as a primary diagnosis of the ER visit (as defined by the ER treating physician), symptoms consistent

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Table 1: Patient Baseline Characteristics at ER and AF Clinic

<table>
<thead>
<tr>
<th>Demographics</th>
<th>N=128</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>63.6 ± 13.2</td>
</tr>
<tr>
<td>Male – no (%)</td>
<td>76 (59%)</td>
</tr>
<tr>
<td>ER Symptoms</td>
<td></td>
</tr>
<tr>
<td>Chest Pain – no (%)</td>
<td>25 (20%)</td>
</tr>
<tr>
<td>Dyspnea – no (%)</td>
<td>48 (38%)</td>
</tr>
<tr>
<td>Fatigue/Effort Tolerance – no (%)</td>
<td>26 (20%)</td>
</tr>
<tr>
<td>Palpitations – no (%)</td>
<td>90 (70%)</td>
</tr>
<tr>
<td>Syncope/Presyncope – no (%)</td>
<td>27 (21%)</td>
</tr>
<tr>
<td>Past Medical History – no (%)</td>
<td></td>
</tr>
<tr>
<td>Known AF/Atrial Flutter (prior to current ER visit)</td>
<td>72 (56%)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>59 (46%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>22 (17%)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>10 (8%)</td>
</tr>
<tr>
<td>CAD</td>
<td>15 (12%)</td>
</tr>
<tr>
<td>Significant valvular heart disease</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Valve surgery</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Left ventricular systolic dysfunction</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>CABG / PCI</td>
<td>12 (9%)</td>
</tr>
<tr>
<td>Prior major bleeding</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Substance abuse including ETOH and street drugs</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>Initial ECG in ER - Type – no (%)</td>
<td></td>
</tr>
<tr>
<td>AF</td>
<td>100 (78%)</td>
</tr>
<tr>
<td>Atrial Flutter</td>
<td>20 (16%)</td>
</tr>
<tr>
<td>Sinus Rhythm*</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>Final ECG in ER - Type – no (%)</td>
<td>N=96†</td>
</tr>
<tr>
<td>AF</td>
<td>33 (34%)</td>
</tr>
<tr>
<td>Atrial Flutter</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Sinus Rhythm</td>
<td>58 (60%)</td>
</tr>
</tbody>
</table>

| CHADS2 – no. (%)      |       |
| 0                     | 51 (40%) |
| 1                     | 37 (29%) |
| ≥2                    | 40 (31%) |
| Rheumatic Heart Disease/Mitral Valve Replacement | 3 (2%) |
| CHA2DS2-VASe – no. (%) |       |
| 0                     | 22 (17%) |
| 1                     | 34 (27%) |
| ≥2                    | 72 (56%) |

| AF Clinic Appointment | N=125 |
| Time from ER to AF Clinic – days (median, IQR) | N=128 |
| 10.5 (5.5-18)        |       |

| Seen by               |
| Nurse Practitioner – no. (%) | 101 (81%) |
| EP Fellow/ Resident – no. (%) | 9 (7%) |
| Physician only – no. (%)     | 15 (12%) |

| AF Type – no. (%) | N=128 |
| Newly documented  | 56 (44%) |
| Paroxysmal AF     | 32 (25%) |
| Persistent AF      | 25 (20%) |

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Figure 1: AFTER3 Patient Recruitment (March 2012 - August 2013)

Admitted - Patients admitted to hospital; Discharged from ER - Patients discharged home from the ED; Not referred to AF Clinic - Patients who did not meet inclusion criteria; Recruited into AFTER3 - Patients who met inclusion criteria and were recruited into the AFTER3 Study.
with AF (no minimum duration was specified), documented AF on a 12-lead ECG, either first or recurrent AF presentation and subsequent discharge from the ER were eligible to participate in the trial. Exclusion criteria included patients with no fixed address, cardiogenic shock, “Do Not Resuscitate (DNR) status”, Class IV congestive heart failure (CHF) symptoms with documented CHF (chest X-Ray, physical exam), unstable angina or myocardial infarction (ischemic ST changes, chest pain suggesting myocardial ischemia, ± abnormal troponin), patients requiring hospitalization and/or serious co-morbidity (terminal cancer, severe COPD, life expectancy < 1 year, dialysis or severe renal failure). The study was approved by the St. Michael’s Hospital Research Ethics Board.

**Development of Toolkit**

Researchers from St. Michael’s Hospital and the Centre for Innovation in Complex Care at the University Health Network, including patient and GP/specialist collaboration, developed five patient education brochures:

1. Introduction to AF.
2. AF treatment options.
3. AF – How to decrease your risk of stroke.
4. What do I do if I think I am having an AF episode.
5. AF – What you need to know about cardioversion.

All of the brochures were reviewed and approved by a Patient Education Specialist from Li Ka Shing Knowledge Institute at St Michael’s Hospital. It was recommended that all patients with documented AF should be given a toolkit at ER discharge.

**ER Recruitment and Referral Process**

Two AF referral processes were implemented sequentially in the ER. Initially, a fax referral form to be completed by the ER physician for anyone who presented with AF was created and triaged by a Nurse Practitioner for early follow-up. However, a 6-month review of the implementation process showed that 27% of patients were not referred to the rapid response AF clinic. Most patients discharged from the ER were either referred to their general practitioner or cardiologist or had unclear referrals without documented early follow-up.

As a result, the referral process was modified. Each patient was provided with a pre-booked appointment in the AF clinic within 7 days of the ER visit. An AF clinic referral binder was implemented to include pre-filled appointment dates that were collected by research staff daily. An appointment slip was provided to each patient at ER discharge along with a patient toolkit. Patients were advised to contact the AF clinic if they were not contacted within 5 business days with an appointment.

At the initial AF clinic visit, patients were seen by a nurse practitioner and a cardiac electrophysiologist. A systematic approach was employed to assess potential causes of AF, symptoms, quality of life, and stroke risk. A treatment plan was developed for each patient, which included either a rate- or rhythm-control strategy and stroke prevention therapy according to Canadian Cardiovascular Society guidelines. Immediately following this process, participants who were found to meet all study inclusion criteria were approached by a research co-ordinator for participation in the AFTER3 Study. A copy of the signed consent form was provided to study participants.

At baseline, participants completed the AF Effect on Quality of Life (AFEQT) Questionnaire, which is an 18-item AF specific validated questionnaire, as well as an additional questionnaire that was divided into 5 parts:

1. Knowledge questions about AF after receiving the patient education toolkit in the ER,
2. Attitudes regarding AF,
3. Follow-up care after ER discharge with a GP or cardiologist, and subsequent visits to the ER,
4. ER Consultation Satisfaction Questionnaire and
5. ER visit satisfaction.

After 3 months, participants were contacted (via telephone, mail and/or in person) and asked to complete the AFEQT questionnaire and answer questions regarding their understanding of AF and any treatment obtained for AF.

**Data Analysis and Statistics**

A convenience sample of 15 months of recruitment was chosen, estimating 150 patients referred to the AF clinic. Descriptive analyses of enrolled patients presenting to the ER with AF and seen in the AF clinic was performed. Patient characteristics were compared between two different groups by unpaired t-test for continuous variables and Fisher’s exact test for categorical variables. P-values <0.05 were considered statistically significant. All statistical analyses were performed using GraphPad Prism version 6 for Windows.

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*CHADS2-VASc≥2 (N=72) – (data is missing for 2 patients), AF – Atrial fibrillation; OAC – oral anticoagulant; D/C – Discharged; AFC – Atrial Fibrillation Clinic; GP – General Practitioner

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www.jafib.com
Baseline ER characteristics of enrolled patients are shown in Table 1. The mean patient age was 63.6±13.2 years old (males 59%). The most common presenting ER symptom was palpitations (70%), with most symptoms starting within the previous 48 hours (71%). Fifty-six percent had a prior history of AF. The initial documented rhythm was atrial fibrillation in 78% and atrial flutter in 16% of cases. Sinus rhythm was present on the initial ECG in 6% of cases. The initial mean ventricular rate was 123.9±35.5 bpm. With respect to stroke risk, 31% had a CHADS² score ≥ 2 and 56% had a CHA²DS²-VASc score ≥ 2. Among the 23 patients presenting to the ER with prior known AF and a CHADS² score ≥ 2, nine (39%) were on an oral anticoagulant; only five (46%) of the 11 patients with AF and on warfarin had an INR in therapeutic range (2.0–3.0) (Table 2a-b).

In the ER, 21 (16%) patients underwent electrical cardioversion and 49 (38%) patients underwent an attempt at pharmacologic cardioversion. Overall, 56 (58%) and 37 (39%) patients were prescribed beta-blockers or calcium channel blockers, respectively, at discharge. Eighty-one percent received a patient toolkit when they were discharged from the ER.

Among the 78 (32%) patients seen in the ER with AF who were not referred to the AF clinic, 62 (79%) were asked to follow-up with their family physician or cardiologist, while 16 (21%) had no specific follow-up documented. Characteristics between patients not referred and those referred to the AF clinic appeared to be similar. Patients with no specific follow-up or specialist referral were less likely to be seen by a cardiologist or arrhythmia specialist (67%), compared to those referred to the AF clinic (87%). The median time from the ER visit to follow-up with their cardiologist was 33.0 days (IQR 18.5–134.5).

The characteristics of enrolled patients seen during their AF clinic visit are shown in Table 1. The median time from ER visit to AF clinic visit was 10.5 (IQR 5.5–18) days, with the majority of patients seen primarily by the nurse practitioner in conjunction with a cardiologist (81%). This was the first ER presentation of AF in 44% of patients. The mean Severity of Atrial Fibrillation (SAF) class was 1.8±1.0. At the time of their first clinic visit, 61% of patients were in sinus rhythm. Three-quarters of all patients seen in the AF clinic were not currently receiving oral anticoagulation therapy (Figure 2a).

Oral anticoagulation therapy was newly prescribed or recommended in 30% and 27% of patients, respectively. When anticoagulation therapy was recommended in the AF clinic, only 54% of patients were actually started on an oral anticoagulant by their family physician or cardiologist at 3 months. In patients with a CHA²DS²-VASc≥2 seen in AF clinic, 66% were not currently taking an oral anticoagulant. Of these patients, oral anticoagulation was newly prescribed in 43% and recommended in 43% of patients. In the remaining 13% (n=6), no anticoagulation was prescribed for various reasons (Figure 2b).

When anticoagulation therapy was recommended in the AF clinic, only 55% of patients were actually started on an oral anticoagulant by their family physician or cardiologist at 3 months.

Results of patient questionnaires regarding AF knowledge, attitudes and quality of life are summarized in Table 3. Over 80% of patients were aware of their diagnosis (87%), increased stroke risk (82%) and possible complications (90%). Most patients were aware that AF could affect quality of life (95%) and that treatment could improve symptoms (86%). There was a significant and moderately large improvement in AFEQT scores, from baseline values of 56.4±25.5 to 76.4±20.0 at 3 months (p=0.0001).

At 3 months after the initial AF clinic visit, follow-up data was obtained in 101 patients (79%). Three patients dropped out of the study, 2 patients died and we were unable to contact 22 patients. Only 62% of patients had seen their family physician since their AF clinic visit and 15% had a repeat visit to the ER for AF. Overall, 93% were satisfied or very satisfied with their understanding of AF and 93% were aware that AF can increase stroke risk.

Discussion

In this study we found that a systematic program to improve transitions of care from the ER to outpatient community care was associated with prompt, guideline-based care, and substantial patient satisfaction. The predominantly nurse-practitioner-led AF clinic resulted in high oral anticoagulant use in guideline-indicated patients, and patients reported improved quality of life at 3 months, compared to the baseline AF clinic visit. The study also demonstrated the feasibility of a process to organize a systematic and rapid “turn-around” referral to a dedicated AF service following ER discharge.

In many clinical settings, particularly after emergency care, a systematic, protocol driven, pattern of care which includes patient education, organized and structured follow-up, and rapid access to expert care, results in improved outcomes compared to “usual care”. In the intermediate term, for example, a systematic protocol-driven pattern of care delivered by nurse practitioners was superior to “usual care” delivered by specialist cardiologists, in a randomized...
controlled trial in the Netherlands. In other studies, follow-up with a cardiologist or specialist was associated with a decreased odds of making a return ER visit and follow-up with a family physician decreased the risk of death. This highlights the importance of having a systematic process to ensure adequate and timely follow-up.

A high proportion of patients presenting to the ER have inadequate or absent guideline-indicated stroke prevention therapies despite a prior diagnosis of AF. Similar findings have been shown in studies of patients with prior known AF, and in patients presenting with stroke. In our study, a high proportion of patients with guideline-indication for anticoagulation for stroke prevention were discharged from the ER on inadequate stroke prevention. There may be several potential explanations for this finding. First, since patients were being referred and promptly seen in the AF clinic, the decision of whether anticoagulation should be started and the most appropriate anticoagulant to use may have been left up to the specialist physicians in the AF clinic as the interim stroke risk is perceived to be low. Second, it may be possible that ER physicians are concerned about starting an anticoagulant in patients in whom follow-up cannot be certain, and who may therefore be at risk of bleeding and relatively unsupervised in the early period following hospital discharge. It is also possible that there may be physician knowledge gaps in stroke risk stratification and therapy.

In this study we also found a low rate of warfarin prescription by family physicians following an explicit recommendation from the AF clinic to start therapy with warfarin. This barrier was not present when the anticoagulation was started in the AF clinic, usually with a direct acting oral anticoagulant. Warfarin was not always started directly in the AF clinic due to concern about incomplete early follow-up without an opportunity for early follow-up of INRs in the community. It is not clear why there was a low rate of warfarin prescription by family physicians, but possible reasons include that they never received the AF clinic recommendations, patients did not see family physicians within the study period or there was “therapeutic inertia” with respect to treatment recommendation. Regardless of the reason, in order to minimize this from occurring, it seems reasonable that patients should be directly given a prescription at the time of the AF clinic encounter.

Distribution of a patient “toolkit”, including educational pamphlets on AF, stroke and stroke prevention, treatment options and letters to family physicians at the time of ER discharge was found to be feasible and resulted in excellent patient satisfaction and adequate patient knowledge about AF and its potential consequences. This contrasts with studies suggesting a lack of patient awareness of stroke risks and details of their illness in most patients with AF. Even though 41% of patients had AF prior to the index ER visit, and thus presumably had a prior opportunity to be educated about the illness, the systematic process was associated with a clinically important improvement in quality of life. It is reasonable to ascribe this improvement, at least in part, to the patient toolkit and information, as well as the prompt follow-up and in-person education and treatment provided in the AF clinic.

There was somewhat inconsistent and incomplete referral of all eligible patients from the ER, possibly due to physicians forgetting, being too busy to complete the referral process or difficulty in identifying the most efficient process for referring patients to the AF clinic. We tested several strategies, including an ER physician completed checklist which was hand delivered, mailed or faxed to the AF clinic; pre-scheduled appointments in a dedicated appointment book which were both given to patients and collected by the AF clinic; and an electronic email/fax based-referral system. In our study, the most effective referral method was a combination of pre-scheduled appointments given to patients and an electronic-based referral system, which resulted in an increased proportion of referrals for patients presenting to the ER with AF. The attrition at all steps in the process, including incomplete referral, patients declining to be seen in the clinic, and a small, non-participation rate all remain important barriers to the wide scale adoption of this program. It is our belief that the most effective and least disruptive referral will need to be decided after discussion between the ER physicians and the referral destination, adapting the process to local needs and resources.

The principal limitation of the current study is its observational nature and it is unclear if “conventional” treatment such as specialist referral would have led to similar improvements in guideline-based therapies and patient satisfaction. Although the best way to study this AF clinic intervention would have been via a randomized trial, this study does highlight the significant gaps in “real-world” practice care and that significant improvements can be achieved through systematic referral to an AF clinic. This was also a single-centre study at an urban academic institution, so generalizability of results to other settings is unknown.

Conclusion

The AFTERT3 program shows that it is feasible to provide a systematic “protocolized” suite of interventions designed to provide optimal outpatient care for patients with AF identified in the ER. This type of intervention seems reasonable to subject to a randomized clinical trial compared to usual care, to test whether this process actually leads to improved outcomes.

References


Idiopathic Ventricular Tachycardia: Transcatheter Ablation Or Antiarrhythmic Drugs?

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Abstract

Introduction: Ventricular tachycardia or frequent premature ventricular contractions (PVCs) can occur in the absence of any detectable structural heart disease. In this clinical setting, these arrhythmias are termed idiopathic. Usually, they carry a benign prognosis and any potential ablative intervention is carried out if patients are highly symptomatic or, more importantly, if frequent ventricular arrhythmias can lead to ventricular dysfunction.

Methods: In this paper, different forms of idiopathic ventricular tachycardia are reviewed. Outflow tract ventricular tachycardia from the right ventricle is the most frequent form of the so-called idiopathic ventricular tachycardia. Other forms of idiopathic ventricular arrhythmias include ventricular tachycardia/PVCs arising from tricuspid annulus, from the mitral annulus, inter-fascicular ventricular tachycardia and papillary muscle ventricular tachycardia. When interventional treatment is deemed necessary, detailed mapping (earliest activation during VT/PVC, pace mapping) is crucial as to identify the successful ablation site. Catheter ablation more than antiarrhythmic drug treatment is usually highly effective in eliminating idiopathic ventricular arrhythmias and providing prevention of recurrence.

Conclusions: Idiopathic VTs are not considered life-threatening arrhythmias and, prevention of recurrences is often achieved by means of catheter ablation that provides an improvement of quality of life. The overall acute success rate of catheter ablation is about 85-90% with a long-term prevention of arrhythmia recurrence of about 75-80%. It is advisable that the procedure is carried out by electrophysiologists with expertise in VT catheter ablation and extensive knowledge of cardiac anatomy as to ensure a high success rate and reduce the likelihood of major complications.

Introduction

We define idiopathic ventricular tachycardia (VT) as all arrhythmias originating from the ventricles not linked to any detectable structural heart disease. They are usually due to focal triggered activity or reentry between fascicular bundles. Detailed mapping of these arrhythmias is crucial because it can guide subsequent ablative intervention, that is often curative. Idiopathic VTs are quite a large group of ventricular arrhythmias that comprises different varieties:

a. Outflow Tract Ventricular Tachycardia
b. Tricuspid Annulus Ventricular Tachycardia
c. Mitral Annulus Ventricular Tachycardia
d. Interfascicular Ventricular Tachycardia
e. Papillary Muscle Ventricular Tachycardia

The scope of this paper is to highlight how to properly deal with VTs and/or frequent premature ventricular contractions (PVCs) in the absence of any detectable organic heart disease. These arrhythmias usually carry a benign prognosis, but patients are frequently symptomatic and, therefore therapy is warranted. Antiarrhythmic drugs (AADs) therapy may constitute a potential strategy of treatment, but generally they need to be administered chronically. Side effects and specific contraindications may limit the use of pharmacologic treatment without reducing the patients’ symptoms. Furthermore, some drugs could induce significant adverse effects that includes negative inotropism and extra-cardiac toxicities, especially harmful if used in young patients.

Therefore, catheter ablation can offer an alternative, effective therapy for preventing arrhythmias.

Outflow Tract Ventricular Tachycardia

Among the group of idiopathic VTs, outflow tract VTs are probably the most frequent occurring arrhythmias due to a discrete focus. Classically, their origin is suggested by QRS morphology and axis. Patients are often symptomatic for non-sustained episodes or long period of premature ventricular contractions (PVCs) with the
Non-invasive clinical criteria to distinguish idiopathic ventricular arrhythmias from right ventricular outflow tract and those due to right ventricular dysplasia/ cardiomyopathy

same ECG morphology of VT. Almost 80% of outflow tract VTs arise from the RV outflow tract and the majority from site 1-2 cm below the pulmonary valve. Typically, a LBBB pattern with transition in the precordial leads at V3-V4 occurs. Transition at the precordial leads V1-V2 is suggestive of left side origin. Precise mapping of single PVCs is required to specifically identify the site of origin and guide successful ablation. Earliest local activation at successful ablation site precedes surface QRS by 20-45 ms; bipolar electrograms often show sharp rapid deflections whilst unipolar recordings typically demonstrate QS morphology. The presence of PVCs of the same VT morphology is critical to mapping and successful ablation; in those cases of sporadic occurrence of PVCs, pace-mapping can be employed to identify the successful ablation site. In case of paucity of PVCs or difficulty to induce VT during mapping at baseline, incremental pacing, burst pacing and sometimes atrial high rate pacing at baseline and during isoproterenol infusion are required to promote arrhythmia occurrence.

Less frequently, outflow tract VTs – PVCs originate from the left ventricle, aortic valve cusps or great arteries. On the other hand, some varieties can originate from the aorto-mitral continuity, the base of the septum or LV epicardium. In these circumstances, QRS complexes show inferior axis, but prominent R waves in V1-V2. Detailed mapping is often improved by using intracardiac

By delivering RF current through an irrigated tip electrode catheter. In the RVOT, not more than 25 W-30 W are used, while less energy power is usually employed for sites like aortic root, aortic cusps and ablation within the coronary venous system. One also could consider to use an non-irrigated ablation catheter as a conventional one, when ablating within the cusps. If the mapping has been carried out systematically in the aortic root, few RF applications are sufficient to achieve the goal, otherwise more careful mapping is required (Fig.2).

Anyhow, the indication to ablate VT from the aortic root, coronary vein system or from the epicardial surface is similar to that for RV outflow tract ablation and, symptoms and clinical presentation constitute the primary clinical indication. Obviously, the rationale to propose catheter ablation in this clinical setting is greater for VT than PVCs. On the other hand, we pay specific attention to those patients with depressed ventricular function and frequent PVCs, due to concern of further detrimental effect on LV function.

One critical issue is the differential diagnosis between a true idiopathic VT and VTs otherwise due to subtle structural heart diseases. In some patients, ARVC/D at initial phase with prominent epicardial involvement and scarce endocardial signs, may produce ventricular arrhythmias mimicking idiopathic RV outflow tract VTs. In those circumstances, an attentive EKG morphology evaluation at baseline is of pivotal importance, since any signs of ventricular repolarization abnormalities may suggest more specific investigations, such as the need to provide a cardiac magnetic resonance imaging (MRI) to rule out an underlying pathologic substrate (i.e. occurrence of late gadolinium enhancement as sign of fatty/fibrous tissue infiltration).

Along with non-invasive investigations, 3-D electroanatomic mapping is advisable to improve the likelihood to make the final diagnosis. (Tab.1) In some occasions, endomyocardial biopsy may
be required to properly distinguish different pathologic entities (RV dysplasia/cardiomyopathy, amyloidosis, sarcoidosis, etc).9-11

Tricuspid Annulus Ventricular Tachycardia

Spontaneous PVCs or VTs (approximately 8% of idiopathic VTs) could arise from the lower body of RV or regions 1-2 cm below the tricuspid valve.10 All these arrhythmias present LBBB pattern. Accurate mapping and subsequent ablation can be effective in promoting prevention of recurrence in > 80% of cases thus, highlighting the critical role of catheter ablation in these forms of arrhythmias. These arrhythmias are often resistant to antiarrhythmic drugs and, ablation is usually considered the most effective strategy of therapy. Also in these patients, it is of pivotal importance to rule out the occurrence of areas of RV scars, as possible signs of arrhythmogenic cardiomyopathy.9 Therefore, detailed voltage maps of the right ventricle is warranted as to identify additional signs of possible RV cardiomyopathy.

Mitrail Annulus Ventricular Tachycardia

Less frequently, idiopathic VTs/PVCs arise from the mitral annulus (about 5% of all idiopathic ventricular arrhythmias). In these circumstances, the most frequently involved area is the anteroseptal region of the annulus. Similar to aortic cusp VTs, a delayed potential is recorded during sinus rhythm at the valve annulus and, this potential precedes the QRS electrogram by 50–70 ms during VT or spontaneous PVCs (11). Endocardial ablation is highly effective in suppressing the arrhythmia and, it should be considered the first line strategy of treatment. Occasionally, an epicardial approach via coronary sinus may be required. Even in this clinical setting, patients are quite symptomatic and the use of AADs is rarely effective for the control of the arrhythmias over time.

Interfascicular Ventricular Tachycardia (Belhassen VT)

This form of VT classically involves the posterior fascicles of left ventricle and demonstrates a RBBB pattern, left axis deviation pattern. It occurs in otherwise healthy patients, sometimes elicited by physical stress and could be terminated by verapamil infusion.12 Two other forms of verapamil-sensitive VT have been described; a left anterior fascicular VT with a narrow QRS complex, RBBB and right axis deviation and an upper septal fascicular VT with narrow QRS complex and normal axis.13 Due to the possible beneficial effect of intravenous verapamil, it has been hypothesized to be a Ca-dependent mechanism. Fascicular VT can usually be initiated with atrial extrastimulation, atrial pacing or ventricular pacing and, sometimes isoproterenol is required to reproduce the arrhythmia. During VT, activation propagates anterogradely, from the basal to the apical part of the LV septum, over the abnormal Purkinje tissue, giving rise to an anterograde late diastolic potential. Subsequently, the reentrant wavefront turns around in the lower third of the septum and activates the conduction Purkinje fibers. Therefore, for the classic form of posterior fascicular VT, RF current is directed at the anterograde apical Purkinje potential; the success rate of ablation is > 85–90%. Intravenous verapamil can slow the tachycardia and then terminate, while long-term oral therapy with verapamil is not as effective as RF catheter ablation. Response of VT to lidocaine, sotalol, procainamide and amiodarone is less consistent and none of these drugs appear to be effective in the long run.

Papillary Muscle Ventricular Tachycardia

This is a distinct form of LV-VT arising form the papillary muscles and it can demonstrate a QRS pattern similar to fascicular VT. This arrhythmia can be catecholamine-sensitive and exercise-sensitive and clinically characterized by frequent PVCs rather than run of sustained VT.14 It is thought they have a focal automatic mechanism with spontaneous QRS variations that lacks in fascicular VTs. Intracardiac echocardiography is the ideal guide to detect the region of the papillary muscle that is the location of the early activation and for guiding the ablation catheter. Like fascicular VT, this variety of ventricular arrhythmia is poorly sensitive to long-term antiarrhythmic treatment.

Conclusion

Even though in the majority of circumstances, idiopathic VTs are not considered life-threatening arrhythmias, prevention of recurrences by means of antiarrhythmic drugs is often ineffective and, the patients’ quality of life remains unaffected. Different options of treatment need to be discussed with the patient, portraying the whole scenario. The overall acute success rate of catheter ablation is about 85–90% with a long-term prevention of arrhythmia recurrence of about 75–80%. The overall complication rate is about 2%, with severe complication rate < 1%. It is advisable that the procedure is carried out by electrophysiologists with expertise in VT catheter ablation and extensive knowledge of cardiac anatomy as to ensure a high success rate and reduce the likelihood of major complications.

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Successful Ablation of Single Reentrant Ventricular Tachycardia Arising from Peri-Aortic Scar in a Patient with an Apparently Normal Heart

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Abstract

Peri-aortic region is one of the arrhythmogenic foci associated not only with idiopathic ventricular tachycardia (VT), but also scar-related VT in patients with an apparently normal heart.1-3 A recent study reported that the patients with scar-related VT were significantly older, had a frequent history of hypertension, and inducibility of multiple monomorphic VTs compared to the patients with idiopathic VT.2 However, whether these clinical features are the causes of the peri-aortic scar or innocent by-standers, remain uncertain. Here, we present a relatively young normotensive patient with a peri-aortic scar and emphasize the importance of cardiac MRI to detect latent arrhythmogenic substrates.

Case Report

A 58-year-old man with a 3-month history of palpitations had a documented sustained VT with a cycle length (CL) 350ms on the 24-hour Holter ECG. A diagnosis of idiopathic VT was made based on the normal findings of the twelve-lead ECG, and no evidence of structural heart disease with coronary angiography and echocardiography. The VT was refractory to the beta-blocker and he was referred to our hospital for further treatment. Cardiac MRI was scheduled for an intensive diagnostic work-up prior to the radiofrequency catheter ablation (RFCA). Cardiac MRI revealed normal right and left ventricular chamber sizes without any abnormalities of the wall motion, which were consistent with the echocardiographic findings. However, contrast enhancement MRI revealed a scar involvement in the peri-aortic region (Figure 1). An electrophysiological study was scheduled after all antiarrhythmic drugs had been discontinued for at least five half-lives. Programmed simulation from the right ventricular apex (RVA) repeatedly induced a hemodynamic tolerable monomorphic VT (CL 350ms) with a right bundle branch block and inferior axis morphology (Figure 1), which was compatible with the scar location and considered as the clinical VT from the tachycardia CL and clinical symptoms. Based on the MRI findings and the reentrant electrophysiological properties, we decided to perform detailed mapping of the outflow tract region in both ventricles using an electroanatomical mapping system (CARTO 3, Biosense Webster Inc, Diamond Bar, CA). Initially, activation mapping in the right ventricle (RV) was performed during the VT using a 4-mm distal tip open-irrigated catheter (NaviStar ThermoCool, Biosense Webster), which revealed the earliest activation site on the RV septum with a local ventricular activation 30ms earlier than the onset of the QRS complex (Figure 2), but with preserved bi-polar voltage signals (> 1.5mV). After terminating the VT with high-rate pacing from the RVA, further voltage mapping of the left ventricle (LV), mainly in the outflow tract, was performed via a transseptal approach based on the previous MRI findings. A total of 57 points were collected to clarify the border of the low voltage area (<1.5mV). The low voltage area with local abnormal ventricular activity was confined in the limited area which was proximal to the His recording site and distributed from the septal to the anterior portion of the peri-aortic region (Figure 1). The QRS morphology during pace mapping in the low voltage area was showed only minor differences in the QRS morphology to the clinical VT-QRS morphology with a stimulus-QRS interval of 73ms (Figure 1). Furthermore, the local ventricular activation at that site during the VT exhibited a fragmented potential preceding the onset of the...
follow-up, no recurrence has been observed.

Discussion

We described a patient with an apparently normal heart, but with a single monomorphic scar-related VT from peri-aortic scar. The peri-aortic region is a common arrhythmogenic focus not only for idiopathic VT, but also VT in dilated cardiomyopathy (DCM) patients. However, VT without any abnormalities in a routine diagnostic work-up including a 12-lead-ECG, transthoracic echocardiography, and coronary angiography, is categorized as idiopathic VT, and further evaluation using cardiac MRI is left to the physician’s decision. Therefore, the clinical features of patients with reentrant VT from peri-aortic scar have only been evaluated in a small study. Nagashima et al. described the clinical features of these patients and mentioned that those patients with scar-related VT were significantly older and had a frequent history of hypertension, and raised the possibility that cardiac remodeling with aging and hypertension might be the cause of the peri-aortic scar. However, our patient characteristics were not consistent with the previous findings and suggested that the peri-aortic scar was more likely to be an early presentation of a cardiomyopathic process. In general, the diagnosis of DCM is masked before the impairment of the LV function or an electrocardiographic abnormality including an emergence of VT. Therefore, cardiac MRI should always be included in the routine diagnostic work-up of VT regardless of the clinical presentation.

Recently, the feasibility of RFCA as the primary management of hemodynamically tolerated monomorphic VT in patients with an LV function >30% has been described. However, data on the clinical course regarding the LV function and/or VT recurrence after the RFCA in patients with peri-aortic scar is scarce. Moreover, a high recurrence rate of the VT after the ablation in DCM patients with anterior septal scar has previously been reported. Therefore, our decision was to follow the patient with an event recorder system.

QRS complex by 68ms and was considered as the presumptive exit of the VT (Figures 2 and 3). Radiofrequency energy was delivered at a power of 40W and the VT was terminated within 6 seconds (Figure 4). After the termination of the VT, energy applications were further delivered at the border zone of the low voltage area for substrate modification. The clinical VT could no longer be induced thereafter under extrastimulation with 3 extrastimuli scanned to a minimum coupling interval of 180ms from the RVA. After the successful RFCA of the single monomorphic VT, an event recorder was implanted. The patient was discharged and after 3 months of...
which enabled us to understand the clinical course of the patient after the successful RFCA of the scar-related VT arising from peri-aortic scar.

References


Elimination Of Triggers Without An Additional Substrate Modification Is Not Sufficient In Patients With Persistent Atrial Fibrillation

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Abstract
Atrial fibrillation (AF) is a multifactorial disease with complex pathophysiology. Although restoring sinus rhythm delays the progression of atrial remodeling, non-pharmacologic intervention, such as radiofrequency catheter ablation (RFCA), should be done based on the background pathophysiology of the disease. While circumferential pulmonary vein isolation (CPVI) has been known to be the cornerstone of AF catheter ablation, a clinical recurrence rate after CPVI is high in patients with persistent AF (PeAF). Step-wise linear ablation, complex fractionate atrial electrogram (CFAE)-guided ablation, rotor ablation, ganglionate plexus ablation, and left atrial appendage isolation may improve the ablation success rate after CPVI. But, there are still substantial AF recurrences after such liberal atrial substrate ablation, and current ablation techniques regarding substrate modification still have limitations. Therefore, more understanding about AF pathophysiology and early precise intervention may improve clinical outcome of AF management. Keeping in mind “more touch, more scar,” operators should generate most efficient substrate modification to achieve better long-term clinical outcome.

Introduction
Radiofrequency catheter ablation (RFCA) is an effective rhythm control strategy for patients with atrial fibrillation (AF), and it has become a standard procedure for anti-arrhythmic drugs (AAD)-resistant AF in current guidelines for AF management. The main target of AF catheter ablation is the pulmonary vein (PV) antrum, and complete durable circumferential PV isolation (CPVI) is the cornerstone of this procedure. However, radiofrequency catheter ablation remains challenging in patients with persistent AF (PeAF) and long-standing PeAF.

As evidenced by a substantially high recurrence rate, CPVI alone is considered insufficient in catheter ablation for PeAF. To overcome this limitation, various ablation strategies have been attempted, including additional linear ablation, complex fractionate atrial electrogram (CFAE) guided ablation, right atrial (RA) ablation, non-PV foci ablation, and rotor ablation. Despite the various ablation strategies for PeAF, the success rate of a single procedure has ranged between 20 and 60%. When 1.3~2.3 additional procedures are performed, long-term AF control rate becomes 72~79% with or without AAD. Although RFCA for L-PeAF significantly reduces AF burden, this procedure still has limitations even when it is performed with current technology at world-class, highly experienced institutions. Here, the mechanism and limitations of RFCA for PeAF are reviewed based on the recent clinical studies.

Pathophysiology of Persistent AF
AF is a progressive disease and the mechanism for generation of AF is not yet fully understood. Coumel suggested that trigger factors or trigger foci initiate AF, and an arrhythmic substrate leads to its persistence. It is known that 70~90% of AF triggers exist around PVs in patients with paroxysmal AF, but non-PV foci are more common in those with PeAF. Generally, PV isolation at the level of PV antrum is the mainstay of catheter ablation for AF, but PV isolation may not be enough for PeAF with multiple non-PV triggers (Figure A). Verma et al considered complex fractionated atrial electrogram (CFAE)- guided ablation to be well-suited for non-PV substrate and trigger ablation, and Lemery et al found CFAE map to co-localize with cardiac autonomic ganglionate plexi detected by nerve stimulation. Another factor to consider in the mechanism of PeAF is AF progression and structural remodeling. AF is a progressive disease associated with increased atrial size, histological change, higher number of co-morbid factors, and more frequent overall cardiovascular events. Significant structural remodeling has atria susceptible to a continuous wavebreak and the maintenance of fibrillation by increasing critical mass. Anti-
fibrillatory effects of critical mass reduction have been proved with RF energy delivery, cut and sew operation, pharmacologic effect, and pacing effects in ex-vivo and in vivo animal model as well as human heart models. Therefore, the reduction of atrial critical mass can be one potential anti-arrhythmic mechanism of linear AF catheter ablation for PeAF patients with significant atrial remodeling.

Role of Circumferential PV Isolation (CPVI) in PeAF

In 1993, Schwartz initially described a catheter-based technique for linear ablation of PeAF [AHA abstract, Circulation.1993;90:335]. In 1998, Haissaguerre et al. reported the importance of PV triggers elimination in patients with paroxysmal AF. Afterward, catheter ablation of AF, a much less invasive procedure compared to the maze operation, was accepted as an effective rhythm control strategy. The efficacy of CPVI has been well established and considered to be the cornerstone of RFCA for AF. In patients with PeAF, however, it is associated with a high recurrence rate due to extensive atrial substrate remodeling and atrial dilatation. However, it still remains the most important step of ablation for PeAF for the following reasons:

1) AF triggers frequently arise from PVs
2) cardiac autonomic nerves reach the heart mainly along the PV antral area and CPVI itself reduces about 15~17% of left atrial critical mass.
3) CPVI is effective in elimination of PV triggers, cardiac autonomic denervation, and substrate modification in both paroxysmal AF and PeAF.

Stepwise Approach for PeAF Ablation: Linear Ablation

A stepwise approach of adding linear ablations to CPVI has been known to be effective for AF substrate modification and improving the clinical outcome. This stepwise AF ablation was first introduced by Haissaguerre et al. and is an important strategy to terminate PeAF or macro-reentrant atrial tachycardias. The benefit of linear ablation in addition to CPVI has been reported in multiple clinical studies and a recent meta-analysis (OR 0.22; 95% CI 0.1-0.49; p<0.001). As AF ablation was performed, AF frequency spectra were organized as increments of linear ablation lesions and were finally terminated. The organization of AF into atrial tachycardia might be a sign suggesting a stepwise reduction of atrial critical mass during RFCA. However, there are several limitations in linear ablation in addition to CPVI:

1) the achievement of complete bidirectional block of linear ablation is sometimes very difficult;
2) incomplete block or reconnection of linear ablation is a major reason for recurrence and aggravates macro-reentrant tachycardia;
3) confirming bidirectional block of linear ablation by differential pacing maneuver is not always accurate, especially in patients with significant substrate remodeling and conduction delay; and
4) excessive ablation to achieve bidirectional block may increase the risk of collateral damage. The anatomical location for linear ablation is also variable depending on the operators. While there is a general consensus for high bidirectional block rate, efficacy, and safety of roof line, left lateral mitral isthmus line showed variable bidirectional block rate between 32% and 92%.

It also frequently requires coronary sinus ablation and long-term maintenance of bidirectional block is doubtful. We previously reported that the anterior linear ablation connecting mitral valve annulus in 12 o’clock direction to the roof line was more effective in achieving bidirectional block and lowering clinical recurrence rate after PeAF ablation than left lateral mitral isthmus ablation (Figure B). However, linear ablations are still limited in producing a long-lasting transmural bidirectional block. In our institution, the bidirectional block rates for roof line and anterior line were 90% and 68%, respectively. During the redo-ablation procedure for recurred patients, previously blocked roof line and anterior line were maintained in only 67% and 37%, respectively (unpublished data).

Complex Fractionated Atrial Electrogram (CFAE) Guided Ablation

CFAE was initially introduced by Konings et al. as an electrogram showing high frequency and irregularity that were recorded by high density mapping of AF at right atrium. Afterwards, Nademanee et al. reported that CFAE area recorded by a bipolar catheter represented an electrophysiologic substrate of AF and an ideal target for ablation to eliminate AF. Clinically, CFAE is known to play a role in maintaining AF, co-localize with the autonomic ganglionate plexi, and act as a target for AF catheter ablation. However, CFAE-guided ablation has its limitations: it...
is somewhat subjective and is based on uncertain pathophysiology. Although Nademanee defined CFAE as fractionated electrograms with a very short cycle length (<120ms), composed of two deflections or more, and/or perturbation of the baseline with continuous deflection of a prolonged activation complex over a 10 second recording period, CFAE can be affected by catheter configuration and direction. The mechanism of CFAE is still controversial as CFAE can be generated by anatomical factors (such as complex anisotropy), histologic factors (focal myocardial fibrotic scar), or functional reentries. We previously reported that CFAE is primarily located in the area of low voltage and conduction velocity, surrounded by high voltage areas, and that CFAE cycle length is longer in patients with remodeled atrium (Figure C). All these factors can result in an abrupt change of AF cycle length, wave-wave interaction, and wave-break, forming pivotal points of multiple reentries. However, CFAE includes both the active driver of AF and passive wave breakers, and extensive CFAE-guided ablation has the risk of unnecessary cardiac tissue damage. Verma et al. considered CFAE ablation after CPVI to be favorable for non-PV substrate and trigger ablation, and reported low recurrence rate of AF in patients with PeAF. However, Oral et al. reported that an additional ablation of CFAE after CPVI did not improve clinical outcome of RFCA. It may be because the definition of CFAE is variable depending on investigators, subjects, and the setting of softwares used for analysis. In a recent meta-analysis, CFAE ablation in addition to CPVI did not show significant reduction of clinical recurrence rate compared to that with CPVI alone (OR 0.64 95% CI 0.35–1.18, p=0.15).

Ablations for Left Atrial Appendage, Right Atrial Ablation, Ganglionic Plexi, or Rotor

Di Biase et al. reported that left atrial (LA) appendage is an arrhythmogenic structure and that electrical isolation of LA appendage reduces AF recurrence after catheter ablation. CFAE area is commonly accumulated at the base of LA appendage and is related to the location of ligament of Marshall and ganglionic plexus. However, the risk of stroke should be considered after LA appendage isolation, because intra-cardiac thrombus is commonly formed in LA appendage.

During the stepwise approach in PeAF ablation, it is often necessary to ablate RA in addition to LA, because previous biatrial mapping has demonstrated multiple biatrial sources of tachycardia in human AF. A divergent prolongation of AF cycle length after LA ablation may suggest that the main driver of AF maintenance exists in RA. In fact, Kim et al. reported over 50% chance of AF termination by additional RA CFAE ablation when LA ablation alone was not successful in patients with longstanding PeAF. A random study on routine RA CFAE ablation did not show incremental efficacy compared with LA ablation, but RA inter-caval linear ablation and superior vena cava (SVC) isolation improved clinical outcome of PeAF and longstanding PeAF ablation. Recently, we reported that linear ablation from SVC to RA septum produced autonomic denervation effects on post-procedural heart rate variability and better clinical outcome in patients with paroxysmal AF. Therefore, RA ablation may have autonomic modulation effects. As ganglionic plexi play a key role in the maintenance and initiation of AF, its ablation in addition to CPVI improved clinical outcome of AF catheter ablation. However, mapping and ablation of the exact location of the ganglionic plexus by endocardial approach remains difficult.

Narayan et al. recorded AF activation with 64-pole basket catheters in both atria, and demonstrated the presence of electrical rotors and repetitive focal beats during AF. Although their definition of rotor is not the same to that of classical basic electrophysiology (unexcited but eminently excitable spiral wave core) and clinical data so far are limited, focal impulse and rotor modulation (FIRM) is promising as it terminated AF and improved clinical outcome.

Surgical Maze Procedures

The recent European Society of Cardiology guidelines on AF management recommend surgical ablation for the following patients;

1) symptomatic AF patients undergoing cardiac surgery (IIA-A);
2) asymptomatic AF patients undergoing cardiac surgery in whom the ablation can be performed with minimal risk (IIB-C); and
3) patients with stand-alone AF who have failed catheter ablation and in whom minimally invasive surgical ablation is feasible (IIA-C).

Surgical maze procedure has some benefits compared with catheter ablation, such as the excision of left atrial appendage, ganglionated plexi ablation, and relatively feasible epicardial approach. Recently, a number of institutions reported that a minimally invasive maze procedure using thoracoscopic surgical ablation combined with ganglionic plexi ablation was able to provide AF free survival in over 80% of patients during the follow-up duration of 12 months. Boersma et al. reported superior clinical outcome of surgical ablation than catheter ablation, but a procedure related adverse events rate was significantly higher in surgical ablation (34.4%) than catheter ablation (15.9%). Therefore, highly selected patients with less amendable factors related to AF may be good candidates of maze procedure.

Balanced Substrate Modification with Limited Tissue Damage

Although CPVI alone is not enough and there have been reports about more extensive substrate ablation resulting in better clinical outcome in patients with PeAF, more touches may generate more scar and increase the risk of complication. Gibson et al. reported that pulmonary hypertension after catheter ablation is detected in 1.4% of patients without pulmonary vein (PV) stenosis, in association with severe LA scarring, small LA dimension (≤45mm), high LA pressure, diabetes and obstructive sleep apnea. The DECAAF (Delayed Enhancement - MRI determinant of successful Catheter Ablation of Atrial Fibrillation) study showed poor clinical outcome after AF ablation in patients with extensive atrial scar.

Recently, we reported that long duration of RF ablation is an independent predictor of AF recurrence in patients with PeAF, and that high LA pressure is associated with advanced LA remodeling related to low LA compliance and more frequent clinical recurrence of AF after catheter ablation. Therefore, balanced substrate modification with limited tissue damage is mandatory to achieve better long-term clinical outcome, minimizing procedure related complication rate.

Future Directions for Persistent AF Ablation

In the last decade, there was an enormous progress in AF ablation skill, technique, mapping system, and catheter design. Although there is no argument that appropriate AF catheter ablation reduces AF burden significantly, a recurrence rate of AF
is still substantial, especially in patients with PeAF. Therefore, it is now essential to also consider patient factors before procedure, including clinical characteristics, biomarkers or genetic factors. As medical technology continues to progress, virtual ablation utilizing patient-specific computer simulation modeling may enable operators to choose the best ablation design for each patient. Better understanding about AF pathophysiology and early precise intervention may improve clinical outcome of AF management.

**Conclusion**

Elimination of triggers without an additional substrate modification is not sufficient in patients with PeAF. However, current ablation techniques regarding substrate modification still have limitations, and recurrence and atrial tissue damage are inevitable. Keeping in mind “more touch, more scar,” operators should generate most efficient substrate modification to achieve better long-term clinical outcome.

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Predictors of Atrial Fibrillation Risk in Hypertrophic Cardiomyopathy

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Abstract
Hypertrophic cardiomyopathy (HCM) is a genetic cardiovascular disease that predisposes individuals to the development of arrhythmias. The most common sustained arrhythmia is atrial fibrillation (AF). Compared with the general population, patients with HCM are more prone to the development of AF. To avoid embolic complications and the clinical deterioration caused by the development of AF in HCM, identifying patients with a tendency toward AF might affect the management of HCM. In this review, we evaluated the predictors of AF development in patients with HCM.

Introduction
Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular disorder, with a prevalence of 1:500 in population-based studies.¹ Diagnosis is based on the demonstration of a hypertrophied left ventricle (LV) with a wall thickness of ≥15 mm that cannot be explained solely by the loading conditions. In most cases, a mutation in the gene that encodes a sarcomeric protein causes the disease, and it is inherited mostly as an autosomal dominant genetic trait.² The disease spectrum is wide, including an asymptomatic state, the development of symptoms of heart failure due to impaired diastolic functions or LV outflow (LVOT) obstruction, sudden cardiac death, progression to LV systolic dysfunction, atrial fibrillation (AF), and related embolic complications.²

AF is the most common sustained arrhythmia in patients with HCM.³ It occurs in ~1% of the general population, but 20–30% of patients with HCM.⁴–⁶ Approximately 2–3.8% of HCM patients are diagnosed with AF annually.⁷–⁹ Since LV filling is dependent mostly on atrial contraction in HCM patients, AF is poorly tolerated by these patients since it reduces LV filling time and causes further impairment in LV diastole. Development of AF causes acute symptoms such as palpitations, dyspnea, and chest pain. The clinical worsening might be more prominent in those with LVOT obstruction and those with severe diastolic dysfunction. In these patients development of AF might cause hypotension, lightheadedness, syncope, and syncope. By decreasing LV diastolic filling time during the tachycardia, AF may also provoke or worsen an LVOT gradient. A study investigating impact of AF on stroke displayed an obviously increased risk in the patients with AF compared with those in sinus rhythm.⁵ AF is associated not only with an increased risk of stroke but also with an increased risk of advanced heart failure,⁶,⁷ and stroke-related deaths⁸ in HCM population. AF was also proved to cause premature deaths in an Italian HCM cohort.¹⁰ Therefore, understanding the predictors of AF and the management of these determinants before AF develops is important clinically. In this review, we evaluated the predictors of AF development in patients with HCM (Table 1 and Figure 1).

Left Atrial Structural Remodeling
Left atrial (LA) enlargement is common in HCM. The LA is a thin-walled cardiac chamber that is exposed to LV end-diastolic pressure (LVEDP). In HCM, elevated LVEDP causes an increase in LA afterload; in response LA enlarges and secondary atrial myopathy is observed.¹¹ Atrial tissue fibrosis was observed in pathological specimens from HCM patients, which might have been a consequence of secondary atrial myopathy.¹² Fibrosis could impair the propagation of sinus impulses in atrial tissue and thereby play an important role in the development of AF.

The size of the LA is strongly associated with the development of AF in patients with HCM.³ Although different thresholds for using the size of the LA to predict AF in HCM populations have been used in different trials, the most accepted LA size is ≥45 mm.⁵,¹³ Guidelines from the European Society of Cardiology
LA Mechanical Remodelling

Three phases of LA mechanical function occur during a cardiac cycle. First, during ventricular systole the LA collects and stores blood to function as a “reservoir”, which is also named the LA total emptying fraction. Second, during the early phase of ventricular diastole the LA transfers blood passively into the LV to serve as a “conduit”, which is also named the LA passive emptying fraction. Third, the LA functions has a “contractile” function to push blood actively into the LV, which is also named the LA active emptying fraction or booster pump function. The phasic functions of the LA have been used to predict the development of AF episodes in patients with HCM. For example, Maron et al. used the LA total emptying fraction (expressed as LAEF <38%) to predict future clinical AF events. However, the authors did not evaluate the value of other two LA phasic functions for predicting the development of AF. Therefore, further data are needed.

LA Electrical Remodelling

Sinus impulses spread homogeneously in the atrial myocardium. The distribution of discontinuous and heterogeneous sinus impulse propagations, an increased dispersion of atrial refractories, and fragmentation of intra-atrial conduction could cause atrial reentry. Two electrocardiographic parameters might provide data regarding the distribution properties of impulses: P wave duration (Pdur), and P-wave dispersion (PWD). The value of Pdur for predicting the development of AF in a HCM cohort was assessed by Cecchi et al. They demonstrated that measuring a Pdur of ≥140 ms in the sinus rhythm using high resolution signal-averaged electrocardiography identified patients with HCM who were likely to develop AF with sensitivity, specificity, and positive-predictive accuracy values of 56%, 83%, and 66%, respectively. Measuring Pdur is a non-invasive technique, but it is not practical for use in routine clinical evaluations. Instead, measuring the maximum P wave duration (Pmax) and PWD using surface 12-lead ECGs is more practical. Ozdemir et al. assessed the value of these two parameters in patients with HCM. They reported that a Pmax of >134.5 ms separated HCM patients with and without AF with a sensitivity of 92%, specificity of 89%, and a positive predictive value of 80%. A PWD of >52.5 ms separated HCM patients with AF from those without AF with a sensitivity of 96%, a specificity of 91%, and a positive predictive accuracy of 84%. In addition, assessing both electrocardiographic parameters as well as atrial electromechanical dysynchrony using echocardiography helps to identify prolonged atrial conduction noninvasively. A chronically elevated LV filling pressure in patients with HCM might cause secondary atrial myopathy, which contributes to atrial dysynchrony and a prolonged PWD; however, a study assessing the predictive value of atrial dysynchrony for the development of AF in a population with HCM has not yet been reported.

Previously, the association between LA electrical and mechanical remodelling in HCM patients with sinus rhythm was investigated. Negative correlations between LA total emptying fraction (LA reservoir function) and PWD and atrial dysynchrony were shown in these patients. No association between LA active emptying fraction and LA electrical remodelling was detected. The LA total emptying fraction was related to AF development; however, the value of LA active emptying fraction in predicting AF development in HCM population was not assessed in a follow-up study.

Genetic Factors

The tendency of some families with HCM to development of AF and incidence of AF in patients with small LA (LA diameter ≤40 mm) have raised suspicions about the genetic inheritance of AF in patients with HCM. This hypothesis is supported indirectly by observations that a specific myosin heavy-chain mutation (Arg663His) increased the risk of developing AF. A study of 24 patients with Arg663His mutations revealed that there was a high prevalence of AF. Specifically, 47% of these individuals developed AF over a 7-year follow-up period. In addition to sarcomeric gene mutations, a group of non-sarcomeric genes have been investigated to assess the genetic predisposition of individuals with HCM to develop AF. The possible role of aldosterone in atrial structural and electrical remodelling, increasing collagen biosynthesis, and cardiomyocyte apoptosis attracted attention toward genes in the renin angiotensin...
aldosterone system (RAAS). Belenko et al. investigated different polymorphisms in various RAAS genes in patients HCM, and showed that 1166/ polymorphisms of AGTR1 was a predictor of AF development, whereas -344 / polymorphisms of CYP11B2 had no association with AF development. However, a recent study that analyzed a Caucasian population with HCM showed a role of the -344T>C CYP11B2 gene polymorphism in the secretion of serum aldosterone, and suggested a link between this polymorphism and AF development in HCM patients. Therefore, further data are needed to better understanding the role of the RAAS genes in predicting AF in HCM.

Age
Age is a well-known predictor of AF in the general population. Increased age also contributes to the development of AF in HCM; however, there is also evidence that a large number of HCM patients aged < 60 years also developed AF. For example, one study reported that AF developed in a wide age range of patients (19–82 years) with HCM. Our previous report explaining that the presence of LA appendage dysfunction in sinus rhythm was independent of age in a HCM cohort also raised concerns over the need for additional AF predictors that could be used in relatively young HCM population. Olivotto et al. reported that an age at diagnosis of > 50 years was a predictor of AF in a multivariate analysis that included LA diameter, functional class, maximum LA wall thickness, and the presence of ≥ 30 mmHg gradient in LVOT; however, LV filling pressure was not studied. Recently, Maron et al. reported an age threshold of ≥ 40 years for predicting AF in their HCM cohort. A late diagnosis of HCM might be associated with a long duration of exposure to a high LV filling pressure. Taken together, these findings suggest that increased age contributes to the development of AF in HCM patients. Nevertheless, more studies are needed to identify young patients at risk of developing AF for the early management of these patients.

Left Ventricular Outflow Obstruction
Confounding data have been reported in studies that assessed the effect of LVOT obstruction or the magnitude of the gradient in LVOT on AF development. The largest retrospective single-center study designed to characterize the prevalence, clinical, and echocardiographic correlates of AF included 3023 patients with HCM who remained in SR and 650 HCM patients with AF, and revealed that AF was less common in patients with an obstructive HCM phenotype. In contrast, Autore et al. suggested that a higher proportion of patients with LVOT obstruction developed either paroxysmal or chronic AF compared with those without LVOT obstruction during follow-up. The discrepancy in these studies might be caused by the dynamic state of the LVOT gradient, rather than the constant state observed in aortic stenosis. It is not possible to estimate the duration and magnitude of the LVOT gradient that an HCM patient is exposed throughout their life because of the dynamic nature of the LVOT obstruction. As such, it is controversial whether LVOT obstruction contributes to LA remodelling. A more severe LVOT gradient causes more a severe systolic anterior motion of mitral valve, which results in a more severe mitral regurgitation that might cause LA function to deteriorate. It could be concluded that the contribution of LVOT obstruction to LA remodelling might be caused by the resultant mitral regurgitation as a result of the systolic anterior motion of the mitral leaflets. Therefore, predicting the development of AF using the duration and degree of mitral regurgitation might be valuable.

Myocardial Fibrosis
Myocardial fibrosis is a known predictor of ventricular arrhythmias in patients with HCM. However, a study investigating pathological specimens of HCM patients with and without AF reported that a greater proportion of myocardial fibrosis in the LV was observed in individuals with AF compared with those without AF, suggesting that the severity of myocardial fibrosis is related to the development of AF in HCM. It is possible that myocardial fibrosis contributes to the development of AF by increasing LV stiffness and elevating LV end-diastolic pressure. However, limited data are available, and larger studies are needed.

Higher levels of brain natriuretic peptide (BNP) are detected in HCM patients with AF compared with those in SR. The predictive value of BNP for the development of AF has not been investigated in a large study. The levels of the N-terminal portion of pro-BNP (NT-pro-BNP) were related to the failure of LA reservoir function. In addition, an impaired LA reservoir function was related to the development of AF in HCM patients. This suggests that BNP might predict AF development in HCM. However, in a study evaluating the relationship between the prevalence of AF and the levels of high-sensitive cardiac troponin T (hs-cTnT) and BNP in obstructive HCM, hs-cTnT, but not BNP, levels were related to the prevalence of AF. Moreover, hs-cTnT levels were significantly higher in patients with persistent AF compared with those with paroxysmal AF or in those without AF. The leakage of troponin from dying atrial myocytes and during AF-induced myocardial ischemia were suggested as the sources of troponin release in HCM. Therefore, larger studies are needed to assess the potential of routine biomarker measurements in clinical practice to identify HCM patients that are likely to develop AF.

Conclusion
It is important to recognize HCM patients who are more prone to the development of AF early to avoid the devastating consequences of AF. LA remodeling remains the cornerstone for predicting AF. ECG also identifies patients with prolonged atrial conduction. In addition, increased age contributes to AF development. Assessing all these predictors on an individual basis and the close follow-up of patients with multiple risk factors before the embolic complications of AF occur might be useful. A risk scoring system for both sudden cardiac death and the development of AF that involves the above predictors might be helpful for the primary prevention of AF in HCM patients.

### Table 1: Predictors of atrial fibrillation risk in hypertrophic cardiomyopathy

<table>
<thead>
<tr>
<th>Study</th>
<th>Variables</th>
<th>Cutoff values</th>
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</thead>
<tbody>
<tr>
<td>Maron et al.18</td>
<td>Age</td>
<td>≥ 40 years</td>
</tr>
<tr>
<td>Olivotto et al.5</td>
<td>LA diameter</td>
<td>&gt; 45 mm</td>
</tr>
<tr>
<td>Maron et al.18</td>
<td>LA end-diastolic volume</td>
<td>≥ 118 mL</td>
</tr>
<tr>
<td>Toni et al.15</td>
<td>LA volume index</td>
<td>≥ 34 mL/cm²</td>
</tr>
<tr>
<td>Maron et al.18</td>
<td>LAEF</td>
<td>&lt; 38 %</td>
</tr>
<tr>
<td>Ozdemir et al.22</td>
<td>Maximum P-wave duration</td>
<td>&gt; 134.5 ms</td>
</tr>
<tr>
<td>Cecchi et al.21</td>
<td>Filtered P-wave duration</td>
<td>≥ 140 ms</td>
</tr>
<tr>
<td>Ozdemir et al.22</td>
<td>P wave dispersion</td>
<td>&gt; 52.5 ms</td>
</tr>
</tbody>
</table>

LA = Left atrium; LAEF = Left atrial ejection fraction

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References


Integrated Chronic Care Management For Patients With Atrial Fibrillation: A Rationale For Redesigning Atrial Fibrillation Care

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Abstract
Atrial Fibrillation (AF) is a highly prevalent heart rhythm disturbance, often associated with underlying (cardio)vascular disease. Due to this the management of AF is often complex and current practice calls for a more comprehensive, multifactorial and patient-centred approach. Therefore an Integrated Chronic Care approach in AF was developed and implemented in terms of a nurse-led specialized outpatient clinic for patients with AF. A randomised controlled trial comparing the nurse-led approach with usual care demonstrated superiority in terms of cardiovascular hospitalization and death as well as cost-effectiveness in terms of Quality Adjusted Life Years (QALYs) and life years, in favour of the nurse-led approach. Implementing such approach can be difficult since daily practice can be persistent. To highlight the importance of integrated care wherein the nurse fulfils a significant role, and to provide a guide in developing and continuing such approach, this paper presents the theoretical framework of the AF-Clinic based on the principles of the Taxonomy for Integrated Chronic Atrial Fibrillation Management.

Introduction
Atrial fibrillation (AF) is a highly prevalent heart rhythm disturbance, associated with an increased risk of thromboembolic events, and often accompanied by underlying heart disease.1,2 Since recurrences in AF are most likely the arrhythmia is considered a chronic condition. The management of AF is a complex process, not only focusing on the arrhythmia (rate or rhythm control) but also on detection and treatment of associated cardio(vascular) diseases and prevention of thromboembolic events. Although international evidence based guidelines are available,3,4 prior research demonstrated that guideline-adherent management of AF throughout Europe is suboptimal,5,6 leading to increased morbidity and mortality in these patients. The prevalence of AF is estimated at 2-3% in general population, accounting for 33.5 million patients globally.7 From a practical and logistical point of view, it is worth mentioning that AF prevalence is age-related8 and due to an aging population it is expected that the number of AF patients will rise dramatically in the near future.9,10 The prognosis is set on a 3-fold multiplication of the prevalence rate until 2050, accounting for 12.1 million AF patients in the US alone.10 This evolution will go hand in hand with capacity shortcomings in providing health care, increasing waiting lists, limited accessibility to care, extremely high healthcare costs, and consequently further fragmentation of healthcare.11 In short, current practice calls for a more comprehensive AF management approach. There is a need for changing the routine delivery of AF care through concepts of integrated and coordinated care management including principles of patient-centred care and collaborating multidisciplinary teams. In fact, it has been demonstrated that involving nurses in the care for specific patient groups improves patient outcomes.12-15 demonstrating the importance of a multidisciplinary approach to care. In daily practice such approaches have scarcely been established in AF-care yet.

As a first response to redesign AF management, an integrated chronic AF approach was developed and implemented in the Maastricht University Medical Centre (MUMC) in terms of a specialized nurse-led outpatient clinic (AF-Clinic).16 This clinic integrates significant care components and focuses on the collaboration between important disciplines and involving patients in the care process, following a patient-centred approach. Based on this approach recognized experts in the field advocate for nurse-coordinated management in AF and outline the rationale and fundamentals of such management approach.17

In a proved intervention as presented here, accountability and monitoring its performance and impact is essential. To this end, qualitative indicators in terms of guideline recommendations
and process variables as well as the intended clinical effects of the intervention, were defined prior to the implementation of the AF-Clinic.\textsuperscript{16} Hence, this integrated approach demonstrates that integrating significant components and evaluable indicators can contribute to more efficient care processes and improved patient outcomes. This reflects the aim of this paper which is to advocate for integrated chronic AF management and illustrate its practicability by presenting the AF-Clinic as a best practice example.

**Redesigning Health Care As A Theoretical Framework In Developing Integrated Care: An Overview**

The increasing prevalence of chronic diseases over the past decades, the associated extremely high healthcare costs and the fragmented nature of care for chronic patients, contributed to increased awareness of the necessity to reorganize medical treatment for chronic illness\textsuperscript{18} Disease management programs were considered suitable for this, since potential benefits of disease management may include improved health outcomes, greater patient satisfaction, better quality of life, and reduced healthcare costs.\textsuperscript{18,19} However, standardization was lacking (e.g. a specific definition of disease management was missing and there was a broad variety in existing disease management models). Although disease management programs were disease specific from the start, their focus was mainly to save money associated with one-size fits all organisation of care. Consequently, in the initial programs patients often received care that they actually did not want or need.\textsuperscript{20} In addition, long term beneficial effects were lacking, both concerning health outcomes as well as costs.\textsuperscript{21,22}

**Chronic Care Model**

As a response to these disease indiscriminate management programs, the Chronic Care Model (CCM) was developed to contribute to improve patient outcomes by changing the routine delivery of care. Wagner et al. advocate the provision of care by fusion of six interrelated elements, in order to deliver patient-centred, evidence-based care.\textsuperscript{23,24} The CCM was developed as a synthesis of the best available evidence of system changes needed to improve the quality of disease management, and covering:

1) the entire community,
2) the healthcare system, and
3) the provider organization.\textsuperscript{24-26}

The CCM pursues high quality management of chronic diseases, by focussing on interrelated elements including self-management support, delivery system design, decision support, clinical information systems, health care organization, and community resources.\textsuperscript{25} These elements are meant to provide a practical system for restructuring the management of chronic care. By coordinating activities in primary care rather than focusing on the roles of specific personnel, the CCM aims to improve organizational and health outcomes.\textsuperscript{21,23,24} This ‘integrated approach to care’ enables to address overall healthcare efficiency (process) and effectiveness (impact),\textsuperscript{28} which is particularly important for multi-problem patients with high-risk conditions like patients with AF.

**The Four Pillars of Integrated Chronic Care Management in Atrial Fibrillation**

Based on the CCM, the integrated chronic care approach in AF is defined by four essential pillars, which together form the comprehensive, integrated approach.\textsuperscript{23,24} The approach consists of a nurse-led, guideline-based, software supported outpatient clinic, named the AF-Clinic. The approach is schematically arranged in the

![Figure 1: Taxonomy of Integrated Chronic Atrial Fibrillation Management](www.jafib.com)
Evidence Based Guidelines

The importance of guideline adherence in the management of AF might be obvious, but prior research demonstrated significant gaps between the evidence-based guidelines on the management of AF and daily practice. Considering the enormous attention given to the guidelines by stakeholders, on websites, in research and publications, and also taking into account the improved accessibility, the availability of pocket versions, and the regular revisions of guidelines in the last decade, one may expect an excellent adherence to guideline recommendations among health care providers these days. In addition, the use of risk assessment schemes is recommended in the guidelines. A remarkable example is the appropriate use of oral anticoagulation conform the individual stroke risk analysis based on the CHADS2-score andCHA2DS2-VASc scores, as demonstrated in the AF-Clinic.

Dedicated Software

The use of clinical decision support technology in patient care, incorporating evidence based guidelines, and primarily used by care providers, has grown tremendously in recent decades. In heart failure, telemonitoring is a well-known example, in which the patient is the primary user, resulting in a reduction of heart failure related hospitalizations and death. In AF, systems are marginally available to determine whether or not to prescribe guideline adherent oral anticoagulation in AF patients. No alternatives are available that focus on the management of AF and the underlying diseases, in terms of guideline adherent diagnostics and therapeutics, and in which input is required from both patient and care provider. Therefore, the development of the dedicated knowledge software system within the AF-Clinic is regarded innovative. The decision support software, based on the current guidelines, is developed as an assisting tool throughout the care process for both the care provider (e.g. guideline-adherent checklist) and the patient (in order to provide tailor-made care, active patient input is required). The system provides an individual patient risk profile and acts as an electronic checklist to ensure adherence to all diagnostic and therapeutic guideline recommendations. Moreover, it ensures a more complete approach by focusing on underlying cardiovascular diseases rather than treating the arrhythmia alone. An additional effect of using the software is that it stimulates and facilitates communication processes in the multidisciplinary team (e.g. discussing guideline deviant decisions) which also has a teaching effect.

Supervision

The multidisciplinary approach is built on the indispensable work relationship between cardiologists and nurse specialists, as these disciplines work closely together within the AF-Clinic. Both disciplines are in charge of care delivery to patients with AF, each in a specified role: the nurse specialist being the case manager and care provider, and the cardiologist being the supervising, and medically responsible health professional. The question always is, which discipline is most suited to provide the care the individual patient needs and at what time? Task substitution contributes to improved accessibility and quality of care, yet depends on additional expertise of medical specialists. Its expression may also be steered by down-to-earth financial incentives. However that may be, the relationship between involved disciplines is based on reciprocal reliance, which is vital in revealing clinically relevant findings on which therapeutic decisions can be made. According to this, staff meetings and feedback loops are of vital importance and contribute to multidisciplinary communication processes. Moreover, the educational level and expertise of the nurse specialist as well as the duration and intensity of the relationship between stakeholders are critical success factors in nurse-led care. Both parties should feel safe to give and receive feedback, as this is an essential cornerstone in the integrated approach. Like in the aviation industry, pilot and co-pilot should cooperate and rely on each other to warrant a safe flight. The same holds for the cardiologist and nurse specialist in the AF-Clinic to secure guideline-based decisions and justify reciprocally guideline-deviant behaviour in order to provide the best available treatment strategy. In this respect, availability of the supervising cardiologist in this redesigned best practice model is of utmost importance.

Implementation of Integrated Care

Implementation of this type of care is often a complex process, which necessitates important changes to the traditional care processes. In fact, integrated care requires a redesign of daily practice. This will only be possible in a system that supports and facilitates the development and implementation of such an approach. On a practical level structural and organizational prerequisites are recommended to facilitate an integrated care approach. This includes an adjustment of the vision of care (including change of professional roles, development of multidisciplinary teams, intensive patient involvement in care and decision making, and deliberately providing guideline-based management), availability and education of skilled personnel (e.g. a nurse specialised in AF and the presence of a supervising cardiologist, practical facilitation of the outpatient clinic and software support). The importance of implement integrated care activities on multiple levels has been described before. On the operational level it is necessary to (re)organize information flows including patient transfers between health care providers. To realize sustainability of integrated care it is necessary to achieve commitment of representatives on a strategic level, while on a macro level the need for performance indicators should be discussed.

Clinical Implications

Patient Centred Care By Means Of Education And Activating Self-Management

AF awareness in patients is increasing since many websites, apps and other supporting tools are available. However, attention for patient education and self-management is often lacking in AF care, while self-care is considered essential in the management of chronic illness. Not surprisingly, patient education is often not structured and therefore insufficiently provided in current practice. It is important to tailor education to the individual patient and his specific situation and abilities. For this reason the nurse specialist in the AF-Clinic extensively informs patients and their carers about pathophysiology and symptoms of AF, possible complications, results of diagnostic tests and personalised treatment options. Also lifestyle management and how to achieve desirable goals is addressed. Moreover, there is a specific focus on activating self-management activities to demonstrate patients how they can contribute to their own care process. This is achieved by assessing patient capabilities for self-management, resulting in an individualized tailored approach matching the patients’ level, capacities and needs.

Nurse-Led Care

Coordination of care is a significant precondition of the continuity
of the care process. In the context of task substitution, nurse specialists are considered suitable professionals to coordinate continued care. Generally, in consulting hours with nurse specialists there is more time reserved for counselling and coordination of care, compared to consulting hours with the physician. Also, nursing education focuses on developing specific communication skills that are required in patient care. These skills might be underlying the fact that clinical outcomes of nurse-led care for specific patient groups are better compared to standard care.\(^5,6,10\) In line with prior findings, the AF-Clinic study demonstrated that nurse-led integrated care is associated with improved outcomes in patients with AF. The challenge of integrated AF care in daily practice is therefore to coordinate the continuum of care across the relevant fields of interest. This requires simultaneously collaboration, differentiation and integration\(^4\) which enables further development of the AF-Clinic concept (e.g. integration of primary care, emergency care). In line with the epidemiological evolution of AF, it is highly recommended to extend the integrated care approach beyond the hospital setting alone.

**Guideline Adherence**

Ten years ago the Euro Heart Survey on AF already demonstrated guideline deviant behaviour in the management of AF and related effects.\(^5,6\) Recent observational research confirmed this behaviour and demonstrated guideline deviant behaviour in prescribing oral anticoagulation, despite the use of stroke risk scores.\(^40\) Apparently the medical society didn’t adapt to research findings and practical guideline recommendations in the last decade. To overcome this issue, integrated care can be a solution in closing the gap between guidelines and daily practice. This is illustrated by the fact that in the AF-Clinic study only 83% of patients in the usual care received appropriate oral anticoagulation treatment compared to 99% of patients in the nurse-led care group. As a consequence, a significant number of patients was not adequately protected against thromboembolic complications. A diagnostic guideline recommendation is to measure thyroid stimulating hormone levels at least once.\(^5,4\) Notably, this procedure was performed in only half of the patients in the usual care (54%) versus 91% in the nurse-led care. These findings reason the fact that integrated chronic care prevents patients from receiving incomplete diagnostic and therapeutic management procedures.

Moreover, implementing dedicated software as an assisting tool in daily practice can be helpful in achieving this goal. This contributes to guideline adherent behaviour but also to downsizing the complexity of AF management. However, one should bear in mind to use the software as an assisting, navigating tool rather than blindly trust it. Clinical thinking is still an essential task of the professional in collaboration with the patient.

**Effectiveness of Integrated AF Care**

In a randomised controlled trial the AF-Clinic was compared with usual care (Clinicaltrials.gov identifier NCT00753259).\(^16\) The trial demonstrated superiority of this approach in terms of major cardiovascular events compared to usual care. The primary outcome – a composite endpoint of cardiovascular hospitalisation or cardiovascular death – occurred in 14.3% of patients in the integrated nurse-led approach versus 20.8% of patients receiving usual care, demonstrating a relative risk reduction of 35% in favour of the AF-Clinic. Moreover, adherence to guideline recommendations in AF management was significantly better in the nurse-led approach versus usual care; adherence to a maximum of six practical guideline recommendations was 82% vs 39% respectively (P<0.001).\(^45\) Although quality of life improved over time in both groups, patients in the nurse-led approach demonstrated higher levels of AF-related knowledge\(^42\) and were more satisfied with the treatment process.\(^31\) In addition, the cost-effectiveness analysis of this study demonstrated this approach to be cost saving in terms of QALYs (0.009 QALY gain with a reduced cost of € 1109 per patient) and life years (0.02 life years gained with a reduced cost of € 735 per patient) compared to usual care and is therefore considered a cost-effective management strategy for patients with AF.\(^45\) These results confirm the beneficial effects of an integrated care approach.

**Research Implications**

**Research and Guidelines**

Since the AF population is growing rapidly, the need for coordination of care within an integrated chronic care setting will be more and more important. The Taxonomy of Integrated Chronic AF Management can act as an important redesign-model to contribute in overcoming ‘the epidemic of this millennium’. Therefore widespread dissemination is needed as well as more clinical research in this area. Currently a multicentre randomized controlled trial in the Netherlands is ongoing to further investigate the effects of specialized AF-Clinics. This ‘IntegRAted CaRe for AF study (RACE-4) aims to include 1716 AF patients from 8 participating centres in the Netherlands and first results are expected in 2016.\(^64\) Despite the current available data it is striking that the current guidelines in the management of AF\(^3\) do not advocate integrated chronic care management yet, while one would have expected that opinion leaders are convinced about the approach by now. Especially in the light of new results that again demonstrate poor management in patients with AF, following the conservative approach.\(^40\)

Many initiatives are undertaken to (re)structure daily practice,\(^17\) but research is missing or still ongoing in this field. This strengthens the necessity of more research in the field of integrated AF management. Moreover, following Nolte et al.\(^65\) the same holds for research to support the implementation of integrated care services. This includes provision of adequate finances to develop new care structures and to incorporate these into daily practice, and to create systems that enable patients to effectively self-manage their care, steered by supportive information technology.

**Conclusion**

To achieve successful integrated chronic care management as demonstrated in the AF-Clinic, it is vital to integrate significant components of care including patients, care providers, infrastructure, finance and research. The AF-Clinic is an example of a best practice model that contributes to efficient care processes and improved clinical outcomes. Given the growing patient population that goes hand in hand with an increasing demand for care and a growing burden of the health care system, necessitates expansion of this approach. Hence, we advocate to go beyond the outpatient borders, in order to create new or improve existing collaborative relationships and achieve sustainable healthcare for patients with AF. This is also reflected in research and innovation programs like Horizon 2020, which aims to break down barriers and create possibilities for research and innovation in Europe. The same holds for the Netherlands organisation for health services research and care innovation (ZonMW) presenting a research theme focussing on integrated care in order to create sustainable healthcare.
References


Significance and Management Strategies for Patients with Asymptomatic Atrial Fibrillation

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Abstract
Atrial fibrillation (AF) is a common and refractory arrhythmia. Prevalence of AF increases with age. Asymptomatic AF is a state of asymptomatic episodes of arrhythmia and its exact prevalence remains unknown. Ablation and therapy with antiarrhythmic agents may predispose to asymptomatic AF. Detection of silent AF is crucial for prevention of ischemic stroke. Progress in continuous ECG monitoring by Holter ECG, telemetry methods or implantable devices can provide a useful tools for identifying silent AF. Simple screening procedures like pulse examination and ambulatory ECG may be helpful in arrhythmia detection and logically – ischemic stroke prevention.

Atrial Fibrillation - Epidemiology
Atrial fibrillation (AF) is the most frequent supraventricular arrhythmia affecting over 3 million people in the USA, over 4.5 million in Western Europe including France, Germany, Italy, Spain and the UK, and over 1.5 million in Japan. A 3 to 4 fold increase in arrhythmia prevalence is expected by 2050. Approximately 15 million people worldwide suffer a stroke each year. AF is associated with at least 15% of all strokes. Of this number, approximately one-third die and another third are left permanently disabled.

In the Rotterdam Study, a large population-based European cohort study, the prevalence of AF was 5.5% and was dependent on the age of the participants. It showed 0.7% in persons aged 55-59 years and 17.8% in those aged 85 years and over. The overall incidence rate was 9.9/1000 person-years and was also strictly associated with age. In the group of 55-59 years of age it was 1.1/1000 person-years and was also strictly associated with age. In the group of 55-59 years of age it was 1.1/1000 person-years, then rose to 20.7/1000 person-years in the group aged 80-84 years and finally stabilized in those aged 85 years and above. AF prevalence and incidence was higher in men than in women. The lifetime risk of developing AF at the age of 55 years was 23.8% in men and 22.2% in women. The lifetime risk of developing AF at the age of 55 years was 23.8% in men and 22.2% in women. In the ATRIA study therapeutic issues in patients with AF in the United States were investigated. A total of 17 974 adults with diagnosed AF were enrolled; 45% of whom were aged 75 years or older. AF was more common in women than in men (1.1% vs 0.8%; P<.001). Prevalence differed from 0.1% among adults younger than 55 years to 9.0% in persons aged 80 years or older. Among persons aged 50 years or older, prevalence of AF was higher in whites than in blacks (2.2% vs 1.5%; P<.001). It was estimated, that approximately 2.3 million US adults currently have AF. The authors of the study expect that this number will increase to more than 5.6 million by the year 2050, with more than 50% of affected individuals aged 80 years or older. AF is usually associated with common cardiovascular conditions, such as arterial hypertension, heart failure, coronary artery disease and diabetes mellitus, etc, which are also associated with abnormal biomarkers of a prothrombotic state. In addition, a prothrombotic state has been identified even in patients with lone AF without vascular risk factors or significant cardiovascular conditions.

Asymptomatic Atrial Fibrillation – Epidemiology
Patients with AF are often asymptomatic. However, in these patients cardioembolic stroke can be caused by short episodes of the arrhythmia especially if AF coexists with other comorbidities (arterial hypertension, diabetes, metabolic syndrome, obstructive sleep apnea syndrome etc).

In a prospective 19-month study of 110 patients with a previous history of AF, indications for pacing were monitored with continuous electrocardiography (ECG) using an implantable device (mean follow-up>18 months). It showed that despite optimal medical therapy, 59% of the patients had at least one period of asymptomatic device–documented AF and 38% had asymptomatic episodes lasting more than 48 hours. A similar conclusion comes from a sub-analysis of the SOPAT (suppression of paroxysmal atrial tachyarrhythmias) trial, that included 1033 patients with symptomatic AF for 60 months. It was observed that of the 6,165 ECG recordings with AF only 46% of patients had symptoms during these episodes. The same study showed that in contrast to sotalol (320 mg/day) combined therapy of quinidine and verapamil (480/240 mg/day or 320/160 mg/day) reduced the ratio of symptomatic to asymptomatic
AF compared with placebo, at least in part by decreasing the heart rate.8

An interesting observation has been made in the DISCERN AF study (Discerning Symptomatic and Asymptomatic Episodes Pre and Post Radiofrequency Ablation of Atrial Fibrillation). In this study patients with symptomatic AF underwent implantation of an implantable cardiac monitor with an automated AF detection algorithm 3 months before and 18 months after ablation. The ratio of asymptomatic to symptomatic AF episodes increased after ablation from 1.1 to 3.7 (p=0.002). Asymptomatic episodes were significantly shorter and slower, with lower heart rate variability. The authors concluded, that post ablation state is the strongest predictor of asymptomatic AF. Symptoms alone underestimate post ablation AF burden, with only 12% of patients having asymptomatic recurrences.9

Clinical Significance Of Asymptomatic AF

Symptomatic Versus Asymptomatic Patients

Important data come from a sub analysis of the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study, which was a randomised controlled trial that included 4,060 patients with AF. It was found that asymptomatic patients (12%) had higher risk of cerebrovascular disease than symptomatic patients (17% vs 13%; p=0.005), but a lower incidence of coronary artery disease (28% vs 40%; p<0.0001). Similarly they were less prone to congestive heart failure and pulmonary disease. They were also more likely to have normal ventricular function as assessed by echocardiography, a slower average and maximum heart rate, longer duration of AF, increased exercise tolerance, and a higher global estimate of quality of life. They received fewer cardiac medications and fewer therapies to maintain sinus rhythm. At 5 years, there was a trend for better survival in asymptomatic patients (81% vs 77%, p=0.058), who were also more likely to be free from disabling stroke or anoxic encephalopathy, major bleeding, and cardiac arrest (79% vs 67%, p=0.024). However, after adjusting for left ventricular ejection fraction and history of coronary artery disease or congestive heart failure, there was no statistically significant difference between the two groups in morbidity and mortality for disabling stroke, disabling anoxic encephalopathy, major central nervous system haemorrhage, and cardiac arrest. Therefore, patients with AF should be treated for underlying heart disease, regardless of the presence or absence of symptoms.6,10

Solely Asymptomatic Patients

The ASSERT study (Asymptomatic AF and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial) has provided another significant observation. In this study subclinical atrial tachyarrhythmias, without clinical AF, occurred frequently in patients with pacemakers and were associated with a significantly increased risk of ischemic stroke or systemic embolism. Up to 2580 patients over 65 years old were enrolled, with hypertension and no history of AF, in whom a pacemaker/defibrillator had recently been implanted. They were monitored for 3 months for subclinical atrial tachyarrhythmias for longer than 6 minutes and afterwards followed for a mean of 2.5 years for the primary outcome of ischemic stroke or systemic embolism. Eleven of the 51 patients who had atrial tachyarrhythmias detected in the 3 month monitoring period specified by the protocol and none had had atrial fibrillation. Subclinical atrial tachyarrhythmias were predictive of the ischaemic stroke and systemic embolism after adjustment for predictors of stroke.11

Temporal relationship between subclinical AF and embolic events has been investigated. Of 51 patients who experienced stroke or systemic embolism during follow-up, 26 (51%) had silent AF. In 18 patients (35%), episodes of silent AF were detected before stroke or systemic embolism. However, only 4 patients (8%) had silent AF detected within 30 days before stroke or systemic embolism, and only 1 of these 4 patients was experiencing silent AF at the time of the stroke. In the 14 patients with asymptomatic arrhythmia AF was detected over 30 days before stroke or systemic embolism, the most recent episode occurred at a median interval of 339 days earlier. Eight patients (16%) had silent AF detected only after their stroke, despite continuous monitoring for a median duration of 228 days before event. In conclusion, although asymptomatic AF is associated with an increased risk of stroke and embolism, very few patients had episodes of the arrhythmia in the month before their event.12

In the study by Glotzer et al. there was a trend to a doubling of the risk of stroke in the 30 days after any day in which there were at least 5.5 hours of AF.13

Morbidity In Atrial Fibrillation In Comparison With Patients Without Documented Arrhythmia

It has been long known, that AF is associated with an increased risk of stroke, death, heart failure, a reduced quality of life and with significant healthcare expenditures related to treating the arrhythmia and its complications.14

The impact of nonrheumatic AF on stroke incidence was examined in 5,070 participants in the Framingham Study after 34 years of follow-up. Compared with subjects free of the arrhythmia there was a near fivefold excess in stroke in patients with AF. In persons with coronary heart disease or cardiac failure AF doubled the stroke risk in men and trebled the risk in women. For those aged 80-89 years it was the sole cardiovascular condition to increase stroke incidence.15

In subjects from the original cohort of the Framingham Heart Study, AF was associated with a 1.5- to 1.9-fold mortality risk after adjustment for the preexisting cardiovascular conditions with which it was related. The decreased survival in persons with AF was present in men and women regardless of age.16

AF often accompanies heart failure. The presence of the arrhythmia in patients with left ventricular systolic dysfunction is associated with an increased risk for all-cause mortality. AF is also associated with progression of left ventricular systolic dysfunction.17 Tachycardia induced cardiomyopathy (TIC) is a reversible form of dilated cardiomyopathy that can occur with most ventricular and supraventricular arrhythmias, including AF. Its pathophysiology is not entirely understood.18 It can develop in patients with asymptomatic AF, who are not aware and not treated for the arrhythmia. It has recently been shown in a small group, that patients with AF who underwent electrical cardioversion presented an immediate increase in left ventricular ejection fraction (LVEF). After 4 to 6 weeks later LVEF increased further in patients who remained in sinus rhythm. Contrary to that, in subjects with AF relapse LVEF returned to initial values.19 Another small study results showed that heart rate control during AF without sinus conversion may result in an incomplete cure of TIC, suggesting the advantages of rhythm control with ablation in patients with TIC.20

Finally, AF is an independent risk factor of all-cause mortality in patients with incident AF, as shown in a recent large trial in Sweden. The concomitant diseases that contributed most were found outside
the thromboembolic risk scores. The highest relative risk of mortality was seen in women and in the youngest patients compared with controls, and the differences between genders in each age category were statistically significant.\textsuperscript{21}

Comparing mortality and morbidity of symptomatic and asymptomatic patients with AF to controls free of arrhythmia requires further research. This subject is difficult to evaluate, because presence of AF may be related to existing comorbidities which additionally influence risk of hospitalizations and mortality.

**Detection Of Asymptomatic AF: The Longer Monitoring The Better Results**

The association between silent AF and ischemic stroke or systemic embolic events seems to be logical and clear. Therefore, the search for a proper monitoring method remains a significant clinical challenge. The arrhythmia can be detected by a standard electrocardiogram (ECG), continuous 24-hour ECG recording, prolonged 7-day ECG recording, telemetric intermittent or continuous recording, implantable loop recorder (ILR) or data can be stored in memory of cardiac implantable devices.

In one of the studies the influence of Holter monitoring duration on the detection of AF episodes recurrences after RF ablation has been observed. A group of 215 patients underwent a 7-day Holter ECG at 6 months after catheter ablation. In 24-hour Holter: 59%, in 48-hour Holter: 67% and in 72-hour Holter: 80% of patients with AF, recurrences were detected, whereas a 4-day recording would have detected 91% of the recurrences that were detected with the complete 7-day recording. In conclusion, a Holter duration of less than 4 days failed to reveal a significant burden of arrhythmia, whereas a 4-day recording might offer a reasonable compromise.\textsuperscript{22}

In another trial 132 patients without known AF presenting to the diabetes, hypertension, and dyslipidaemia clinics (76 outpatients in the different clinics), or to the stroke unit (56 stroke survivors) were screened for unknown AF using a simple patient-operated, single-channel ECG recorder. Silent AF was found in 7 patients (5.3%; median CHADS2 score: 2). The prevalence of AF was in direct proportion with a number of risk factors for stroke and AF: AF was found in 3% (1/32) of patients with hypertension and no other risk factors for AF, but in 7% (5/71) of patients with two risk factors including stroke patients (diabetes and hypertension, stroke, or stroke and hypertension), and in 11% (1/9) of patients with stroke, hypertension, and diabetes.\textsuperscript{21}

Asymptomatic AF identification is extremely important in patients with an ischemic stroke. A meta-analysis of randomized controlled trials and prospective cohort studies of patients with acute ischemic stroke has been performed. Five studies including 736 participants were analysed. All studies evaluated Holter monitoring, two also evaluated event loop recording. In studies that evaluated Holter monitoring (588 participants), new AF/atrial flutter was detected in 4.6% (95% CI: 0% to 12.7%) of patients with ischemic stroke. Duration of monitoring ranged from 24 to 72 hours. Two studies (140 participants) evaluated event loop recorders after Holter monitoring. New AF/atrial flutter was detected in 5.7% and 7.7% of consecutive patients in these two studies. The authors concluded, that screening consecutive patients with ischemic stroke with routine Holter monitoring will identify new AF/atrial flutter in approximately one in 20 patients. Extended duration of monitoring may improve the detection rate.\textsuperscript{24,25} Prolonged ECG monitoring may be reasonable, but according to another trial, detection of AF in patients with ischemic stroke is often delayed. In this study, in 68% of patients AF was identified over 48 hours after presentation with stroke.\textsuperscript{25,26} Large trials are needed before firm recommendations can be proposed. A currently ongoing trial is CRYSTAL AF (A Study of Continuous Cardiac Monitoring to Assess Atrial Fibrillation After Cryptogenic Stroke), which has a purpose of assessing long-term ECG monitoring in patients with cryptogenic ischemic stroke and cryptogenic transient ischemic attack.\textsuperscript{25,27}

The question of screening for silent AF in the general population is extremely important. According to current guidelines of European Society of Cardiology (ESC) every patient aged 65 years and older who attends their general practitioner should be screened by checking the pulse, followed by an ECG in case of irregularity.\textsuperscript{28} An interesting experiment of stepwise screening of arrhythmia in an older population group study (mean age 75 years) has recently been made in Sweden. All 1330 inhabitants in the municipality of Halmstad aged 75 to 76 years were invited to a stepwise screening program for AF, 848 (64%) of whom participated. As a first step, participants had 12-lead ECG and reported their relevant medical history. Those with sinus rhythm on 12-lead ECG, no history of AF, and ≥2 risk factors according to CHADS2 score underwent a 2-week recording using a handheld ECG and were asked to record 20 or 30 seconds twice daily and if palpitations occurred. Silent AF was first found in 10% (1%) among 848 individuals who recorded 12-lead ECG. Among 403 persons with ≥2 risk factors for stroke, who completed the hand-held ECG event recording, 30 (7.4%) were diagnosed with paroxysmal AF. In conclusion, stepwise risk factor-stratified AF screening in a 75-year-old population yields a large share of candidates for oral anticoagulation treatment on AF indication.\textsuperscript{29}

According to current guidelines, in patients 65 years or older, opportunistic screening by pulse palpation, followed by an ECG in those with an irregular pulse, is important to detect AF prior to the first stroke.\textsuperscript{26,30}

**Current Recommendation for Management of AF**

Treating asymptomatic AF is not different from management of symptomatic form of arrhythmia. In both cases prevention of thromboembolism is crucial. Current guidelines by European Society of Cardiology emphasise that antithrombotic therapy is recommended in all patients with AF except those at low risk or with contradictions. However, selection of therapy should be based on individualised prognosis of risk and benefit and patient preferences. CHA2DS2-VASC score is recommended for initial assessing stroke risk and HAS-BLED score should be used to calculate bleeding risk. Novel oral anticoagulants may be used alternatively to vitamin K antagonists.\textsuperscript{28,30}

Rate control should be the initial approach in elderly patients with AF and minor symptoms. Rate control agents are: β-blockers, non-dihydropyridine calcium channel antagonists and digitalis.\textsuperscript{28,30}

In contrast, rhythm control as an initial approach should be considered in young symptomatic patients in whom catheter ablation treatment has not been ruled out and in patients with AF secondary to a trigger or substrate that has been corrected (e.g.ischaemia, hyperthyroidism). Depending on underlying heart disease the following antiarrhythmic drugs are recommended: amiodarone, dronedarone, flecainide, propafenone, sotalol. In patients without significant structural heart disease, initial antiarrhythmic therapy
should considered dronedarone, flecainide, propafenone, and sotolol. In subjects with severe heart failure, NYHA class III and IV or recently unstable NYHA class II, amiodarone should be the drug of choice.28,30

Catheter ablation for paroxysmal AF should be considered in symptomatic patients who have previously failed a trial of antiarrhythmic medication. It may also be considered in paroxysmal AF prior to antiarrhythmic drug therapy in symptomatic patients despite adequate rate control with no significant underlying heart disease. In these patients catheter ablation is more effective than antiarrhythmic drug therapy for the maintenance of sinus rhythm.28,30

Further detailed recommendations concerning therapeutic issues in AF can be found in Guidelines for the management of atrial fibrillation 2010 and 2012 focused update of the ESC Guidelines for the management of AF.28,30

Conclusion
Silent AF is a significant clinical problem especially for prophylaxis of ischemic stroke. Various methods of identifying AF are being investigated for their effectiveness in detecting the arrhythmia. The role of wide screening in the primary care should be emphasized.

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Catheter Ablation Of Atrial Fibrillation Without Radiation Exposure Using A 3D Mapping System

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Abstract

Transcatheter ablation procedures have been traditionally performed under fluoroscopic guidance. However, x-ray exposure is afflicted by the risk of developing malignancies as well as other deterministic effects of radiation. For this reason, radiation doses in the interventional laboratory should be reduced ‘As Low As Reasonably Achievable’, with respect to the safety of the patients and the medical staff. This is of utmost importance in atrial fibrillation (AF) ablations, which are usually lengthy procedures. With the improvement of technology, the development of additional imaging tools and the widespread of 3D electroanatomic mapping systems (EAM), near-zero fluoroscopy AF ablation procedure is becoming a reality, limiting fluoroscopy use mainly to guide transseptal puncture.

In the present paper we reviewed the risks to health related to x-ray exposure and we discussed the current state of knowledge of catheter ablation of AF without fluoroscopy in the 3D EAM system era.

Introduction

Catheter ablation is nowadays a well-established therapy for treatment of atrial fibrillation (AF).¹ Historically, conventional fluoroscopy-guided ablations were lengthy procedures, posing a risk to the patient and the physician related to radiation exposure. This risk of radiation-related dermatitis, cataracts, reproductive system damage and malignancy is cumulative and lifelong, and is of a greater concern for particularly sensitive population groups like children and pregnant women, but also for patients who are potentially exposed to multiple ablation procedures, as for AF ablation.²⁻⁴

As technology and operator experience improved, procedural and fluoroscopic times have progressively decreased.⁵ In the past few years, development of new tools like 3D navigation systems have enabled a potential non-fluoroscopic approach to almost all right-sided arrhythmias.⁶ However, left-sided ablations, especially AF ablation, currently represent the majority of everyday electrophysiological (EP) practice. The main limitation in fluoroscopy reduction or complete x-ray elimination for AF ablation is due to safety concerns, mainly related to transseptal puncture. With the improvement of technology, the development of tools like intracardiac echocardiography (ICE) and the widespread of 3D electroanatomic mapping systems (EAM), near-zero fluoroscopy AF ablation procedure is becoming a reality.⁷⁻⁸

This review discusses the current state of knowledge of catheter ablation of AF without radiation exposure in the 3D mapping system era.

Radiation risks

Biological Effects Of Radiation

Nowadays, we are exposed to a variety of radiation sources in our everyday life, at least in the developed countries. Harley et al. reported that natural background radiation was responsible for an effective annual dose equivalent of 3 mSv in the United States and Canada.⁹ Moreover, the major cause of human-made radiation source is certainly attributable to exposure related to medical imaging and tests.¹⁰ The American College of Cardiology guidelines recommend that all invasive catheterization laboratories adopt the ALARA principle, that is to say reducing the radiation dose ‘As Low As Reasonably Achievable’ in order to protect the patient and the medical staff.¹¹

The biological effect of radiation is related to hydroxyl radical creation and to its interaction with DNA, causing DNA ionization, strand breaks and base damage. Two injury mechanisms to DNA have been described: the stochastic mechanism caused by unrepaired damage of a single viable cell, and the deterministic effect, in which a significant number of cells are involved and sufficiently damaged so as to cause observable injury. The stochastic effect occurs by chance and without a threshold level of dose. The main stochastic effect of radiation exposure is cancer, whose probability is proportional to the dose of radiation but its severity is independent of the dose. Deterministic effects, on the other side, have a threshold below which the effect does not occur. Examples of deterministic effects
of radiation include skin erythema, hair loss, cataracts and sterility.

**Radiation Exposure To The Patient**

One hour of fluoroscopy for lengthy and complex EP procedures like AF ablation was the rule and not the exception until a few years ago. Lickfett et al. demonstrated that catheter ablation of AF required significantly greater fluoroscopy duration and radiation exposure (more than four-fold) than simpler catheter ablation procedures. Similar data have been reported also by Macle et al., although using a less sensitive method to assess the peak skin doses. Kidouchi et al. reported that the mean fluoroscopy time for AF ablation (70 minutes) was 2 to 3 times longer than for patients undergoing ablation for other forms of tachycardia (34 minutes). These investigators found that the average entrance skin dose for the AF group was 1.5 to 3 times bigger than for the non-AF group. The more recent position document of the ESC Association of Cardiovascular Imaging, Percutaneous Cardiovascular Interventions and Electrophysiology, showed that, in patients undergoing an AF ablation procedure, the effective radiation dose was 16.6 mSv (ranging from 6.6 to 59.2 mSv), equivalent to 830 chest x-rays.

The lifetime risk for a fatal malignancy associated with a single AF ablation procedure has been estimated to be 0.15% for female and 0.21% for male patients.

<table>
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<th>Procedural time (min)</th>
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<td>Brooks et al., Int J Cardiol 2013</td>
<td>CartoSound</td>
<td>PVI + LL + CFAE</td>
<td>30</td>
<td>50.8 ± 12.2</td>
</tr>
</tbody>
</table>

CFAE: complex fractionated atrial electrograms; EAM: electroanatomic mapping; GP: ganglionic plexi; LL: linear lesions; PVI: pulmonary vein isolation

**Figure 1:** A – upper panel: Carto 3 electroanatomic reconstruction of the left atrium obtained with the mapping catheter (postero-anterior view). A – lower panel: MRI of the left atrium. B – left panel: NavX electroanatomic reconstruction of the left atrium obtained with the mapping catheter (antero-posterior view). B – right panel: MRI of the left atrium. With both EAM systems, the reconstructed cardiac anatomy is very similar to that obtained with MRI.
Table 2: Main studies evaluating the impact of imaging integration on AF ablation

<table>
<thead>
<tr>
<th>Fluoroscopy time (min)</th>
<th>Long-term success rate (%)</th>
<th>Complication rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carto</td>
<td>CartoMerge</td>
</tr>
<tr>
<td>Kistler et al., JCE 2006</td>
<td>62 ± 26</td>
<td>49 ± 27</td>
</tr>
<tr>
<td>Martinek et al., PACE 2007</td>
<td>55</td>
<td>63</td>
</tr>
<tr>
<td>Kistler et al., Eur Heart J 2008</td>
<td>57 ± 23</td>
<td>53 ± 18</td>
</tr>
<tr>
<td>Tang et al., Chin Med J 2008</td>
<td>28 ± 13</td>
<td>20 ± 7</td>
</tr>
<tr>
<td>Bertaglia et al., Europace 2009</td>
<td>55 ± 23</td>
<td>54 ± 25</td>
</tr>
<tr>
<td>Caponi et al., Europace 2010</td>
<td>34 ± 1</td>
<td>15 ± 1</td>
</tr>
</tbody>
</table>

patients respectively. Beir et al. showed the same results (0.065% fatal cancer risk from a radiofrequency ablation procedure requiring 60 minutes of fluoroscopy), and also found a 0.0001% genetic defect risk in the United States population, meaning that, in 1 million patients undergoing a typical radiofrequency (RF) ablation procedure, 650 extra malignancies and 1 birth defect were expected in addition to the naturally occurred events. Therefore, the individual cancer risk (fatal and non-fatal) of a patient admitted in a modern cardiology ward has been estimated as 1/200. Moreover, obese patients have been shown to receive significantly higher radiation exposure during pulmonary vein isolation for AF than the general population. Ector et al. reported effective radiation doses of 15 ± 8 mSv in non-obese patients compared to 27 ± 12 mSv in obese patients (BMI greater or equal to 30 kg/m2). In the latter group of patients, the mean attributable lifetime risk of malignancy is increased to 0.15%. The radiation risk is further increased if a pre-procedural computed tomography (CT) scan is performed to define the anatomy of the left atrium and the pulmonary veins, and by possible repetitive ablation procedures for AF recurrences. For this reason, our and several other groups decided to perform a magnetic resonance imaging (MRI) in order to avoid this additional risk. Although single-procedure radiation exposure appears to constitute a very low cancer risk, repeated procedures may indeed begin to cause a measurable increased risk.

Radiation Exposure To The Medical Staff

If the safety of the patient is of utmost importance, the exposure of the physician performing the ablation procedure should be considered as well. Even if interventional procedures account for the 2% of all radiological procedures, they are responsible for an exposure of the interventional cardiologist per-head per-year 2 to 3 times higher than that of a radiologist. The risk coefficient for cancer induction in medical staff is 5% per Sv of effective dose, which for an interventional cardiologist corresponds to receiving a maximal occupational dose each year (50 mSv) for 20 years of work. The evaluated risk of fatal cancer to the operator per EP procedure ranges between 1/500,000 and 1/1,000,000, but the lifetime attributable risk of fatal cancer following a 15-year radiological exposure exceeding 50 mSv is 1/200 exposed subjects. Somatic DNA damage has also been described in interventional cardiologists compared with clinical cardiologists, implying reproductive system and birth defects. Moreover, occupational risks related to x-ray exposure include orthopedic complications such as neck and back pain, which could be reduced or avoided with apron lead elimination.

3D EAM Systems

The advent of EAM systems, able to reconstruct the cardiac chambers of interest and to simultaneously visualize multiple catheters, has allowed to perform ablation reducing or completely eliminating radiation exposure without affecting the safety of the procedure, giving the high level of accuracy and spatial resolution of 3D EAM. To date, there are 2 main non-fluoroscopic 3D systems that allow catheter visualization and mapping.

EnSite NavX

EnSite NavX (St. Jude Medical, St. Paul, Minnesota, USA) bases its methodology on the principle of applying an electrical current between surface patches positioned on the patient’s chest. Electrodes from standard EP catheters sense the electrical signals transmitted between the patches and interact with the electrical field, so that the system reproduces and shows catheters’ position and real-time motion. With the EnSite NavX system, an additional patch is positioned on the abdomen of the patient and is used as a reference during venous axis navigation at the initial phase of the procedure.

Carto

In the Carto system (Biosense Webster, Diamond Bar, California, USA) location of the sensor at the tip of a dedicated EP catheter is triangulated with three magnetic fields created by skin patches on patient’s chest and back. This system allows 3D reconstruction of the chamber of interest and navigation within the map. Carto3, the new generation of the system, includes a hybrid technology that combines
the magnetic location technology with current-based visualization data, allowing an even more accurate visualization of the tip and curve of the ablation catheter itself combined with the visualization of all the other diagnostic catheters.\textsuperscript{30}

**Reduction Of Fluoroscopy**

One of the first papers reporting the ability of EAM in reduction of fluoroscopy time during EP procedures was published in 2000.\textsuperscript{31} Since that year, several studies have demonstrated that EAM systems permitted to decrease or eliminate radiation exposure, especially in pediatric populations, with a similar success and complication rate compared to standard ablation procedures.\textsuperscript{32–35} In our personal experience, we demonstrated that the combination of EAM systems with cryoablation and RF energy allowed to perform fluoroless slow-pathway ablation for atrioventricular nodal reentrant tachycardia in children and adolescents, with a high efficacy and safety, comparable to conventional fluoroscopy guided procedures.\textsuperscript{36}

AF ablation procedure is technically challenging and highly fluoroscopy and time consuming, because of the need of targeting large ablation areas. The left atrium is a complex 3D structure, with variability of structure and pulmonary vein anatomy.\textsuperscript{37} Ablation usually involves pulmonary vein isolation at the ostium level, carefully avoiding ablation inside the veins to reduce the risk of pulmonary vein stenosis. Moreover additional ablation such as linear lesions (roof, mitral isthmus lines, etc.) and ablation of complex fractionated atrial electrograms is sometimes required. These difficulties have encouraged the use of EAM to reconstruct cardiac anatomy, thus facilitating the procedure.

Moreover, EAM systems have permitted to significantly reduce x-ray exposure in the setting of AF ablation. Since the advent of EAM, literature reports a huge number of experiences using EAM to guide AF ablation. In the majority of the studies, fluoroscopy times ranged from around 5 minutes to one hour and a half, depending on the ablation strategy (Table 1). With technological improvements of the EAM systems, further x-ray reduction has been demonstrated. Our group showed a significant reduction in total fluoroscopy time between patients assigned to fluoroscopy alone, EAM integration with CartoMerge (Biosense Webster, Diamond Bar, California, USA), that allows to visualize only the ablation catheter, and EAM integration with Carto3, that permits visualization of either the ablation and other diagnostic catheters (18'09'' ± 5'00'', 9'48'' ± 3'41'' and 22'8'' ± 1'40'' respectively; \( p < 0.001 \)).\textsuperscript{38} Stabile et al.\textsuperscript{39} showed a significant reduction of fluoroscopy exposure with Carto3 compared to CartoXP (Biosense Webster, Diamond Bar, California, USA): 15.9 ± 12.3 minutes and 26.0 ± 15.1 respectively; \( p < 0.001 \). Despite this last work was not able to replicate the same minimal fluoroscopy time as reported in our paper, it demonstrated anyway that every physician was able to reduce his own fluoroscopy time thanks to the EAM system. This result supports the use of EAM system in daily AF ablation practice.

Furthermore, improved visualization of the anatomy of the pulmonary veins and the left atrium by merging techniques can provide an opportunity to tailor the ablation strategy to an individual’s anatomy. For this reason, many centers started to perform an imaging study, such as CT scan or MRI, before the procedure to know the anatomy in advance and to obtain a more reliable model after chamber reconstruction, so that the operator could be more confident in manipulating catheters without direct fluoroscopy visualization. However, CT scan is inherently characterized by a significant amount of x-ray exposure. To overcome this limitation, our center decided to choose the MRI instead of the CT scan.\textsuperscript{31} Indeed, Caponi et al.\textsuperscript{32} comparing AF ablation procedures guided by CartoXP and CartoMerge, demonstrated that merging the pre-acquired MRI of the left atrium with the 3D EAM reconstruction did not modify the outcome of the ablation procedure, but permitted instead to obtain a significant reduction of x-ray exposure in the CartoMerge group (22.1 ± 11.4 minutes with CartoMerge vs. 40.4 ± 13.5 minutes with CartoXP in the paroxysmal AF group; 28.8 ± 14.3 minutes with CartoMerge vs. 58.0 ± 8.7 minutes with CartoXP in the persistent forms of AF). The same trend of x-ray reduction was reported by Kistler et al.\textsuperscript{39} On the other side, Bertaglia et al.\textsuperscript{40} did not confirm the previous results. One possible explanation of this conflicting result could be related to the multicenter fashion of the study, which involved a great number of EP centers with different level of expertise. Concerning clinical outcomes, similar conflicting results are reported in the literature.\textsuperscript{41} A recent meta-analysis,\textsuperscript{42} indeed, concluded that image integration for AF ablation does not result in better clinical outcomes compared to EAM alone, and therefore the usefulness of 3D EAM seems to be confined to x-ray reduction. Moreover, although displaying an ablation catheter and integrating its position within the CT/MRI geometry is possible, the accuracy of the 3D EAM is highly dependent on image quality and, more importantly, on the merge process. Possible image errors caused by the cardiac chamber volume, rhythm or respiratory state may influence the procedure parameters and outcomes. In addition, regardless the use of EAM system or fluoroscopy-guided approach, successful AF ablation remains critically dependent on appropriate catheter-tip-tissue contact. Nonetheless, 3D EAM is not sufficiently predictive of good contact-derived lesions, which may make the clinical outcome uncertain.\textsuperscript{43} Furthermore, an important additional feature is that image integration for AF ablation didn’t change the total procedural time as well as the complication rate (Table 2).\textsuperscript{41,42} However, up to now, despite the use of 3D EAM systems, the majority of experiences still report few minutes of fluoroscopy, mainly used to guide the transseptal puncture.

**Zero-Fluoroscopy**

Two reports evaluated the feasibility and safety of pulmonary vein isolation with zero-fluoroscopy use combining 3D EAM and ICE.\textsuperscript{7,8} ICE has emerged as one of the most helpful tools in the EP laboratory, thanks to its ability of conveying real-time images during the procedure. Until recently, ICE was mainly used to assist with challenging transseptal puncture and anatomy, and to guide AF ablation with 8 mm-tip catheters to monitor over-heating and microbubble formation.\textsuperscript{44} Nowadays, it is increasingly utilized as a guide to manipulate catheters in the left atrium.\textsuperscript{45} Ferguson et al.\textsuperscript{7} enrolled 21 patients undergoing AF ablation and utilized ICE to perform a double transseptal puncture. In 19 out of 21 cases, no fluoroscopy was used and the EP staff did not wear any protective lead, whereas in 2 cases 2-16 minutes of fluoroscopy were required. Reddy et al.\textsuperscript{8} combined ICE and a 3D EAM system to perform a completely fluoroless procedure of pulmonary vein isolation in 20 patients. Transseptal puncture was deemed successful in every patient and no complication occurred. In eleven patients CT scan was used and integrated with the left atrium anatomy rendered with the 3D EAM. Despite these promising results, we have to consider that ICE still requires a dedicated operator, an additional venous puncture, potentially increasing the risk of vascular complications, and can
result in longer ablation procedures, up to 4 hours. Thanks to its ability to generate multiple 2D ultrasound fans, ICE has also been used to reconstruct a 3D object with the CartoSound (Biosense Webster, Diamond Bar, California, USA) software algorithm, becoming a valuable tool for physicians to have a reliable anatomy reconstruction without the need of an imaging technique prior to the ablation procedure. However, the resolution of 2D ICE imaging is lower compared to CT and MRI. Acoustical shadowing and incomplete penetration can hinder a complete 3D CartoSound rendering, which is operator dependent. Brooks et al. performed a randomized controlled trial to compare image integration with CartoSound with conventional EAM system (CartoXP) in a mixed cohort of AF patients. In both groups, virtual geometries were merged to the previously acquired reconstructed CT scan. Whereas total procedure, ablation and mapping times were similar in each group, CartoSound reduced total x-ray time (51 ± 12 vs. 65 ± 18 min; p = 0.001), via a reduction in both mapping and remaining procedural time. It also demonstrated a reduced left atrial access time, while navigation accuracy, complication rate and AF ablation success at follow-up were similar in both groups.

Another strategy is using real-time 3D transesophageal echocardiography to guide AF ablation procedures, since it allows precise point-by-point navigation in the left atrium and visualization of both circular mapping and ablation catheter. All that considered, this is the question that might arise: is it really of utmost importance trying to reach zero-fluoroscopy by any means? Since EAM systems may reduce the fluoroscopy time to very few minutes confined to guide transseptal puncture, trying to reach zero-fluoroscopy at any cost, with the additional cost of tools like ICE or transesophageal echocardiography, the discomfort for the patient, additional vascular accesses and longer procedures, is probably not always justified. Last but not least, we should remember to apply the already existing protocols and strategies to decrease ionizing radiation exposure, such as minimizing the radiation tube-to-intensifier distance, the collimation of x-ray beam, the standard use of individual lead aprons, thyroid shields, lead glasses, x-ray protecting sterile gloves and radiation adsorbing sterile drapes together with the implementation of radiation safety programs.

Future Directions

Nowadays, 3D EAM systems alone do not allow a completely zero-fluoroscopy approach to AF ablation, at least until the visualization of the transseptal needle by the non-fluoroscopic mapping system is possible. Besides 3D EAM systems, new technologies are constantly evolving to reduce fluoroscopy times and help the physician in the desirable transition between fluoroscopy and fluoroless procedures. New tools such as the contact-force sensing catheters, the MediGuide (St. Jude Medical, St. Paul, Minnesota, USA) and the CartoUniv (Biosense Webster, Diamond Bar, California, USA) mapping systems, and the real time remote magnetic catheter navigation system (Steroaxis Inc., St. Louis, Missouri, USA and Biosense Webster, Diamond Bar, California, USA) have been introduced in the clinical practice showing favorable results.

Conclusion

The importance of fluoroscopy reduction during AF ablation procedures cannot be ignored, with regards to both the patient and the operator. The availability of 3D EAM systems, in addition to ICE and dedicated protocols, contributes to a substantial decrease in radiation exposure. However, the reduction extent still remains operator-dependent, it requires specific training and learning curve and, above all, a mind changing. The current 3D EAM systems allow avoiding fluoroscopy, without harming the safety profile of the procedure, and potentially confining x-ray use only to guide transseptal puncture. Taking all that into account, fluoroscopy reduction shouldn’t be pursued by any means, even in the zero-fluoroscopy era, and x-ray should still be used in particular situations where its lack would influence the safety of the procedure.

References


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