Pen Bay Healthcare
MaineHealth

PREDICTION AND MAINTENANCE OF SINUS RHYTHM AMONG ATRIAL FIBRILLATION PATIENTS

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List of Abbreviations

AF: Atrial Fibrillation
EPIC: the electronic medical record system utilized by Pen Bay Medical Center
COPD: Chronic Obstructive Pulmonary Disease
LA GLS - left atrial global longitudinal strain
LAVI (Left atrial volume index)
PBMC: Pen Bay Medical Center
PHI: Protected Health Information
REDCap: Research Electronic Data Capture
TOMTECH – ARENA: echocardiographic software program

1 Introduction

Atrial fibrillation (AF) is the most common heart rhythm disorder seen in clinical practice, with an estimated 2.7-6.1 million people in the U.S. affected by the disorder [1]. Previous studies have demonstrated that left atrial volume is a predictive measure of incident atrial fibrillation [2]. This study aims to add to the literature by investigating predictive measures of left atrial global longitudinal strain (LA GLS) that would be suggestive of maintenance of normal sinus rhythm post cardioversion. If we could gain insight on the connection between LA GLS and cardioversion among patients with atrial fibrillation, we could potentially help the clinical management of patients pre/post cardioversion, and potentially change poor outcomes.

Background

Atrial fibrillation (AF) is a heart rhythm disorder in which the normal beating in the upper chambers of the heart is irregular, leading to poor blood flow to the lower chambers. Risk factors include older age, high blood pressure, obesity, European ancestry, diabetes, heart failure, ischemic heart disease, hyperthyroidism, chronic kidney disease, heavy alcohol use, and enlarged heart chambers on the left side [3]. AF increases a person's risk for stroke and contributes to an estimated 130,000 deaths each year [1]. Treatment generally includes medication, surgery, and/or healthy lifestyle changes [1]. Electrical cardioversion, in which the patient must undergo sedation or general anesthesia, is also used to convert patients with persistent AF to normal sinus rhythm. Electrical cardioversion has been associated with a high initial success rate of 68-98% [4], but long-term maintenance of sinus rhythm has proved challenging [5]. Due to the potential risks incurred to the patient, it is important to understand which patients are good candidates for cardioversion therapy. A review article describes that duration of AF, sex, age, weight smoking status, number of shocks at cardioversion, post-ablation procedure, medications, hypertension, diabetes, Chronic Obstructive Pulmonary Disease (COPD), obstructive sleep apnea, renal impairment, hyperthyroidism, coronary artery disease, congestive heart failure, left systolic dysfunction, left diastolic dysfunction, left ventricular hypertrophy, valvular heart disease, and left atrial size have each been found to be associated with maintenance of sinus rhythm [6].

Echocardiography has been increasing used in understanding the cardiac structure and risk of stroke among patients with AF, with left atrial size, left ventricular wall thickness, and left ventricular dysfunction recognized as independent predictors of AF [7]. Increasing evidence supports that the left atrial strain measurements can be a predictor of outcomes among AF patients, including stroke and AF recurrence after catheter ablation [8], [9]. We aim to further explore left atrial strain measurements, including left atrial global longitudinal strain (LA GLS), as predictors of maintenance of normal sinus rhythm post-cardioversion. We anticipate to find that a lower LA GLS will predict AF recurrence. To do this, we will study patients with AF at Pen Bay Medical Center who have undergone cardioversion, measuring their LA GLS pre-cardioversion, and assess maintenance of sinus rhythm 6 months post-cardioversion. We anticipate that our study will confirm LA GLS as a marker for maintenance of sinus rhythm post-cardioversion.

Hypothesis

A lower left atrial global longitudinal strain is a predictor of atrial fibrillation recurrence post- electrical cardioversion.

Specific Aims

Include patients from the MaineHealth system into a retrospective study to explore the relationship between left atrial global longitudinal strain (LA GLS) and AF. Patient data will derive from existing EPIC data for MaineHealth patients from January 1, 2017 to June 30, 2021. The EPIC data extract will include: diagnosis of atrial fibrillation, documented echocardiogram, and electrical cardioversion during the study time period. For patients who meet the study criteria outlined in Section 3 below, we will collect demographic and clinical data from EPIC manually (see Section 5 below). The primary outcome measure to be collected includes maintenance of sinus rhythm at least six months post-cardioversion.

Include patients from Pen Bay Medical Center (PBMC) into the same study, however in a prospective portion of the study. These patients will be consented and followed prospectively until six months after cardioversion.

2. We will assess LA GLS using an automated measurement tool called AutoSTRAIN by TOMTEC-ARENA (https://www.tomtec.de/products/application-finder/autostrain/). The historic echocardiograms from patients who meet the study inclusion criteria will be uploaded into this software, which was newly acquired by the PBMC Cardiology Department. MaineHealth Information Services are currently working with study staff to assure appropriate security compliance within the network. LA GLS has not been routinely collected previously from echocardiograms performed at PBMC because of a lack of such technology.

3. We will use statistical methods to describe the relationship between LA GLS and maintenance of sinus rhythm six months post-cardioversion among the AF patients included in this study.

2 Study Design

This study has both retrospective and prospective components. There is an enrollment goal of 500 subjects.

For the retrospective portion, patients will be identified for inclusion in the study based on a previous documented diagnosis of AF, have a documented echocardiogram done prior to the cardioversion with images available in the MaineHealth electronic medical record (EMR), and have undergone electrical cardioversion at a MaineHealth institution.

For the prospective portion of the study, patients will be identified by the PBMC echocardiographic technicians prior to elective cardioversion. The patient will be consented prior to the administration of any sedative. If the patient consents, they will be followed for 6 months after the procedure via the EMR only. The prospective portion of the study will only be conducted at PBMC and not at other MaineHealth institutions due to the lack of staffing capacity at the investigative site.

3 Subject Selection and Withdrawal (if applicable)

3.1 Inclusion Criteria

- Patients identified at any MaineHealth site with a documented diagnosis of AF (at any point in time prior to the cardioversion) and who have undergone any cardioversion.
- The patient would also need to have had an echocardiogram within six months pre-cardioversion (performed for any reason) with a well visualized atrial roof in order to perform the measurements accurately using the TOMTEC-ARENA software.
- For the prospective portion of the study – must be willing to provide informed consent

3.2 Exclusion Criteria

- Patients with a mitral regurgitation greater than moderate (effective regurgitant orifice >= .2 mm^2)
- Patients who have undergone surgical valve repair or replacement, if the procedure was done with a thoracotomy
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- Echocardiographic images not of sufficient quality to obtain the study measurements as determined by the investigator

3.3 Subject Recruitment and Screening

Subjects will be identified using a retrospective chart review within EPIC,between January 1, 2017, through June 30, 2021. These patients will have a diagnosis of atrial fibrillation, a documented echocardiogram, and cardioversion therapy. The study staff will review the medical records in EPIC of these patients and screen for the other inclusion/exclusion elements described above.

For the prospective portion of the study, potential subjects will be identified by the PBMC echocardiographic technicians prior to cardioversion. Either one of the echocardiographic technicians or one of the PBMC Clinical Research coordinators will explain the study to the patient and obtain informed consent.

4 Storage of Study Materials

Study data will be entered into and maintained in a web-based, HIPAA-compliant REDCap database which has a password protected login and only accessed by appointed study staff. These staff include a cardiac sonographer, the clinical research manager at PBMC, and the Rural Research Navigator at the Center for Outcomes Research and Evaluation (CORE), each of which will have full read/write access to the database. Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Once the dataset is complete, all identifiers (medical record numbers and dates of health events or services) will be deleted and subjects will be identified by a unique study ID#, assigned by REDCap. Only de-identified data will be downloaded for analysis.

5 Data collection and management

The study staff- one cardiac sonographer, the clinical research manager at PBMC, and the Rural Research Navigator at CORE- will request an extract of EPIC patient data from Enterprise Reporting based on the inclusion criteria of atrial fibrillation, a documented echocardiogram, and electrical cardioversion therapy, including these codes:

	ICD-9	ICD-10	CPT
Atrial fibrillation	427.31		
Atrial flutter	427.32		
Paraoxysmal atrial fibrillation		I48.0	
Persistent atrial fibrillation		I48.1	
Chronic atrial fibrillation		I48.2	
Tyipical atrial flutter		I48.3	
Atypical atrial flutter		I48.4	
Unspecified atrial fibrillation		I48.91	
Unspecified atrial flutter		I48.92	
Transthoracic stress echo, complete			93350
Transthoracic stress echo, complete w cont EKG			93351
Transthoracic echo cardiac anomalies			93303
Transthoracic echo cardiac anomalies, limited			93304
Transthoracic echo complete w color & spectral			93306
Transthoracic echo complete wo color & spectral			93307
Transthoracic echo limited			93308
Cardioversion (nonemergency), elective, electrical			92960

The study staff will review the medical records in EPIC of these patients and screen for the other inclusion/exclusion elements described above. Patients who meet this criteria will be included in the study and have their medical record number documented in REDCap (a secure, HIPAA compliant, web-based database portal). If these patients are living and scheduled for a follow-up visit at PBMC, they will be consented to be included in the study by one of the study staff. If they do not consent to be included in the study, their information will be deleted from the REDCap database. If they are no longer living or have already had a follow-up visit at the time of the study start date, consent will not be obtained. For those included in the study, medical record numbers, along with demographics, BMI, date of atrial fibrillation diagnosis, antiarrhythmic medications, date(s) of echocardiogram(s) and cardioversion(s) performed, and whether sinus rhythm was maintained at least six months post-cardioversion either by electrocardiogram (ECG), holter monitor, telemetry monitoring or cardiologist dictated note. These patients' echocardiography images will be obtained pre-cardioversion from EPIC and uploaded to the TOMTEC software in order to obtain the LA GLS measurements (as continuous data).

GLS is derived via validated methods [10] using a calculation of: $\epsilon = \frac{L1 - L0}{L0} \times 100\%$.

It has proven to be clinically reproducible as reported in a prior study [11]. While the TOMTEC vendor does not provide normal range values for clinical interpretation, the literature provides GLS measurement data for comparison among nine different software vendors, including TOMTEC [12].

In short, we will:

1. Identify patients at with AF, who obtained an echocardiogram and cardioversion.
2. Consent patients who meet the inclusion criteria who are living and who will be returning for their six month follow-up visit.
3. For patients who have consented or who are deceased, or who have already presented for their six month follow-up visit by the time the study has started, the following information will be collected:
    a. Dates of echocardiogram(s) and cardioversion(s) performed
    b. Determine maintenance of sinus rhythm at least six months post cardioversion
    c. Medical Record Number
    a. Sex
    b. Age
    c. Race/ethnicity
    d. Weight
    e. Date of first atrial fibrillation diagnosis
    f. Number of AF recurrence visits
    g. Antiarrhythmic medications
    h. Smoking status
    i. Number of shocks at cardioversion
    j. Post-ablation procedure
    k. Hypertension
    l. Diabetes
    m. COPD
    n. Obstructive sleep apnea
    o. Renal impairment
    p. Hyperthyroidism
    q. Coronary artery disease
    r. Congestive heart failure
    s. Left systolic dysfunction
    t. Left diastolic dysfunction
    u. Left ventricular hypertrophy
    v. Valvular heart disease
4. Also within this population, obtain echocardiographic features/ measurements:
    a. GLS of LA of 4 chamber
    b. GLS of LA of 2 chamber

c. LAVI (Left atrial volume index)

Aside from the echocardiographic features, all of the above data elements will be in EPIC and extracted into a REDCap database. The echocardiographic features will be obtained by the two cardiac sonographers utilizing the TOMTEC software, and will document these in REDCap. Patient medical record numbers and dates of health events or services (date of cardioversion, date of atrial fibrillation diagnosis, and date of echocardiogram) will be removed from the database after the six month follow-up visit and documentation of normal sinus rhythm occurs. Time lapsed between echocardiogram(s) and duration of atrial fibrillation will be calculated fields created in REDCap based on dates of echocardiogram(s) and date of first atrial fibrillation diagnosis, respectively. Once the time lapsed variables have been created, the date variables will be removed from the database.

Subject information will be kept in the PBMC Echocardiographic lab and the PBMC Clinical Research office, which are both locked when unattended. Information entered into a REDCap database which is password protected. Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

- Protected health information (PHI), which will be collected from subject charts in this study, include demographics (age, sex), echocardiogram results, and maintenance of normal sinus rhythm. Patient medical record numbers will be used for linking the prospective information related to maintenance of normal sinus rhythm, and will be deleted after this information is documented in REDCap.
- Time lapsed between echocardiogram(s) and duration of atrial fibrillation will be calculated fields created in REDCap based on dates of echocardiogram(s) and date of first atrial fibrillation diagnosis, respectively. Once the time lapsed variables have been created, the date variables will be removed from the database.
- Only the cardiac sonographers and the PBMC clinical research nurse manager will have access to this information.

6 Analysis Plan

The duration of AF will be calculated for each patient utilizing the date of first AF diagnosis and the date(s) of cardioversion(s). Descriptive statistics will be used to summarize the demographic and clinical characteristics of patients included in the study, with continuous variables presented as a mean +- standard deviation and categorical variables as frequencies/percentages of the total.

A t-test will be utilized to compare the mean LA GLS among patients documented to have maintenance of sinus rhythm at 6 months to those who have not.

A binary logistic regression model will be developed in order to model any predictive factors (independent variable: echocardiographic features/measurements) among those who have maintained sinus rhythm vs. those who have not (dependent variable: sinus rhythm yes/no) within six months of cardioversion. Criteria for selecting other variables listed above for entry into the logistic regression model will be based on univariate analysis of each variable. Variables determined to have a significant univariate test with a p-value cutoff of 0.05 will be included in the model. Variables deemed not significant will be assessed for confounding by observing parameter estimate changes >10% when variables are excluded from the full model. Analyses will be performed using SAS by the Rural Research Navigator at the Center for Outcomes Research and Evaluation at the Maine Medical Center Research Institute.

7 Confidentiality

Subject information will be kept in the PBMC Echocardiographic lab and the PBMC Clinical Research office, which are both locked when unattended. Information entered into a REDCap database which is password protected. Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

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- Only the cardiac sonographers and the PBMC clinical research nurse manager will have access to this information.

8 Potential problems

The number of patients included (since early 2017) could be too small to meet our target number of 500.

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