Atrial Fibrillation: Rate, Rhythm and Stroke

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Objectives

- Understand arrhythmia management options for atrial fibrillation.
  - Rate versus rhythm control
  - Importance of early ablation
- Understand anticoagulation management for atrial fibrillation.
  - Anticoagulants versus Watchman
IT'S NOT NICE TO FIB
AF is a Growing Problem Associated with Greater Morbidity and Mortality

- Higher stroke risk for older patients and those with prior stroke or TIA
- 15-20% of all strokes are AF-related
- AF results in greater disability compared to non-AF-related stroke
- High mortality and stroke recurrence rate

AF = most common cardiac arrhythmia, and growing

AF increases risk of stroke

5x greater risk of stroke with AF²

~5 M people with AF in U.S., expected to more than double by 2050¹


Current AF Treatment Options

AF

Arrhythmia Management

And

Anticoagulation Management
Current AF Treatment Options

AF

Symptoms

Arrhythmia Management

Anticoagulation Management

Rate Control

Rhythm Control

NO

YES

NO

YES

NO

YES
Arrhythmia Management

SYMPTOMS

- **NO**
  - Rate control
    - Beta blockers
    - Calcium channel blockers
    - Digoxin
    - AV node ablation and Pacemaker
  - Irreversible long term

- **YES**
  - Rhythm Control
    - Antiarrhythmic Drugs
      - Flecainide
      - Propafenone
      - Sotalol
      - Dronedarone
      - Dofetilide
      - Amiodarone
    - Ablation
      - No cure
      - Better at reducing recurrences

**ANTICOAGULATION** Based on CHA₂DS₂-VASc score
Not arrhythmia management
Ablation

- Consider earlier rather than later
- Paroxysmal patients have higher success
- Class I
  - Symptomatic paroxysmal AF who have not responded to or tolerated AAD
- Class IIa
  - Symptomatic, paroxysmal AF prior to trial of medical therapy
- Refer before they become persistent (AF >7 days and/or requires cardioversion to return to SR)
- Ablation does not change need for anticoagulation
  - Based on $\text{CHA}_2\text{DS}_2$-$\text{VASc}$ score
- 2019
  - 30% paroxysmal
Success rate

- **Paroxysmal**
  - 70-80%
  - Higher after second procedure

- **Persistent**
  - 60-75%
  - Some studies report 50% with one ablation procedure
“Billy and I are playing doctor. So far, I've kept him waiting three hours.”
Current AF Treatment Options

- Arrhythmia Management
- Anticoagulation Management

AF (Atrial Fibrillation) with And connection
Current AF Treatment Options

AF

Symptoms

Arrhythmia Management

Rate Control

NO

Rhythm Control

YES

Anticoagulation Management

CHA2DS2-VASc Score

0-1

No Anticoagulation

≥ 2

Anticoagulation NOAC Coumadin

Bleeding Risk

Watchman
Assess stroke risk with CHA$_2$DS$_2$-VASc score

- Score 1 in men & 2 in women: Annual stroke risk 1%-2%, oral anticoagulants or aspirin may be considered
- Score ≥2 in men & ≥3 in women: Annual stroke risk 2%-15%, oral anticoagulants are recommended

Balance stroke risk reduction benefit vs. bleeding risk

<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc Score in Men</th>
<th>CHA$_2$DS$_2$-VASc Score in Women</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>No anticoagulant</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>Aspirin (81-325 mg daily) or oral anticoagulants may be considered</td>
</tr>
<tr>
<td>≥ 2</td>
<td>≥ 3</td>
<td>Oral anticoagulants are recommended*</td>
</tr>
</tbody>
</table>

*DOACS (dabigatran, rivaroxaban, apixaban, and edoxaban) recommended over warfarin in DOAC-eligible patients
Connection Between Non-Valvular AF-Related Stroke and the Left Atrial Appendage

AF Creates Environment for Thrombus Formation in Left Atrium

- Stasis-related LA thrombus is a predictor of TIA\(^1\) and ischemic stroke\(^2\).
- In non-valvular AF, >90% of stroke-causing clots that come from the left atrium are formed in the LAA\(^3\).

LAAO Rationale

- 90% of embolism come from the LAA
- If we occlude (occlusion devices like Watchman) or tie off (Lariat) the LAA then that will reduce the risk for stroke
- Protect AF
  - Supported hypothesis
- Prevail
  - Supported safety
- Led to FDA approval of Watchman
2019 ACC/AHA/HRS Focused Update on Atrial Fibrillation
WATCHMAN included in AF Guidelines

4.4. Nonpharmacological Stroke Prevention

4.4.1. Percutaneous Approaches to Occlude the LAA

<table>
<thead>
<tr>
<th>Recommendation for Percutaneous Approaches to Occlude the LAA</th>
</tr>
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<tbody>
<tr>
<td>Referenced studies that support the new recommendation are summarized in Online Data Supplement 4.</td>
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</table>

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-NR</td>
<td>1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation (S4.4.1-1–S4.4.1-5). NEW: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.</td>
</tr>
</tbody>
</table>

“Oral anticoagulation remains the preferred therapy for stroke prevention for most patients with AF and elevated stroke risk. However, for patients who are poor candidates for long-term oral anticoagulation (because of the propensity for bleeding or poor drug tolerance or adherence), the Watchman device provides an alternative.”
WATCHMAN LAAC Device: A One-Time Procedure

- One-time implant that does not need to be replaced
- Performed in a cardiac cath lab/EP suite by a Heart Team
- Transfemoral Access:
  - Catheter advanced to the LAA via the femoral vein
  - Does not require open heart surgery
- General anesthesia (typical)
- 1 hour procedure (typical)
- 1-2 day hospital stay (typical)
- Some same day discharges
WATCHMAN LAAC Device Overview

Minimally Invasive, Local Solution
- Available Sizes: 21, 24, 27, 30, 33mm diameter

Intra-LAA Design
- Avoids contact with left atrial wall to help prevent complications

Nitinol Frame
- Conforms to unique anatomy of the LAA to reduce embolization risk
- 10 active fixation anchors designed to engage tissue for stability

Proximal Face
- Minimizes surface area facing the left atrium to reduce post-implant thrombus formation
- 160 micron membrane PET cap designed to block emboli and promote healing

Designed Specifically for the left atrial appendage
Using a standard percutaneous technique, a guidewire and vessel dilator are inserted into the femoral vein.
The interatrial septum is crossed using a standard transseptal access system and the procedure is performed with fluoroscopy and transesophageal echocardiography (TEE).
Access sheath is advanced over the guidewire into the left atrium and then navigated into the distal portion of the LAA over a pigtail catheter.
WATCHMAN Implant Procedure: Navigating to the LAA

WATCHMAN is then deployed and released in the LAA.
Device released when position confirmed
Heart tissue grows over the WATCHMAN Implant, and the LAA is permanently sealed after approximately 45 days.
TEE Guided Transeptal Puncture
Evaluating LAA
LAA Arteriogram
Deployment of the Watchman Device
Post Deployment Arteriogram
Tug Test
Post Deployment
Detaching the Device
Timeline of Adjunctive Pharmacotherapy in WATCHMAN Device Patients

*If leak > 5mm, patients remain on warfarin + ASA until seal documented, skipping the clopidogrel + ASA pharmacotherapy

**Post Procedure Therapy**
- Warfarin + ASA (81mg) daily
- Clopidogrel (75mg) + ASA (325 mg) daily

**Destination Therapy**
- ASA (325mg) daily

Implant

45 days*

6 months
Methods & Objectives

Two registries of patients implanted with WATCHMAN LAAC devices provides the largest source of follow-up data

CAP

A continued access registry to the PROTECT-AF RCT

- 566 patients who continued follow-up through their 5-year visit or until study exit
- Inclusion/exclusion criteria identical to those in PROTECT-AF
- Endpoints identical to those in PROTECT-AF
  - **Primary Efficacy:** composite of stroke, CV/unexplained death, systemic embolism
  - **Safety:** occurrence of life-threatening events
- Average Follow-up Time: 50.1 months (2293 pt-yrs)

CAP2

A continued access registry to the PREVAIL RCT

- 578 patients with follow-up data available through 4 years on all patients remaining in trial
- Inclusion/exclusion criteria identical to those in PREVAIL
- Endpoints identical to those in PREVAIL
  - **Primary Efficacy:**
    - Composite of stroke, CV/unexplained death, systemic embolism, and
    - Ischemic stroke and systemic embolism, excluding events occurring within 7-days post-procedure
  - **Safety:** occurrence of life-threatening, procedure-related events within the first 7 days after implant
- Average Follow-up Time: 50.3 months (2227 pt-yrs)

Holmes, DR et al. JACC 2019; In Press
CAP & CAP2 Hemorrhagic Stroke Rates in Perspective

Lowest reported rate of hemorrhagic stroke to date

Holmes, DR et al. JACC 2019; In Press
CAP & CAP2 Ischemic Stroke Rates

Significant relative reductions in ischemic stroke, when compared to expected rates

Events / 100 pt-yrs

Chi2DS2-VASc if untreated
Observed

Ischemic Stroke CAP
5.86% 1.30% RRR 78%

Ischemic Stroke CAP2
7.10% 2.20% RRR 69%

*Effectiveness in stroke reduction vs. estimated in the absence of therapy for comparable CHA2DS2-VASc scores based on Friborg et al. EHJ 2012

Holmes, DR et al. JACC 2019; In Press
High rate of procedural success and low rates of procedure-related complications, consistent with post-approval rates

**Procedural Success**

94.3%

In both CAP\(^1\) and CAP\(^2\)

**Major Procedural Complications within 7 Days**

1.2% CAP\(^1\)

1.4% CAP\(^2\)

1.5% NESTed SAP\(^2\)

*Major Procedural Complications defined as death, ischemic stroke, systemic embolism, or device/procedure-related events necessitating cardiac surgery or major endovascular intervention within either 7-days post-implant or hospital discharge, whichever occurred later.

**Procedural success defined as delivery and release of the device into the LAA

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1 Holmes, DR et al. JACC 2019; In Press
CAP & CAP2: Warfarin Cessation

At one year, greater than 95% of patients were able to discontinue warfarin

<table>
<thead>
<tr>
<th></th>
<th>CAP</th>
<th>CAP2</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-Day</td>
<td>96%</td>
<td>93%</td>
</tr>
<tr>
<td>1 Year</td>
<td>96%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Holmes, DR et al. JACC 2019; In Press
Conclusions from CAP & CAP2 Long-Term Follow-Up

- Final 5- and 4-year data presented from the CAP and CAP2 Registries provides the longest and largest follow-up data of patients with the WATCHMAN device.

- Data from CAP and CAP2 documents the lowest rate of hemorrhagic stroke yet documented in this patient population.

- Results from the CAP and CAP2 Registries add to increasing information that LAAC is an effective and safe alternative to long term anticoagulation in patients with NVAF who are at increased risk for stroke.

Holmes, DR et al. JACC 2019; In Press
Our Data

- Program started January 2019
- 42 total cases to date
  - 5 cancelled or aborted secondary to clot or valvular disease
- 6 months
  - 100% off anticoagulation
Summary

- Previous studies and registries have shown
  - the noninferiority of the LAAC device to warfarin for stroke or systemic embolism
  - its superiority in reducing hemorrhagic stroke, cardiovascular mortality, and nonprocedure-related bleeding
- The device has been found to result in improved quality of life
- Procedural success rates remain high
- Overall, procedural complications are low
- For patients who cannot tolerate long term anticoagulation, Watchman is an excellent alternative to consider
What is the best management for atrial fibrillation?

Get an iWatch?
Giant Study Suggests Apple Watch Accurately Catches Atrial Fibrillation

- 400,000 participants
  - already owned their own Apple Watch (series 1-3) and compatible iPhone
  - did not evaluate the latest Apple Watch model, series 4, which has a built-in electrocardiogram (ECG) app
- 2161 or 0.5% got an AF alert
- The watch and its app use a light sensor technology to measure blood flow at discrete intervals and detect any changes, which could suggest an irregular heartbeat. It measures the interval between beats, called a tachogram. If 5 of 6 of these intervals over 48 hours falls outside the algorithm, the app triggers an alert to the user.
- In this study, those who got an alert were asked to have a video consultation with a doctor, who decided whether the person should wear an ECG patch for 7 days. One-third of those who were sent the patch based on their AF reading on their watch were found to have it on the patch as well; the study authors said this is normal, as AF can “come and go.”
57% who received an alert sought medical attention

Researchers did report anxiety among 16 users as an adverse event.

What’s noteworthy is when users wore the patch and the watch at the same time, the positive predictive value for tachogram was 71%, and the predictive value of the notification was 84% (meaning if the watch notified the user of AF, so did the patch).

Personal experience

- Seems to correlate well with AF
- ECG is helpful
- Sometimes is just PAC’s so need to be wary
Apple watch could do more harm than good

- Still do not know the real overall effect on health
  - Not randomized control trial
- No idea of the false negatives
  - Patients may be reassured that no alert received
- False positives
  - Anxiety
  - Unnecessary doctor visits
- Personal Experience
  - Unnecessary referrals for slow heart rate or fast heart rate
All Arrythmias
Straighten Themselves Out in
THE END
THANK YOU!!
“We wanted to make the stress test as realistic as possible.”
Challenges in Treating AF

Warfarin is not always well-tolerated

- Narrow therapeutic range (INR between 2.0 – 3.0)
- Effectiveness is impacted by interactions with some foods and medications
- Requires frequent monitoring and dose adjustments

Major Complications

- Major bleeding with warfarin use is estimated to occur at a frequency as high as 16%²
- Warfarin associated bleeding experience a rate of mortality, hospitalization, life threatening disability or intervention as high as 90%²

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[i] Eligible patients using warfarin

[i] Eligible patients not using warfarin

Time in therapeutic INR³

Outside therapeutic INR³

66% 34%
Case

- BC is a 78 Y male with history of chronic atrial fibrillation s/p PM
- Previously on coumadin c/b spontaneous SDH when INR was 2.8
- Coumadin is now held.
- CHADSVASC score is 4 (age, HTN, atherosclerosis of aorta)
  - 4% per year adjusted stroke rate
- HASBLED score is 3 (age, bleeding history, medications to predispose to bleeding)
Treatment Options

- Before 2015, what would you do?
  - A. Continue on aspirin only knowing patient is at 4% risk per year for embolic stroke
  - B. Retry Coumadin again knowing patient is at very high risk for repeat SDH
  - C. Treat with new oral anticoagulant like pradaxa or apixiban or rivarouxaban? Still is at risk for repeat SDH but may be less than Coumadin. GI bleeding is increased.
Treatment Options

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  - D. Refer for left atrial appendage occlusion device
Treatment Options

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  - D. Refer for left atrial appendage occlusion device
Case BC

- Are at increased risk for stroke and systemic embolism based on CHADS\textsubscript{2} or CHA\textsubscript{2}DS\textsubscript{2}-VASc scores and are recommended for anticoagulation therapy
  - Yes - Chadsvasc score 4
- Are deemed by their physicians to be suitable for warfarin
  - Yes - cleared by neurology for short term coumadin
- Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin
  - Yes - is at increased risk for rebleeding with long term warfarin and new oral anticoagulants
2014 AHA/ACC/HRS Treatment Guidelines to Prevent Thromboembolism in Patients with AF

- Assess stroke risk with CHA$_2$DS$_2$-VASc score
  - Score 0 male, 1 female: No anticoagulation recommended
  - Score 1: Annual stroke risk 1%, oral anticoagulants or aspirin may be considered
  - Score ≥2: Annual stroke risk 2%-15%, oral anticoagulants are recommended

- Balance benefit vs. bleeding risk
Embolic Management/ Anticoagulation

- **CHA$_2$DS$_2$-VASc** score guides management
  - MDCalc.com

- Score $> 2$
  - Anticoagulate
    - Coumadin
    - NOAC
      - Pradaxa
      - Apixiban
      - Rivaroxaban
      - Edoxaban
  - For non valvular AF recommend NOAC over Coumadin
    - Valvular AF= Mechanical mitral valve or moderate-severe MS

- Bleeding issue consider Watchman
LAAO Devices

- Watchman
  - FDA approved March 2015
  - Device is deployed in the left atrial appendage via transeptal puncture
  - Requires anticoagulation pre and post procedure
  - Does not electrically isolate the left atrial appendage
The WATCHMAN Device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on CHADS₂ or CHA₂DS₂-VASc scores and are recommended for anticoagulation therapy;
- Are deemed by their physicians to be suitable for warfarin; and
- Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin

WATCHMAN™ is **not** intended to be a broad replacement for Oral Anticoagulants (OAC)
WATCHMAN LAA Closure Technology - P130013
Watchman Procedure

- Under general anesthesia
- TEE probe throughout the procedure
- Fluroscopically guided
- One venous puncture via right femoral vein
Clinical Trial Device Arm Drug Protocol

*Cessation of warfarin is at physician discretion provided that any peri-device flow demonstrated by TEE is ≤ 5mm. Before 6 months, when seal is adequate, patients can cease warfarin and should begin clopidogrel 75 mg daily and increase aspirin dosage to 300-325 mg daily. This regimen should continue until a total of 6 months have elapsed after implantation.
**Implant Success & Warfarin Cessation**

Implant success defined as deployment and release of the device into the left atrial appendage.

### Warfarin Cessation

<table>
<thead>
<tr>
<th>Study</th>
<th>45-day</th>
<th>12-month</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROTECT AF</td>
<td>87%</td>
<td>&gt;93%</td>
</tr>
<tr>
<td>CAP</td>
<td>96%</td>
<td>&gt;96%</td>
</tr>
<tr>
<td>PREVAIL</td>
<td>92%</td>
<td>&gt;99%</td>
</tr>
</tbody>
</table>

**PREVAIL Implant Success**

No difference between new and experienced operators.

- Experienced Operators
  - n=26
  - 96%
- New Operators
  - n=24
  - 93%
  - p = 0.28

**PREVAIL**: Holmes, DR et al. JACC 2014; 64(1):1-12.
Long Term PROTECT AF
All-Cause Mortality

Event free probability (%)

Year

0 0.5 1 1.5 2 2.5 3 3.5 4 4.5

WATCHMA
N
Control

463 404 389 381 373 360 352
341 330 294 202 194 177
244 233 222 216 204
163 150 125 92

Circulation. 013;127:720-729.
Long Term Data/Meta Analysis

- LAAC similar benefit to warfarin for primary efficacy endpoint (stroke, SE, CV death)
- LAAC improvement in survival, particularly from freedom from CV death
- All cause bleeding similar
  - Exclude procedure related bleeding, then bleeding was higher in the coumadin group
- All cause stroke rates similar but
  - Warfarin patients have more hemorrhagic strokes
  - LAAC patients have more ischemic strokes
    - Strokes from other sources
### Major Complication Rates Across Watchman Clinical Studies

<table>
<thead>
<tr>
<th>Procedural Parameters</th>
<th>Aggregate Clinical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Procedures</td>
<td>6,720</td>
</tr>
<tr>
<td>Implantation Success, %</td>
<td>94.9%</td>
</tr>
</tbody>
</table>

### Complication Rates

- Pericardial Tamponade: 1.24%
- Procedure-Related Stroke: 0.18%
- Device Embolization: 0.25%
- Procedure-Related Death: 0.06%

![Graph showing complication rates across clinical studies](image)

Watchman Pitfalls

- Requires anticoagulation pre and post with Coumadin or NOAC
- ASAP II Trial pending
  - Evaluate Watchman device with asa and Plavix only
- Not applicable to all shapes and sizes of LAA
- Alternatives
  - Amulet (St. Jude)
  - Coherex Wavecrest (Coherex Medical)
  - Lariat procedure
  - Atri Clip