Reducing Stroke Risk Using Left Atrial Appendage Closure Devices

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Disclosures

• Honoraria
  • Medtronic, St. Jude Medical, Biotronik

• Research Grants
  • Biosense Webster, Biotronik
Learning Objectives

- Understand procedural options to occlude the left atrial appendage and reduce stroke risk
- Critical evaluate data supporting reduced stroke risk after LAAO

Background

• Atrial fibrillation (AF) is the most common cardiac arrhythmia

• In those older than 40 years of age, an estimated 1 in 4 lifetime risk

• Large projected increase in prevalence by the year 2050
The Aging U.S. Population - Risk for AF

Background

- The most serious, common complication of AF is arterial thromboembolism
  - Most clinically evident embolic event is ischemic stroke
AF and Stroke

Thrombus

LEFT ATRIUM
Background

- Antithrombotic therapy with warfarin (and now novel oral anticoagulants) has been shown to:
  - Lower the risk of thromboembolism in patients with AF
    - Regardless of duration
      - Paroxysmal AF
      - Persistent AF
Risk of Embolization

- Risk of embolization in AF patients varies according to the presence or absence of clinical risk factors
- Risk rates have been assessed by different risk-stratification systems
  - $\text{CHADS}_2$-Score
    - Traditionally used
  - $\text{CHA}_2\text{DS}_2$-VASc Score
    - New guideline recommended
Lack of Appropriate OAC

Original Investigation

Oral Anticoagulant Therapy Prescription in Patients With Atrial Fibrillation Across the Spectrum of Stroke Risk Insights From the NCDR PINNACLE Registry

Jonathan C. Hsu, MD, MAS; Thomas M. Maddox, MD, MSC; Kevin F. Kennedy MS; David F. Katz, MD; Lucas R. Marvez, MD; Steven A. Lubitz, MD, MPH; Ari K. Gehl, MD; Minlu P. Turakhia, MD, MAS; Gregory M. Marcus, MD, MAS

**Importance** Patients with atrial fibrillation (AF) are at a proportionally higher risk of stroke based on accumulation of well-defined risk factors.

**Objective** To examine the extent to which prescription of an oral anticoagulant (OAC) in real-world US cardiology practices increases as the number of stroke risk factors increases.

**Design, Setting, and Participants** Cross-sectional registry study of outpatients with AF enrolled in the American College of Cardiology National Cardiovascular Data Registry’s PINNACLE (Practice Innovation and Clinical Excellence) Registry between January 1, 2008, and December 30, 2012. As a measure of stroke risk, we calculated the CHADS2 score and the CHA2DS2-VASc score for all patients. Using multinomial logistic regression models adjusted for patient, physician, and practice characteristics, we examined the association between increased stroke risk score and prescription of an OAC.

**Main Outcomes and Measures** The primary outcome was prescription of an OAC with warfarin sodium or a non-vitamin K antagonist OAC.

**Results** The study cohort comprised 429,417 outpatients with AF. Their mean (SD) age was 71.3 (12.9) years, and 55.8% were male. Prescribed treatment consisted of an OAC (92.6%), aspirin only (10.3%), aspirin plus a thienopyridine (23.4%), or no antithrombotic therapy (87.2%). Each 1-point increase in risk score was associated with increased odds of OAC prescription compared with aspirin-only prescription using the CHADS2 score (adjusted odds ratio, 1.08; 95% CI, 1.04-1.12; P < .001) and the CHA2DS2-VASc score (adjusted odds ratio, 1.15; 95% CI, 1.12-1.19; P < .001). Overall, OAC prescription prevalence did not exceed 50% even in higher-risk patients with a CHADS2 score exceeding 3 or a CHA2DS2-VASc score exceeding 4.

**Conclusions and Relevance** In a large quality improvement registry of outpatients with AF, prescription of OAC therapy increased with a higher CHADS2 score and CHA2DS2-VASc score. However, a plateau of OAC prescription was observed, with less than half of high-risk patients receiving an OAC prescription.

Oral Anticoagulant Use Does Not Top 50%, Even in the Highest Stroke Risk AF Patients

Aspirin Instead of Oral Anticoagulant Prescription in Atrial Fibrillation Patients at Risk for Stroke

Jonathan C. Hsu, MD, MAS, Thomas M. Maddox, MD, MSc, Kevin Kennedy, MS, David F. Katz, MD, Lucas N. Marzec, MD, Steven A. Lubitz, MD, MPH, Anil K. Gehi, MD, Mintu P. Turakhia, MD, MAS, Gregory M. Marcus, MD, MAS

ABSTRACT

BACKGROUND Oral anticoagulation (OAC), rather than aspirin, is recommended in patients with atrial fibrillation (AF) at moderate to high risk of stroke.

OBJECTIVES This study sought to examine patient and practice-level factors associated with prescription of aspirin alone compared with OAC in AF patients at intermediate to high stroke risk in real-world cardiology practices.

- 38-40% of patients at moderate to high risk of stroke treated with Aspirin alone

Hsu, et al. JACC 2016.
Left Atrial Appendage Exclusion Devices for Stroke Prevention in AF

A new era
Overview

• Outline novel treatments for ligation or occlusion of the left atrial appendage (LAA)
  • Left atrial appendage occlusion
    • WATCHMAN device (Boston Scientific)
  • Left atrial appendage ligation
    • LARIAT device (SentreHeart, Inc)

• Review literature on outcomes after LAA exclusion
Role of LAA

Source of over 90% of thrombus in nonvalvular AF

Surgical Ligation

- Open chest visualization with ligation or amputation of LAA
  - Often performed in patients undergoing cardiac surgery for other indications
  - Limited data suggesting this approach can reduce the risk of stroke
- Feasibility of a stand alone thorascopic approach to LAA ligation

Surgical Ligation

- Retrospective study of 205 patients
  - Concomitant LAA ligation with mitral valve replacement (83% for rheumatic heart disease, 86% in AF)
    - 6 year f/u data of incidence of an embolic event
      - LAA ligation – 3%
      - No LAA ligation – 17%

Left Atrial Appendage Occlusion

WATCHMAN Device
LAA Occlusion- WATCHMAN

• Manufactured by Boston Scientific
• Recent FDA approval 3/13/15
• Left atrial appendage occlusion device
  • Implanted with transseptal puncture and TEE guidance
• Goal
  • Reduce stroke risk
  • Comparator
    • Warfarin anticoagulation
LAA Occlusion- WATCHMAN

- Nitinol cage covered by a layer of polyethylene terephthalate (PTFE)
  - Deployed inside the LAA
  - Fabric of the WATCHMAN device is permeable to blood
  - Requires conventional thromboembolic prophylaxis with warfarin
    - At least 45 days post-implant
    - TEE then performed to ensure endothelialization
  - Then treated with both aspirin 81 mg and clopidogrel 75 mg for 6 mo
Left atrial appendage closure

A device is placed in the left atrial appendage to close it off from the rest of the left atrium.
Watchman Device

- Nitinol frame
  - Radial expansion
  - 10 anchors
- 5 sizes – 21, 24, 27, 30, 33 mm
- 160 micron membrane polyethylene terephthalate
Watchman Data

- ~1700 pts in clinical trials
- Implantation success 91-95%
- Transseptal puncture
- Difficult anatomy may exist
  - Ostium diameter > LAA length
  - Chicken wing LAA
- Complication rate 3-10%
Percutaneous Left Atrial Appendage Closure for Stroke Prophylaxis in Patients With Atrial Fibrillation

2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) Trial

Vivek Y. Reddy, MD; Shephal K. Doshi, MD; Horst Sievert, MD; Maurice Buchbinder, MD; Petr Neuzil, MD, PhD; Kenneth Huber, MD; Jonathan L. Halperin, MD; David Holmes, MD; on behalf of the PROTECT AF Investigators
PROTECT-AF Data

- Non-inferiority trial, >700 patients with nonvalvular, randomization 2:1 ratio to device or long term warfarin

- Inclusion criteria:
  - paroxysmal, persistent, or permanent AF
  - CHADS2 score ≥1

- Device implantation was successful in 91%

PROTECT-AF Data

• Composite primary efficacy end point:
  • Stroke, systemic embolism, and cardiovascular death

• Primary safety end point:
  • Composite of major bleeding, pericardial effusion, procedure related stroke, and device embolization

PROTECT-AF Data

• Mean f/u 18 months
  • Primary efficacy event rate was similar:
    • 3.0 events per 100 / pt years (device)
    • 4.9 events per 100 / pt years (warfarin), rate ratio 0.62, 95% Bayesian credible interval 0.35-1.25).
  • Non-inferior
  • Primary safety end point more in device
    • 7.4 events per 100 / pt years (device)
    • 4.4 events per 100 / pt years (warfarin)
      • Most safety issues occurred early
        • 50% effusion requiring drainage

Protect AF- Endpoints

Figure 2. Kaplan-Meier curves of the primary efficacy end point. Incident probabilities for the intention-to-treat analysis are shown with time calculated as the days since randomization for the composite primary efficacy end point of stroke, systemic embolism, and cardiovascular death; stroke alone; and all-cause mortality.

Primary Safety Endpoint

Original Investigation

Percutaneous Left Atrial Appendage Closure vs Warfarin for Atrial Fibrillation
A Randomized Clinical Trial

Vivek Y. Reddy, MD; Horst Sievert, MD; Jonathan Halperin, MD; Shephal K. Doshi, MD; Maurice Buchbinder, MD; Petr Neuzil, MD, PhD; Kenneth Huber, MD; Brian Whisenant, MD; Saibal Kar, MD; Vijay Swarup, MD; Nicole Gordon, BSEE; David Holmes, MD; for the PROTECT AF Steering Committee and Investigators

IMPORTANT While effective in preventing stroke in patients with atrial fibrillation (AF), warfarin is limited by a narrow therapeutic profile, a need for lifelong coagulation monitoring, and multiple drug and diet interactions.

OBJECTIVE To determine whether a local strategy of mechanical left atrial appendage (LAA) closure was noninferior to warfarin.
# PROTECT-AF Long Term F/U

## Table 2. Intention-to-Treat Primary Efficacy and Safety Outcomes According to Treatment Group by Bayesian Model

<table>
<thead>
<tr>
<th>Event</th>
<th>Device Group (n = 463)</th>
<th>Warfarin Group (n = 244)</th>
<th>Device/Warfarin Rate Ratio (95% Credible Interval)</th>
<th>Posterior Probabilities, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events/Patient-Years</td>
<td>Observed Rate(^a)</td>
<td>Events/Patient-Years</td>
<td>Observed Rate(^a)</td>
</tr>
<tr>
<td>Primary efficacy end point(^b)</td>
<td>39/1720.2</td>
<td>2.3 (1.7-3.2)</td>
<td>34/900.8</td>
<td>3.8 (2.5-4.9)</td>
</tr>
<tr>
<td>Stroke</td>
<td>26/1720.7</td>
<td>1.5 (1.0-2.2)</td>
<td>20/900.9</td>
<td>2.2 (1.3-3.1)</td>
</tr>
<tr>
<td>Ischemic</td>
<td>24/1720.8</td>
<td>1.4 (0.9-2.1)</td>
<td>10/904.2</td>
<td>1.1 (0.5-1.7)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>3/1774.2</td>
<td>0.2 (0.0-0.4)</td>
<td>10/916.2</td>
<td>1.1 (0.5-1.8)</td>
</tr>
<tr>
<td>Disabling(^c)</td>
<td>8/1771.3</td>
<td>0.5 (0.2-0.8)</td>
<td>11/912.7</td>
<td>1.2 (0.6-1.9)</td>
</tr>
<tr>
<td>Nondisabling(^c)</td>
<td>18/1723.7</td>
<td>1.0 (0.7-1.7)</td>
<td>9/907.7</td>
<td>1.0 (0.4-1.7)</td>
</tr>
<tr>
<td>Systemic embolization</td>
<td>3/1773.6</td>
<td>0.2 (0.0-0.4)</td>
<td>0/919.5</td>
<td>0</td>
</tr>
<tr>
<td>Cardiovascular or unexplained death</td>
<td>17/1774.3</td>
<td>1.0 (0.6-1.5)</td>
<td>22/919.4</td>
<td>2.4 (1.4-3.4)</td>
</tr>
<tr>
<td>Primary safety end point(^d)</td>
<td>60/1666.2</td>
<td>3.6 (2.8-4.6)</td>
<td>27/878.2</td>
<td>3.1 (2.0-4.3)</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

\(^a\) Events per 100 patient-years (95% credible interval).

\(^b\) Primary efficacy defined as composite of stroke, systemic embolization, or cardiovascular/unexplained death.

\(^c\) Disabling or fatal strokes were those with a Modified Rankin Score of 3-6 after the stroke. Nondisabling strokes were those with Modified Rankin Scores of 0-2 after the stroke.

\(^d\) Safety defined as procedure-related events (pericardial effusion requiring intervention or prolonged hospitalization, procedure-related stroke, or device embolization) and major bleeding (intracranial or bleeding requiring transfusion).
PROTECT-AF Long Term F/U

Figure 2. Kaplan-Meier Curves for the Primary Efficacy and Safety End Points

- **A** Primary efficacy end point
  - HR (95% CI), 0.61 (0.38-0.97)
  - \( P = .04 \)

- **B** Primary safety end point
  - HR (95% CI), 1.21 (0.78-1.94)
  - \( P = .41 \)

Figure 3. Kaplan-Meier Curves for Ischemic Stroke, Cardiovascular Mortality, and All-Cause Mortality

- **A** Ischemic stroke
  - RR (95% CI), 1.26 (0.72-3.28)
  - \( P = .49 \)

- **B** Cardiovascular mortality
  - HR (95% CI), 0.40 (0.21-0.75)
  - \( P = .005 \)

- **C** All-cause mortality
  - HR (95% CI), 0.66 (0.45-0.98)
  - \( P = .04 \)

PROTECT-AF Quality of Life

- Quality of life compared:
  - 361 device vs
  - 186 warfarin patients
  - Quality of life was assessed using the Short-Form 12 Health Survey
    - At 12 months, patients treated with the closure device had improvement in health related QOL measures
    - QOL declined among patients treated with warfarin

PROTECT-AF Quality of Life

Figure 2 Change in QOL in All Subjects, Device Versus Control

(A) The change in quality of life (QOL) in all patients for the mental and physical component scores, device (blue bars) compared to warfarin (red bars), is shown. (B) The relative change in QOL among individual patients within each group is depicted. Green areas = improved; blue areas = no change; red areas = worsened/death.
WATCHMAN - FDA Approval

- Increased risk for stroke based on CHADS$_2$ or CHA$_2$DS$_2$-VASc scores and are recommended for anticoagulation therapy
- Are deemed by their physicians to be suitable for warfarin
- Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin
WATCHMAN Post-Approval

• More questions than answers?
  • PREVAIL and PROTECT both used warfarin as the comparator arm to WATCHMAN
    • Is equivalence the same in the era of non-vitamin K antagonist oral antagonists?
    • Future studies will be forthcoming
  • Patients with contra-indication to anticoagulation—Can WATCHMAN be used?
    • Small ASAP Trial performed
    • Larger studies and registry data needed
Percutaneous Left Atrial Appendage Ligation

Procedures to reduce stroke risk in patients, particularly those not able to tolerate oral anticoagulation
LARIAT LAA Ligation

- Non-surgical, percutaneous device
  - Dry epicardial puncture for epicardial access of the LAA
  - Transseptal access for endocardial access of LAA
  - Approved by the US FDA for soft tissue closure ("approximation") only
    - Particularly those who cannot take oral anticoagulation and are at high risk for stroke due to AF
Subxyphoid Puncture-Appendage Ligation Access
Subxyphoid Puncture—Dry Pericardial Access
Percutaneous Left Atrial Appendage Suture Ligation Using the LARIAT Device in Patients With Atrial Fibrillation

Initial Clinical Experience
Percutaneous Left Atrial Appendage Suture Ligation Using the LARIAT Device in Patients With Atrial Fibrillation

Initial Clinical Experience
LARIAT Long-Term Followup

Short and long-term outcomes of percutaneous left atrial appendage suture ligation: Results from a US multicenter evaluation

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LARIAT Long-Term Followup

• 712 consecutive LARIAT
  • Successfully deployed in 682 patients (95.5%)
  • Complete closure in 669 patients (98%)
    • 13 patients (1.8%) had a trace leak (<2 mm)
  • 1 death related to the procedure
  • 10 patients (1.44%) had cardiac perforation necessitating open heart surgery
    • Another 14 (2.01%) did not need surgery
  • Risk of cardiac perforation decreased significantly after the introduction of a micropuncture needle for pericardial access
LARIAT Long-Term Followup

- Delayed complications:
  - Pericarditis requiring >2 weeks of treatment with nonsteroidal anti-inflammatory drugs/colchicine and pericardial and pleural effusion after discharge occurred in 34 (4.78%) patients
  - Risk decreased significantly with the periprocedural use of colchicine

- Follow-up TEE (n =480) showed a leak of 2–5 mm in 6.5% and a thrombus in 2.5%
LARIAT and Electrical Activity

The effects of LAA ligation on LAA electrical activity

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Figure 1  (A) Mean unipolar and (B) mean bipolar left atrial appendage (LAA) voltage pre- and post-LAA closure.

LARIAT and AF Burden

Impact of left atrial appendage exclusion using an epicardial ligation system (LARIAT) on atrial fibrillation burden in patients with cardiac implantable electronic devices

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The Future of LARIAT

• Recent FDA Approval of AMAZE Trial
  • LARIAT ligation for adjunctive treatment of AF
  • Randomized controlled trial
    • LARIAT + PVI ablation vs. PVI ablation alone
  • Persistent or longstanding persistent AF
  • Background:
    • Only percutaneous device with potential mechanical and electrical isolation of LAA myocardium by devascularization
LARIAT- AMAZE TRIAL

• Study plan
  • Enroll a maximum of 600 persistent or longstanding persistent AF patients
  • Candidates for PVI catheter ablation
  • Up to 50 center study
    • The first stage of the AMAZE Trial will enroll up to 175 patients at 15 centers

• Outcome: recurrent atrial fibrillation

• Will use of LARIAT as adjunct to PVI decrease AF?
Key Differences

- Requirement of dry pericardial access
  - LARIAT
- Epicardial ligation versus endocardial plug
  - Oral anticoagulation implications
- Left atrial appendage tissue characteristics after exclusion
  - AF rhythm control implications
  - Reduction of recurrent AF
Summary

• AF is common and can result in stroke
  • LAA ligation can be safe and effective to reduce stroke risk in patients that cannot be anticoagulated
  • LAA occlusion devices, mainly Watchman in the United States, have shown equivalence compared to warfarin and will be important as a procedural option in preventing strokes in AF patients
THANK YOU

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76 year old woman with DM, HTN, atrial fibrillation and spontaneous intracerebral hemorrhage on coumadin with INR 2.8

Discharged from hospital and now recovered, taken off of coumadin
Lack of Appropriate OAC

Original Investigation

Oral Anticoagulant Therapy Prescription in Patients With Atrial Fibrillation Across the Spectrum of Stroke Risk Insights From the NCDR PINNACLE Registry

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Importance Patients with atrial fibrillation (AF) are at a proportionally higher risk of stroke based on accumulation of well-defined risk factors.

Objective To examine the extent to which prescription of an oral anticoagulant (OAC) in real-world US cardiology practices increases as the number of stroke risk factors increases.

Design, Setting, and Participants Cross-sectional registry study of outpatients with AF enrolled in the American College of Cardiology National Cardiovascular Data Registry’s PINNACLE (Practice Innovation and Clinical Excellence) Registry between January 1, 2008, and December 30, 2012. As a measure of stroke risk, we calculated the CHADS2 score and the CHA2DS2-VASc score for all patients. Using multinomial logistic regression models adjusted for patient, physician, and practice characteristics, we examined the association between increased stroke risk score and prescription of an OAC.

Main Outcomes and Measures The primary outcome was prescription of an OAC with warfarin sodium or a non-vitamin K antagonist OAC.

Results The study cohort comprised 4,294,417 outpatients with AF. Their mean (SD) age was 71.3 (12.9) years, and 55.9% were male. Prescribed treatment consisted of an OAC (42,600 [4.9%]), aspirin only (111,134 [25.9%]), aspirin plus a thienopyridine (25,545 [5.9%]), or no antithrombotic therapy (102,229 [23.8%]). Each 1-point increase in risk score was associated with increased odds of OAC prescription compared with aspirin-only prescription using the CHADS2 score (adjusted odds ratio, 1.13; 95% CI, 1.11-1.15; P < .001) and the CHA2DS2-VASc score (adjusted odds ratio, 1.16; 95% CI, 1.15-1.17; P < .001). Overall, OAC prescription prevalence did not exceed 50% even in higher-risk patients with a CHADS2 score exceeding 3 or a CHA2DS2-VASc score exceeding 4.

Conclusions and Relevance In a large-quality improvement registry of outpatients with AF, prescription of OAC therapy increased with a higher CHADS2 score and CHA2DS2-VASc score. However, a plateau of OAC prescription was observed, with less than half of high-risk patients receiving an OAC prescription.

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Figure 1. Prevalence of Patients With AF Across the Spectrum of the CHADS₂ Score and the CHA₂DS₂-VASc Score

A. Distribution of CHADS₂ scores within the cohort

B. Distribution of CHA₂DS₂-VASc scores within the cohort

Shown is the distribution of patients with AF in the cohort characterized by the CHADS₂ score (A) and the CHA₂DS₂-VASc score (B). AF indicates atrial fibrillation.
Figure 2. Prevalence of Antithrombotic Therapies in Patients With AF Across the Spectrum of Stroke Risk by the CHADS$_2$ Score and the CHA$_2$DS$_2$-VASc Score

A) Prevalence of treatment strategies across the spectrum of CHADS$_2$ score

B) Prevalence of treatment strategies across the spectrum of CHA$_2$DS$_2$-VASc score

Shown is the proportion of patients treated with different antithrombotic therapies based on the CHADS$_2$ score (A) and the CHA$_2$DS$_2$-VASc score (B). Oral anticoagulant therapy was defined as prescription of either warfarin sodium, dabigatran, or rivaroxaban, further stratified by warfarin (dark blue) vs dabigatran or rivaroxaban (dark brown). Other treatment strategies included prescription of aspirin only (light brown), aspirin plus a thienopyridine (light blue), or no antithrombotic therapy (light grey). Treatment with a thienopyridine was defined as prescription of clopidogrel bisulfate, ticlopidine hydrochloride, or prasugrel. AF indicates atrial fibrillation.
Inappropriate Anticoagulation

LESS IS MORE

Oral Anticoagulant Prescription in Patients With Atrial Fibrillation and a Low Risk of Thromboembolism: Insights From the NCDR PINNACLE Registry

In patients with atrial fibrillation (AF) who are at risk for thromboembolism, anticoagulation therapy with warfarin or the newer novel anticoagulants reduces morbidity and mortality.⁴ Because oral anticoagulant use carries a risk of bleeding, the drugs are not recommended in patients with AF who are at a particularly low risk for stroke. Specifically, previous AF guidelines recommend against the use of oral anticoagulation in patients younger than 60 years without heart disease or other known risk factors for thromboembolism,³ and more recently updated guidelines do not recommend the use of oral anticoagulation in patients with AF without any established risk factor for stroke.⁴ We sought to examine the prevalence of oral anticoagulant prescription that does not adhere to the guidelines in young and healthy patients with AF who were at the lowest risk for thromboembolism, as well as the clinical predictors of this practice.

Methods | Of 1,711,326 patients enrolled in the National Cardiovascular Data Registry’s PINNACLE (Practice Innovation and Clinical Excellence) Registry between January 1, 2008, and December 30, 2012, a total of 359,315 (21.0%) had received a diagnosis of AF. Our final study cohort, derived from 76 cardiology practices from 287 different geographic office sites in 33 states, comprised 10,995 young (<60 years) and healthy patients with AF and no structural heart disease who were at low risk for thromboembolism. While all these patients by definit-

Results | In the cohort of patients with a CHADS₂ score of 0 and the cohort of those with a CHA₂DS₂-VASc score of 0, a total of 2561 (23.3%) and 1787 (26.6%) patients with AF, respectively, were prescribed an oral anticoagulant. Demographics and clini-

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Inappropriate Anticoagulation

**Figure. Relative Risk of Oral Anticoagulant Prescription in Patients With Atrial Fibrillation Who Have Low Stroke Risk**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A CHADS(_2) Cohort</td>
<td></td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.48 (1.41-1.56)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.34 (1.22-1.46)</td>
</tr>
<tr>
<td>Body mass index (per 5 kg/m(^2))</td>
<td>1.18 (1.14-1.22)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.93 (0.85-1.01)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>0.07 (0.56-1.67)</td>
</tr>
<tr>
<td>Insurance: Medicare vs private</td>
<td>1.32 (1.17-1.49)</td>
</tr>
<tr>
<td>Insurance: Medicaid vs private</td>
<td>1.07 (0.87-1.31)</td>
</tr>
<tr>
<td>Insurance: other vs private</td>
<td>0.80 (0.52-1.22)</td>
</tr>
<tr>
<td>Insurance: no insurance vs private</td>
<td>1.13 (0.99-1.30)</td>
</tr>
<tr>
<td>Region: South vs Northeast</td>
<td>0.69 (0.49-0.98)</td>
</tr>
<tr>
<td>Region: West vs Northeast</td>
<td>0.76 (0.55-1.05)</td>
</tr>
<tr>
<td>Region: Midwest vs Northeast</td>
<td>0.84 (0.57-1.22)</td>
</tr>
<tr>
<td>Tobacco: current vs never</td>
<td>0.93 (0.81-1.06)</td>
</tr>
<tr>
<td>Tobacco: quit &lt;12 months vs never</td>
<td>1.05 (0.84-1.31)</td>
</tr>
<tr>
<td>Tobacco: quit &gt;12 months vs never</td>
<td>1.01 (0.92-1.11)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B CHADS(_2)-VASc Cohort</td>
<td></td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.44 (1.36-1.54)</td>
</tr>
<tr>
<td>Body mass index (per 5 kg/m(^2))</td>
<td>1.19 (1.15-1.23)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.92 (0.83-1.02)</td>
</tr>
<tr>
<td>Insurance: Medicare vs private</td>
<td>1.29 (1.13-1.47)</td>
</tr>
<tr>
<td>Insurance: Medicaid vs private</td>
<td>0.93 (0.80-1.25)</td>
</tr>
<tr>
<td>Insurance: other vs private</td>
<td>0.77 (0.52-1.14)</td>
</tr>
<tr>
<td>Insurance: no insurance vs private</td>
<td>1.19 (1.03-1.37)</td>
</tr>
<tr>
<td>Region: South vs Northeast</td>
<td>0.67 (0.47-0.96)</td>
</tr>
<tr>
<td>Region: West vs Northeast</td>
<td>0.73 (0.54-1.00)</td>
</tr>
<tr>
<td>Region: Midwest vs Northeast</td>
<td>0.79 (0.54-1.17)</td>
</tr>
<tr>
<td>Tobacco: current vs never</td>
<td>1.02 (0.87-1.19)</td>
</tr>
<tr>
<td>Tobacco: quit &lt;12 months vs never</td>
<td>1.10 (0.87-1.39)</td>
</tr>
<tr>
<td>Tobacco: quit &gt;12 months vs never</td>
<td>1.11 (1.00-1.23)</td>
</tr>
</tbody>
</table>

Characteristics associated with oral anticoagulant prescription after multivariable adjustment in patients with atrial fibrillation and low thromboembolic risk, as defined by a CHADS\(_2\) (defined as 1 point each for congestive heart failure, hypertension, age 75 years or older, and diabetes mellitus, and 2 points for prior stroke, transient ischemic attack, or thromboembolism) score of 0 (A) and those with a CHADS\(_2\)-VASc (defined as 1 point each for congestive heart failure, hypertension, age 65 to 74 years, diabetes mellitus, vascular disease, and female sex, and 2 points each for prior stroke, transient ischemic attack, or thromboembolism and age 75 years or older) score of 0 (B). Error bars denote 95% CIs. Body mass index is calculated as weight in kilograms divided by height in meters squared. RR indicates relative risk.
ASAP Trial

- 150 patients with nonvalvular AF and CHADS$_2$ ≥1, who were considered ineligible for warfarin
  - Primary endpoint was the combined events of ischemic / hemorrhagic stroke, and death.
  - Mean duration of follow-up was 14.4 ± 8.6 mo
  - Serious procedure- or device-related safety events occurred in 8.7% of patients (13 of 150 patients).
    - All-cause stroke or systemic embolism occurred in 4 patients (2.3% per year)
  - Ischemic stroke rate was less than that expected (7.3% per year) based on the CHADS$_2$ scores
Amplatzer LAA Cardiac Plug
Amplatzer LAA Cardiac Plug

- St. Jude Medical
  - Nitinol-only cage
    - Consists of a left atrial disk and a distal plug connected to the left atrial disk by a short waist
    - Distal plug contains six pairs of barbs designed to increase stability within the appendage
  - Shorter than the Watchman device
  - May be more advantageous in individuals with variable morphology of the appendage given more flexible waist
  - CE Mark approval in Europe, not FDA approved
WaveCrest Device
WaveCrest Device

- Coherex Medical
  - Nitinol based, similar design as the Watchman
    - However, WaveCrest is covered by a foam layer on the LAA side and PTFE on the side facing the left atrium
    - Anchors along the LAA side
    - Designed to be deployed at the entrance of the LAA rather deep within the structure
    - May be alternative to Watchman if the LAA is too small to accommodate larger devices
  - CE Mark approval in Europe, not FDA approved