Atrial Fibrillation 2016
Quality of Life and Preventing Stroke

The 14 Clinical Challenges

ACC-New York, Dec. 12, 2015
No Disclosures
Circulation Research Compendium

Atrial Fibrillation
Editor: Stanley Nattel

2014

ACC / AHA / HRS - JACC 2014; 64: 2246
ESC - EHJ 2013; 34:1471
### AF - CLINICAL CHALLENGES (14) - 2016

<table>
<thead>
<tr>
<th></th>
<th>Presentation: Prevalence / Stroke / Death vs Sx (2)</th>
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<tbody>
<tr>
<td>2</td>
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ACC / AHA / HRS - JACC 2014; 64: 2246 - ESC - EHJ 2013; 34:1471
1a). Prevalence of Adults With AF
The European Union Between 2000 And 2060

BP Krijthe et. al. Eur Heart J. 2013;34:2746
Over Age 50 yr.- AF: 1/2 1<sup>st</sup> yr of Age, -
Isq. Stroke: 1<sup>st</sup> yr of Age, Hem. Stroke: 1-2%
Stroke: A Significant Cause Of Poor Health

- Stroke accounts for nearly 10% of all deaths worldwide.
- The number of strokes per year is predicted to rise dramatically as the population ages.
- About 30% strokes are cardioembolic & 15% relate to AF
- Strokes in patients with AF are more severe and have worse outcomes than strokes in people without AF.
- AF almost doubles the death rate from stroke. AF increases the risk of remaining disabled following stroke by almost 50%.

ESC Guidelines EHJ 2010;31:2369 - Working Group Report, EU 2010
1c). Death, Causes & Influencing Factors in AF
A Competing-Risk Analysis From the Randomized Evaluation of Long-Term Anticoagulant Therapy Study

RE-LY (E Marijon et. al.) Circulation. 2013;128:2192
DP Leong, et al EHJ 2013; 34: 1027 – Association & Causation (Stroke)
## 2) AF Symptoms / Etiology

**EHRA Score**

<table>
<thead>
<tr>
<th>EHRA class</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHRA I</td>
<td>‘No symptoms’</td>
</tr>
<tr>
<td>EHRA II</td>
<td>‘Mild symptoms’; normal daily activity not affected</td>
</tr>
<tr>
<td>EHRA III</td>
<td>‘Severe symptoms’; normal daily activity affected</td>
</tr>
<tr>
<td>EHRA IV</td>
<td>‘Disabling symptoms’; normal daily activity discontinued</td>
</tr>
</tbody>
</table>

1. **Presentation:** Prevalence / Stroke / Death vs Sx (2)

2. **Etiology:** General vs Specific (2)

3. **AC Rx:** When / Bridge / NSAID vs SCI / NSR (2)

4. **Aging:** TE & Bleeding vs Warfarin (2)

5. **AF / Stent:** Triple Rx vs Double Rx (2)

6. **Warf. / NOACs:** Efficacy vs Safety (2)

7. **Ablat. Yes / No** AC vs LAA Closure (2)

**ACC / AHA / HRS - JACC 2014; 64: 2246 - ESC - EHJ 2013; 34:1471**
1). General Etiologies of AF – Think !!!!!

- d) Alcohol
  - (0.5 – 5.0%)
  - < Connexins

- a) Environmental risk factors
  - HTN, diabetes, valve disease,
  - HF, obesity, smoking, SDB

- b) Structural substrate
  - Inflammation
  - Abnormal innervation
  - Metabolic changes
  - Atrial remodeling & fibrosis
  - Hypertrophy

- c) Epigenetic, transcriptional, proteomic and metabolomic modification

- Genetic variation
  - Primary genes
    - PITX2, ZFHX3, KCNN3
  - Modifier genes

- Electrical substrate
  - Membrane ionic currents
  - Regional heterogeneity
  - Calcium dynamics

- Endophenotypes
  - LA enlargement, P wave indices

- Atrial Fibrillation

2a). **Obesity - Peri-atrial EAT Volume Indexes (CT)**

**AF Events According To LA Volume Index**

K Nakanishi et. al. Circ J 2012;76:2748 (Osaka)- Adipocytokines

HS Abed et. al. JAMA. 2013;310:2050 - <Weight, <AF
2b). **AF Substrate: Towards Specific Fibrotic Atrial Cardiomyopathy**

![Box plot diagram showing the ratio of collagen I to GAPDH in different cardiac conditions: SR, Lone AF, and MVD with AF. The diagram illustrates statistical significance with P-values of 0.01 in two comparisons.](image)

**H Kottkamp Eur Heart J. 2013; 34: 2731**
2c) AF - LAA Morphologies (CT, MRI) – N=932

Chicken Wing LAA Morphology

Windsock LAA Morphology

Cactus LAA Morphology

Cauliflower LAA Morphology

L Di Biase et. al. J Am Coll Cardiol 2012;60:531 (Austin, Foggia, Turin)
J H Yoon et al., Clin Cardiol 2013; 36:235 (Korea) – LA Function > Volume
2d). Genetics in AF – Familial 5%

Novel Genetic Markers Associate With Atrial Fibrillation Risk in Europeans and Japanese

Steven A. Lubitz, MD, MPH,1,2 Kathryn L. Lunetta, PhD,3,4 Honghuang Lin, PhD,5,6 Dan E. Arking, PhD,7,8 Stella Trompeter, PhD,9 Guo Li, MS,5 Bouwe P. Krijthe, MSc,10,11 Daniel I. Chapman, PhD,12,13 John Barnard, PhD,14 Marcus E. Kleber, PhD,15 Marcus Dörö, MD,16,17 Kouichi Ozaki, PhD,18 Albert V. Smith, PhD,19 Martina Müller-Nurssyid, MSc, PhD,20 Stefan Walter, PhD,21 Suni K. Agawal, MD, PhD,22 Joshua C. Bis, PhD,23 Jennifer A. Brody, BA,24 Lin Y. Chen, MD, MS,25 Brendan M. Everett, MD, MPH,26,27 Ian Ford, PhD,27 Oscar H. Franco, MD, PhD,26,28 Tamara B. Harris, MD,26 Albert Hofman, MD, PhD,26,28 Stefan Kääb, MD, PhD,26,28 Saagar Mahida, MB, ChB,27 Sekar Kathiresan, MD, MPH,26,28 Michiaki Kubo, MD, PhD,29 Lenore J. Launer, PhD,28 Peter W. Macfarlane, DSc,28 Jared W. Magnani, MD, MSc,30,31 Barbara McKnight, PhD,32 David D. McManus, MD, ScM,32 Annette Peters, PhD, MPH,32 Bruce M. Psaty, MD, PhD,32,33,34 Lynda M. Rose, MSc,31 Jerome I. Rotter, MD,32 Guenterth Silbernagel, MD,31 Jonathan D. Smith, PhD,31 Nuna Sotoodehnia, MD, MPh,31,32 David J. Stott, MD,31 Kent D. Taylor, PhD,31 Andreas Tornowitzki, MD,31 Tatsuhiko Tsumoda, PhD,31 Andre G. Uitterlinden, PhD,31,32,33,34 David R. Van Wagoner, PhD,31 Uwe Völker, PhD,31,32 Henry Volzke, MD,31,32 Joanne M. Murabito, MD, ScM,31,32 Moritz F. Sinner, MD, MPH,30 Vilmundur Gudnason, MD, PhD,31 Stephan B. Felix, MD,31,32,33,34 Winfried März, MD,31,32,33,34 Mina Chung, MD,31,32 Christine M. Albert, MD, MPh,31,32,33,34 Bruno H. Stricker, MB, PhD,31,32,33,34,36 Toshihiro Tanaka, MD, PhD,31,32,33,34,36 Susan R. Heckbert, MD, PhD,31,32,33,34,36 J. Wouter Jukema, MD, PhD,31,32,33,34,36 Alvaro Alonso, MD, PhD,31,32 Emelia J. Benjamin, MD, ScM,31,32,33,34,36 Patrick T. Ellinor, MD, PhD,31,32

Arrhythmia/Electrophysiology

Integrating Genetic, Transcriptional, and Functional Analyses to Identify 5 Novel Genes for Atrial Fibrillation

Moritz F. Sinner, MD, MPH; Nathan R. Tucker, PhD; Kathryn L. Lunetta, PhD; Kouichi Ozaki, PhD; J. Gustav Smith, MD, PhD; Stella Trompeter, PhD; Joshua C. Bis, PhD; Honghuang Lin, PhD; Mina K. Chung, MD; Jonas B. Nielsen, MD; Steven A. Lubitz, MD, MPH; Bouwe P. Krijthe, PhD; Jared W. Magnani, MD, MSc; Jiangchuan Ye, MD, PhD; Michael H. Gollob, MD, Tatsuhiko Tsumoda, PhD; Martina Müller-Nurssyid, PhD; Peter Lichtner, PhD; Annette Peters, PhD; Elena Dolmatova, MD; Michiaki Kubo, MD, PhD; Jonathan D. Smith, PhD; Bruce M. Psaty, MD, PhD; Nicholas L. Smith, PhD; J. Wouter Jukema, MD, PhD; Daniel I. Chapman, PhD; Christine M. Albert, MD, MPH; Yusuke Ebana, MD, PhD; Tetsushi Funakawa, MD, PhD; Peter W. Macfarlane, DSc; Tamara B. Harris, MD, MS; Dawood Darbar, MD; Marcus Dörö, MD; Anders G. Holst, MD, PhD; Jesper H. Svendsen, MD, DMS; Albert Hofman, MD, PhD; Andre G. Uitterlinden, MD, PhD; Vilmundur Gudnason, MD, Mitusuki ike, MD, PhD; Rainer Malik, PhD; Martin Dingga, MD; Jonathan Rosand, MD, MSc; David R. Van Wagoner, PhD, MASTROBE Consortium; AFGen Consortium; Emelia J. Benjamin, MD, ScM; David J. Milan, MD; Olle Melander, MD, PhD; Susan R. Heckbert, MD, PhD; Ian Ford, PhD; Yongmee Liu, MD, PhD; John Barnard, PhD; Morten S. Olsen, MD, MSc, PhD; H.C. Stricker, MB, PhD; Toshihiro Tanaka, MD, PhD; Stefan Kääb, MD, PhD; Patrick T. Ellinor, MD, PhD

J Am Coll Cardiol 2014;63:1200 - Circulation 2014;130:1225
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ACC / AHA / HRS - JACC 2014; 64: 2246 - ESC - EHJ 2013; 34:1471
# 1a) Stroke Risk Stratification In AF

## Components of CHA\textsubscript{2}DS\textsubscript{2}-VASc

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac failure</td>
<td>1</td>
</tr>
<tr>
<td>HTN</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥75 y</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (MI, PAD, aortic atherosclerosis)</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74 y</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (female)</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHA\textsubscript{2}DS\textsubscript{2}-VASc Score</th>
<th>Annual Risk of Stroke (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>3</td>
<td>3.2</td>
</tr>
<tr>
<td>4</td>
<td>4.0</td>
</tr>
<tr>
<td>5</td>
<td>6.7</td>
</tr>
<tr>
<td>6</td>
<td>9.8</td>
</tr>
<tr>
<td>7</td>
<td>9.6</td>
</tr>
<tr>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
</tr>
</tbody>
</table>

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ATRIA - HA van den Ham et. al. J Am Coll Cardiol 2015;66:1851 – Points by

CHA$_2$DS$_2$VASc:
- CHADS$_2$ = 0: Prefer no treatment rather than aspirin
- CHADS$_2$ = 1: Prefer OAC rather than aspirin

V Fuster, JS Chinitz, Circ. 2012; 125: 2285
Swedish AF Cohort Register (L Friberg, GYH Lip et al) Circ. 2012; 125: 2298
A/C Prevention - Emboli >>> Bleeding, Thrombosis > Bleeding
1b) Bridging AC and Associated Outcomes During AC Interruption in Patients With AF

The ORBIT-AF is a prospective, observational registry study of US outpatients with AF. Of 7372 patients treated with oral A/C, 2803 overall interruption events occurred in 2200 patients or 30% at a median follow-up of 2 years. Bridging A/C were used in 24% (n=665), predominantly LMW heparin (73%, n=487) and unfractionated heparin (15%, n=97). Bridged patients were more likely to have had prior cerebrovascular events (22% versus 15%; \( P=0.0003 \)) and mechanical valve replacements (9.6% versus 2.4%; \( P<0.0001 \)); however, there was no difference in CHA\(_2\)DS\(_2\)-VASc scores (scores \( \geq 2 \) in 94% versus 95%; \( P=0.5 \)). Bleeding events were more common in bridged than nonbridged patients (5.0% versus 1.3%; \( P<0.0001 \)). The incidence of MI, stroke or systemic embolism, major bleeding, hospitalization, or death within 30 days was also significantly higher in patients receiving bridging (13% versus 6.3%). These data do not support the use of routine bridging, and additional data are needed to identify best practices concerning A/C interruptions.

\( \text{ORBIT-AF (BA Steinberg et al.), Circulation 2015; 131:488} \)
1c) **NSAID Exposure in Patients on Antithrombotic Rx**

**Risks For Serious Bleeding At 3 Mo & 2 Yrs,**

<table>
<thead>
<tr>
<th>Serious Bleeding (3 mo)</th>
<th>Absolute Risk Difference (95% CI)</th>
<th>Serious Bleeding (2 y)</th>
<th>Absolute Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antithrombotic Treatment</strong></td>
<td></td>
<td><strong>Antithrombotic Treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>Overall</td>
<td></td>
</tr>
<tr>
<td>No NSAID</td>
<td>1.9 (1.6–2.3)</td>
<td>No NSAID</td>
<td>1.3 (1.0–1.6)</td>
</tr>
<tr>
<td>NSAID</td>
<td></td>
<td>NSAID</td>
<td></td>
</tr>
<tr>
<td>OAC plus single antiplatelet</td>
<td></td>
<td>OAC plus single antiplatelet</td>
<td></td>
</tr>
<tr>
<td>No NSAID</td>
<td>2.6 (1.6–3.7)</td>
<td>No NSAID</td>
<td>1.8 (1.1–2.6)</td>
</tr>
<tr>
<td>NSAID</td>
<td></td>
<td>NSAID</td>
<td></td>
</tr>
<tr>
<td>OAC</td>
<td></td>
<td>OAC</td>
<td></td>
</tr>
<tr>
<td>No NSAID</td>
<td>2.5 (2.1–3.0)</td>
<td>No NSAID</td>
<td>1.9 (1.4–2.3)</td>
</tr>
<tr>
<td>NSAID</td>
<td></td>
<td>NSAID</td>
<td></td>
</tr>
<tr>
<td>Single antiplatelet</td>
<td></td>
<td>Single antiplatelet</td>
<td></td>
</tr>
<tr>
<td>No NSAID</td>
<td>2.1 (1.7–2.5)</td>
<td>No NSAID</td>
<td>1.4 (1.0–1.8)</td>
</tr>
<tr>
<td>NSAID</td>
<td></td>
<td>NSAID</td>
<td></td>
</tr>
<tr>
<td>No treatment</td>
<td></td>
<td>No treatment</td>
<td></td>
</tr>
<tr>
<td>No NSAID</td>
<td>1.6 (1.3–2.0)</td>
<td>No NSAID</td>
<td>1.0 (0.7–1.3)</td>
</tr>
<tr>
<td>NSAID</td>
<td></td>
<td>NSAID</td>
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</tbody>
</table>
**2a). Silent Cerebral Infarcts (SCI)**

Cardiac Disease And Procedures

- Cardioembolic heart disease
  - Atrial fibrillation
  - Left ventricular thrombus
  - Cardiomyopathy
  - Patent foramen ovale

Cardiac procedures
- Left heart catheterization
- CABG surgery
- Transcatheter aortic valve implantation
- Pulmonary vein isolation
- Closure of patent foramen ovale

- Stroke
- Cognitive decline
- Dementia
- Depression

*ME Hassell et. al. Nat. Rev. Cardiol. 2013;10:696*
Silent Cerebral Ischemia in AF
Correlation With Cognitive Function

F Gaita et. al. J Am Coll Cardiol 2013;62:1990 (Italy)
2b) LAA Structure / Function – AF but Stroke in NSR

Cardiac Imaging For Assessment

J Romero et. al. Nat Rev Cardiol. 2014;11:470
ENGAGE AF (DK Gupta et al.) EHJ 2014; 35:1457 – LA Function / NSR ?
ASSERT (M Brambatti, et al.) Circ. 2014; 129:2094- LV Function / NSR ?
ATs detected by implanted devices are often AF/AFI associated with stroke. We randomized 2718 patients with dual-chamber and biventricular defibrillators to start and stop AC based on remote rhythm monitoring vs. usual office-based follow-up with AC determined by standard clinical criteria. Although AT burden was associated with thromboembolism, there was no temporal relationship between AT and stroke. In other words, in patients with implanted defibrillators, the strategy of early initiation and interruption of anticoagulation based on remotely detected AT did not prevent thromboembolism and bleeding.

**IMPACT** (DT Martin et al.) Eur Heart J 2015; 36:1660
Temporal Relation Of Daily Atrial Tachyarrhythmia Burden And Thromboembolism

IMPACT (DT Martin et. al.) EHJ. 2015;36:1660
**CHA2DS2-VASc Score in Predicting Stroke, Thromboembolism, and Death in HF With AF (closed) and Without AF (open)**

L Melgaard et. al. JAMA 2015;314:1030 – Danish Registry in HF (n=42,987)
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1) NVAF - ODDS OF INTRACRANIAL HEMORRHAGE & AGE IN 145 CASE-PATIENTS (INR 2.0-3.0) AND 870 CONTROLS

MC Fang et al., Ann Intern Med 2004; 141:745 (UCSF, Boston, Oakland)
2) **The Net Clinical Benefit Of Warfarin By Age Group**

![Graph showing the net clinical benefit of warfarin by age group.](image)

- **Age ≥ 85**: Net Clinical Benefit = 2.34 (events per 100 person years)
- **Age 75-84**: Net Clinical Benefit = 1.00 (events per 100 person years)
- **Age 65-74**: Net Clinical Benefit = 0.44 (events per 100 person years)
- **Age <65**: Net Clinical Benefit = -0.65 (events per 100 person years)

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1a). **Triple vs Double Antithrombotic Regimens, AF Post MI and PCI (N=11480) – PI / AC**

*Nationwide Reg (M Lamberts et. al.) Circ. 2012;126:1185 (Denmark)*
In the WOEST trial, 573 patients were randomized to dual therapy with oral anticoagulation and clopidogrel (75 mg daily) or to triple therapy with oral anticoagulation, clopidogrel and aspirin 80 mg daily. Treatment was continued for one month after bare metal stenting and one year after drug eluting stent placement.

<table>
<thead>
<tr>
<th>Bleeding events (TIMI criteria)</th>
<th>Dual therapy (%)</th>
<th>Triple therapy (%)</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All bleeding Events</td>
<td>19.5</td>
<td>44.9</td>
<td>0.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.26-0.50)</td>
<td></td>
</tr>
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Significant reduction in minor bleeding, < Major bleeding (NS)

Stent thrombosis | 1.5 | 3.2 | NS

**WOEST** (*W DeWilde et al.*) *NEJM 2012* - *2014 AHA/ACC/HRS – AC+Clop IIB*
2). **AF - Choice Of Antithrombotic Therapy, Including Combination Strategies**

[Flowchart image]

**STEP 1** — Stroke risk

- **CHA₂DS₂-VASc = 1**
  - Low to intermediate (e.g., HAS-BLED = 0–2)
  - Stable CAD, ACS
  - If PCI is performed

- **CHA₂DS₂-VASc ≥ 2**
  - High (e.g., HAS-BLED ≥ 3)
  - Stable CAD, ACS
  - If PCI is performed

**STEP 2** — Bleeding risk

- **HAS-BLED = 0–2**
  - Stable CAD, ACS
  - Stable CAD, ACS
  - Stable CAD, ACS

- **HAS-BLED ≥ 3**
  - Stable CAD, ACS
  - Stable CAD, ACS
  - Stable CAD, ACS

**STEP 3** — Clinical setting

- **Stable CAD**
  - ACS
  - Stable CAD
  - ACS
  - Stable CAD

- **Acute Coronary Syndromes (ACS)**
  - Stable CAD
  - ACS
  - Stable CAD

**STEP 4** — Antithrombotic therapy

- **Oral anticoagulation**
- **Aspirin 75–100 mg daily**
- **Clopidogrel 75 mg daily**

**Time from PCI/ACS**

- 0 weeks
- 4 weeks
- 6 months
- 12 months
- Lifelong

**Choice of Antithrombotic Therapy**

- **Triple therapy**
  - O A C
  - O A or C
  - O A or C
  - O A or C

- **Dual therapy**
  - O A or C
  - O A or C
  - O A or C
  - O A or C

- **Monotherapy**
  - O

**References:****

- **GYH Lip et. al. Eur Heart J 2014;35:315**
- **2014 AHA/ACC/HRS – AC+Clop IIB**
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3. AC Rx: When / Bridge / NSAID vs SCI / NSR (2)
4. Aging: TE & Bleeding vs Warfarin (2)
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ACC / AHA / HRS - JACC 2014; 64: 2246 - ESC - EHJ 2013; 34:1471
New Oral Anticoagulants - 1) Efficacy & 2) Safety

Stroke or systemic embolism

- Category
  - W vs placebo
  - W vs W_{low-dose}
  - W vs aspirin
  - W vs aspirin + clopidogrel
  - W vs ximelagatran
  - W vs dabigatran 110
  - W vs rivaroxaban
  - W vs dabigatran 150
  - W vs apixaban 5

- Relative hazard ratio (95% CI)

Intracranial hemorrhage

- W vs dabigatran 110
- W vs rivaroxaban
- W vs dabigatran 150
- W vs apixaban 5

- Major bleeding

- W vs dabigatran 110
- W vs rivaroxaban
- W vs dabigatran 150
- W vs apixaban 5

Favors warfarin
Favors other treatment

*Dialogues in Cardiovascular Medicine* 2012;17:189
Randomized controlled trials in patients with AF were identified. 100,913 patients (21 studies) were allocated to placebo/control, aspirin and/or clopidogrel, vitamin K antagonists (VKAs), or new NOACs. Based on utility, NOACs were better than VKA or anti-platelet therapy; dabigatran 150 mg was ranked highest (21% chance of being best). Ranked by cost, the 3 factor Xa inhibitors were very similar (16-18% chance of being best). When haemorrhagic events were weighted more than ischaemic events, edoxaban 30 mg was ranked higher (22%), while rivaroxaban (23%) was most preferred when ischaemic events were rated worse than haemorrhagic events. Differences between NOACs were modest and dependent upon the order of ranking of clinical events.

A Dogliotti and RP Giugliano. Eur Heart J – Cardiovasc Pharmacol 2015; 1:15
# NOACs - Kidney & Prosthetic Heart Valves

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHADS(_2)-VASc</strong> score recommended to assess stroke risk</td>
<td>I</td>
</tr>
<tr>
<td>With prior stroke, TIA, or CHADS(_2)-VASc score ≥2, oral anticoagulants recommended. Options include:</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>I</td>
</tr>
<tr>
<td>Dabigatran, rivaroxaban, or apixaban</td>
<td>I</td>
</tr>
<tr>
<td>Evaluate renal function before initiation of direct thrombin or factor Xa inhibitors, and reevaluate when clinically indicated and at least annually</td>
<td>I</td>
</tr>
<tr>
<td><strong>Direct thrombin dabigatran and factor Xa inhibitor rivaroxaban are not recommended in patients with AF and end-stage CKD or on dialysis because of a lack of evidence from clinical trials regarding the balance of risks and benefits</strong></td>
<td>III: No Benefit</td>
</tr>
<tr>
<td><strong>Direct thrombin inhibitor dabigatran should not be used with a mechanical heart valve</strong></td>
<td>III: Harm</td>
</tr>
</tbody>
</table>

*CT January et. al. J. Am. Coll. Card. 2014; 64: e1*
### AF - CLINICAL CHALLENGES (14) - 2016

1. **Presentation:** Prevalence / Stroke / Death vs Sx  (2)
2. **Etiology:** General vs Specific  (2)
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**ACC / AHA / HRS - JACC 2014; 64: 2246 - ESC - EHJ 2013; 34:1471**

EN Prystowsky et. al. JAMA 2015; 314: 278 - Rhythm
1a). AF Burden - After Catheter Ablation
Several Strategies (Linq Recorder etc)

El Charitos et. al. Circulation. 2012;126:806 (Luebeck, Germ.)
1b). **CHA\(_2\)DS\(_2\)-VASc (Recurrent AF) in Predicting Clinical Outcomes in AF After Catheter Ablation**

T-F Chao et al., *JACC* 2011; 58:2380 (Japan) – 565 Pts
2). Primary Efficacy Outcome of Watchman LAA Closure For Embolic Protection In AF PROTECT AF Over 60 Months

- RP Whitlock et. al. Circulation. 2015;131:756
Percutaneous occlusion of the left atrial appendage: An expert consensus statement

Consensus d’experts sur les modalités de l’occlusion percutanée de l’auricule gauche

Didier Kluga,*, Philippe Commear, Pascal Defayec, Jean-Benoît Thanb, Daniel Grase, Pierre Aubryf, Jean-Luc Pasquieg, Patrice Guerin, Emmanuel Teigeri, René Konings, Olivier Piotk, for the Heart Rhythm, Pacing Group, the Atheroma, Interventional Cardiology Group of the French Society of Cardiology

Archives of Cardiovasc Dis 2015;108:460
| 1. **Presentation:** | Prevalence / Stroke / Death vs Sx | (2) |
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**ACC / AHA / HRS - JACC 2014; 64: 2246 - ESC - EHJ 2013; 34:1471**