Absolute contraindications to oral anticoagulation and when to refer for left atrial appendage occlusion

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How well are we doing with OACs (best case scenario)?

31% on warfarin had TTR < 65%
12% NOAC patients had incorrect dose

Survey of 500 Canadian patients

<table>
<thead>
<tr>
<th>Medication persistence and discontinuation of rivaroxaban and dabigatran etexilate among patients with non-valvular atrial fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winnie W. Nelson, Xue Song, Erin Thomson, David M. Smith, Craig I. Coleman, C.V. Damaraju &amp; Jeffrey R. Schein</td>
</tr>
<tr>
<td>Current Medical Research and Opinion 2015</td>
</tr>
<tr>
<td>30,000 US patients on dabigatran or rivaroxaban</td>
</tr>
</tbody>
</table>

Self-reported adherence to anticoagulation and its determinants using the Morisky medication adherence scale

<table>
<thead>
<tr>
<th>Self-reported adherence,</th>
<th>VKA (n = 361)</th>
<th>DOAC (n = 126)</th>
<th>Rivaroxaban (n = 90)</th>
<th>Dabigatran (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate Adherence*</td>
<td>56.2%</td>
<td>57.1%</td>
<td>59.6%</td>
<td>48.0%</td>
</tr>
<tr>
<td>Non-adherence</td>
<td>43.8%</td>
<td>42.9%</td>
<td>40.4%</td>
<td>52.0%</td>
</tr>
</tbody>
</table>

* Defined as Morisky score = 0.
Compliance and persistence with OACs

Thrombosis and Haemostasis 115.1/2016

<table>
<thead>
<tr>
<th>Type of AC treatment</th>
<th>N</th>
<th>90 days %</th>
<th>180 days %</th>
<th>270 days %</th>
<th>365 days %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete VKA/NOAC-treated cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>NOAC</td>
<td>914</td>
<td>94.7</td>
<td>85.9</td>
<td>82.4</td>
<td>79.2</td>
</tr>
<tr>
<td>VKA</td>
<td>12307</td>
<td>87.2</td>
<td>76.5</td>
<td>69.3</td>
<td>63.6</td>
</tr>
<tr>
<td>P value*</td>
<td></td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CHA₂DS₅VASC &lt;2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOAC</td>
<td>139</td>
<td>91.9</td>
<td>74.5</td>
<td>64.5</td>
<td>57.6</td>
</tr>
<tr>
<td>VKA</td>
<td>1519</td>
<td>85.0</td>
<td>69.1</td>
<td>58.7</td>
<td>51.4</td>
</tr>
<tr>
<td>P value*</td>
<td></td>
<td>0.0266</td>
<td>0.1652</td>
<td>0.1749</td>
<td>0.1679</td>
</tr>
<tr>
<td>CHA₂DS₅VASC ≥2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOAC</td>
<td>775</td>
<td>95.2</td>
<td>88.0</td>
<td>85.6</td>
<td>83.0</td>
</tr>
<tr>
<td>VKA</td>
<td>10788</td>
<td>87.5</td>
<td>77.5</td>
<td>70.8</td>
<td>65.3</td>
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<tr>
<td>P value*</td>
<td></td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Intracerebral bleeds on oral anticoagulants

The most feared consequence of oral anticoagulation

Subdural (traumatic/non-traumatic), sub-arachnoid and parenchymal

0.1 – 0.5% per year

Deep (subcortical) haemorrhage
Commonly due to hypertension
Recurrence 2% 1 year, 4% 2 year

Lobar haemorrhage
Commonly due to cerebral amyloid
Recurrence 15% 1 year, 21% 2 year, 36% at 3 year (15% per year)

Intracerebral bleeds on warfarin have a 40-50% in-hospital mortality
What about subdurals?

- Subdural haematomas are a common reason to stop/avoid OAC
- Not always easy to distinguish between traumatic and spontaneous
- Burr hole treatment more likely to recur than conservative therapy
- Was it in the setting of high INR?
- 15% recurrence at 1 year (L Schmidt PLoS 2015)
Reintroducing OAC after intracerebral bleeds

Data available from small registries and case series, principally in patients on warfarin for prosthetic heart valves.

- Canadian Registry suggest no difference in recurrent bleeds in those restarted on warfarin and those not – but patients restarted on warfarin had suffered smaller hemorrhagic strokes. *Canadian Journal of Cardiology* 2012;28:33–39.

- Swedish and Canadian Cohort. Recurrent hemorrhage in 14% who restarted warfarin and 8% who didn’t. *Stroke* 2010;41:2860-66

- Markov modelling balancing ischemic stroke risk vs rebleeding risk, for lobar hemorrhages reintroduction of warfarin resulted in net harm. Same applied for deep hemorrhages with CHA$_2$DS$_2$-VASc score <5, less clear if 5 or more. *Stroke* 2003;34:1710-16

German Registry 719 pts, 20% restarted on warfarin
Reintroducing OAC after intracerebral bleeds

6 studies looking at both ischaemic and haemorrhagic events
AF and prosthetic valve patients
2044 patients
38% had warfarin restarted
Intracerebral bleeds on oral anticoagulants

Deep (subcortical) hemorrhage
- Commonly due to hypertension
- Recurrence 2% 1 year, 4% 2 years

Lobar hemorrhage
- Commonly due to cerebral amyloid
- Recurrence 15% 1 year, 21% 2 years, 36% at 3 years (15% per year)

Intracerebral bleeds on warfarin have a 40-50% in-hospital mortality

No randomised trial data
Almost exclusively based on vitamin K antagonists
Decision to restart OAC heavily biased by physician selection
### NOACs and intracerebral bleeds

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dabigatran 150mg</th>
<th>Dabigatran 110mg</th>
<th>Rivaroxaban 20mg</th>
<th>Apixaban 5mg</th>
<th>Edoxaban 60mg</th>
<th>Edoxaban 30mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual severe bleeding rate</td>
<td>3.11 vs 3.36</td>
<td>2.71 vs 3.36</td>
<td>3.6 vs 3.4</td>
<td>2.13 vs 3.09</td>
<td>2.75 vs 3.43</td>
<td>1.61 vs 3.43</td>
</tr>
<tr>
<td>Annual hemorrhagic stroke rate</td>
<td>0.10 vs 0.38</td>
<td>0.12 vs 0.38</td>
<td>0.32 vs 0.49</td>
<td>0.24 vs 0.47</td>
<td>0.16 vs 0.47</td>
<td>0.26 vs 0.47</td>
</tr>
<tr>
<td>Annual intracranial bleed rate</td>
<td>0.3 vs 0.74</td>
<td>0.23 vs 0.74</td>
<td>0.5 vs 0.7</td>
<td>0.33 vs 0.8</td>
<td>0.39 vs 0.85</td>
<td>0.26 vs 0.85</td>
</tr>
</tbody>
</table>
Apixaban and a history of bleeding

ARISTOTLE analysis De Caterina et al Am Heart J 2016

17% of 18,167 enrolled patients had a history of bleeding.

Apixaban better than warfarin, but “bleeders” more likely to bleed than “non-bleeders”
Apixaban versus Antiplatelet drugs or no antithrombotic drugs after anticoagulation-associated intraCerebral HaEmorrhage in patients with Atrial Fibrillation (APACHE-AF): study protocol for a randomised controlled trial

van Nieuwenhuizen et al.

**Methods/Design:** APACHE-AF is a phase II, multicentre, open-label, parallel-group, randomised clinical trial with masked outcome assessment. One hundred adults with a history of atrial fibrillation and a recent intracerebral haemorrhage during treatment with anticoagulation in whom clinical equipoise exists on the optimal stroke prevention strategy will be enrolled in 14 hospitals in The Netherlands. These patients will be randomly assigned in a 1:1 ratio to either apixaban or to avoiding oral anticoagulation. Patients in the control group may be treated with antiplatelet drugs at the discretion of the treating physician. The primary outcome is the composite of vascular death or non-fatal stroke during follow-up. We aim to include 100 patients in 2.5 years. All patients will be followed-up for the duration of the study, but at least for 1 year.
Cerebral amyloid angiopathy

A cerebrovascular disease caused by the deposition of β-amyloid in the walls of cerebral arteries, arterioles, and capillaries. It is followed by disruption of the blood vessel wall leading to microaneurysm formation and fibrinoid necrosis.

- Common cause of lobar ICH
- Recurrent ICH is common
- Higher risk of ICH if anticoagulated
- 70% bleeds lead to disability or death

Microbleeds = risk of ICH
> 10 = OAC contraindicated (ESC 2016 AF guidelines)

Nb. Deep microbleeds = hypertension / arteriosclerosis
GI bleeding
GI bleeding with NOACs

Impact of new oral anticoagulants on gastrointestinal bleeding in atrial fibrillation: A meta-analysis of interventional trials

Lorenzo Loffredo*, Ludovica Perri, Francesco Violi


Effectiveness and Safety of Dabigatran, Rivaroxaban, and Apixaban Versus Warfarin in Nonvalvular Atrial Fibrillation

Xiaoxi Yao, PhD; Neera S. Abraham, MD, MSCE; Lindsey R. Sangareffingham, MPH; M. Fernando Bekhle, MD, MS; Robert D. McAllister, MD; Niall D. Smith, PhD; Peter A. Noseworthy, MD

*J Am Heart Assoc. 2016;5:e003725
76,000 patients in US database

<table>
<thead>
<tr>
<th>Event Rate per 100 person-years</th>
<th>Hazard Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban vs. Warfarin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=7,695</td>
<td>n=7,695</td>
<td></td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>2.33</td>
<td>4.45</td>
</tr>
<tr>
<td>Intracranial</td>
<td>0.29</td>
<td>1.06</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1.78</td>
<td>3.04</td>
</tr>
<tr>
<td>Dabigatran vs. Warfarin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=14,307</td>
<td>n=14,307</td>
<td></td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>2.37</td>
<td>3.03</td>
</tr>
<tr>
<td>Intracranial</td>
<td>0.28</td>
<td>0.79</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1.97</td>
<td>1.95</td>
</tr>
<tr>
<td>Rivaroxaban vs. Warfarin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=16,175</td>
<td>n=16,175</td>
<td></td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>4.04</td>
<td>3.64</td>
</tr>
<tr>
<td>Intracranial</td>
<td>0.44</td>
<td>0.79</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>3.26</td>
<td>2.53</td>
</tr>
</tbody>
</table>

Favor NOAC: 1.0
Favor Warfarin
GI bleeding with NOACs

Not all NOACS are equal (although never directly compared)

| Table 1. Direct Comparisons of DOACs With Regard to Efficacy and Safety Profile<sup>10,11</sup> |
|---|---|---|---|---|---|---|
| | Rivaroxaban vs Dabigatran | Apixaban vs Dabigatran | Apixaban vs Rivaroxaban |
| | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value |
| Efficacy | | | | | | | | | |
| Stroke or systemic embolism | 1.00 | 0.75-1.32 | .99 | 0.82 | 0.51-1.31 | .41 | 1.05 | 0.64-1.72 | .85 |
| Ischemic stroke | 0.91 | 0.66-1.27 | .58 | 0.93 | 0.55-1.57 | .79 | 1.27 | 0.73-2.23 | .39 |
| Hemorrhagic stroke | 1.70 | 0.84-3.43 | .14 | 0.72 | 0.18-2.86 | .84 | 0.66 | 0.16-2.78 | .57 |
| Safety | | | | | | | | | |
| Major bleeding | 1.30 | 1.10-1.53 | <.01 | 0.50 | 0.36-0.70 | <.001 | 0.39 | 0.28-0.54 | <.001 |
| Intracranial bleeding | 1.79 | 1.12-2.86 | .02 | 0.65 | 0.25-1.65 | .36 | 0.56 | 0.21-1.45 | .23 |
| GI bleeding by age (y) | | | | | | | | | |
| 18-84 | 2.03 | 1.06-3.90 | <.05 | 0.38 | 0.08-1.84 | NS | 0.38 | 0.08-1.89 | NS |
| 65-74 | 1.44 | 1.00-2.06 | <.05 | 0.25 | 0.10-0.65 | <.01 | 0.18 | 0.07-0.47 | <.001 |
| ≥75 | 1.06 | 0.84-1.34 | NS | 0.45 | 0.29-0.71 | <.001 | 0.39 | 0.25-0.61 | <.001 |
| Bleeding by HAS-BLED score | | | | | | | | | |
| 0-2 | 1.41 | 1.08-1.85 | <.05 | 0.43 | 0.24-0.77 | <.01 | 0.35 | 0.20-0.63 | <.001 |
| ≥3 | 1.27 | 1.03-1.56 | <.01 | 0.54 | 0.36-0.81 | <.01 | 0.39 | 0.26-0.59 | <.001 |

DOAC, direct oral antagonist; CI, confidence interval; GI, gastrointestinal; HA-BLED, hypertension, abnormal renal and liver function, stroke, bleeding, labile International Normalized Ratio (INR) ratios, age ≥65 years, drugs or alcohol; HR, hazard ratio; NS, not significant.

Apixaban safer than Dabigatran, which is safer than Rivaroxaban
Restarting Anticoagulation and Outcomes After Major Gastrointestinal Bleeding in Atrial Fibrillation

Wajid Qureshi, MD, Chetan Mittal, MD, Iram Patlas, MD, Kiran Garikapati, MD, Aishwarya Kochi, MD, Gagandeep Cheema, MD, Mohammad Elborn, MD, Zaid Alhakim, MD, and Fatima Khalil, MD

Am J Cardiol 2014;113:662–668

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Adjusted Hazard Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolism</td>
<td>0.71 (0.54–0.93)</td>
<td>0.01</td>
</tr>
<tr>
<td>Recurrent gastrointestinal bleeding</td>
<td>1.18 (0.94–1.10)</td>
<td>0.47</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.67 (0.56–0.81)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CI = confidence interval.

Freedom from recurrent GI bleeding

Freedom from thromboembolism
4602 patients discharged from hospital on antithrombotic treatment after a GI bleed
• Many forms of GI bleeding can be addressed

• Anaemia can be screened for and addressed with iron replacement therapy/transfusion

• Patients are more concerned about strokes than GI bleeds
Frequent falls

Risk of Falls and Major Bleeds in Patients on Oral Anticoagulation Therapy

Prospective study. Prior to initiation of OAC, 515 patients answered questionnaire on falls in last 12 months and history of balance/gait problems

60% were deemed “high risk”
8 bleeds/100 pt years (vs 6.8 bleeds/100 pt years), p=ns
Only 3 major bleeds directly after a fall (0.6 /100 pt years

Atrial fibrillation, anticoagulation, fall risk, and outcomes in elderly patients
Matthew R. Selbers, MD, * and L. Kristin Newby, MD, MHS.*** Durham, NC

(Am Heart J 2011;161:241-6.)

In elderly at risk of falls, anticoagulation benefits outweigh risks once annual stroke risk is >2% (i.e. CHA₂DS₂-VASc ≥2 or CHADS2 ≥1)

Have to fall >297 times a year before risk outweighs anticoagulation benefit
Do Not Do Recommendation

Do not withhold anticoagulation solely because the person is at risk of having a fall.

Do Not Do Recommendation Details

Recommendation: Do not withhold anticoagulation solely because the person is at risk of having a fall.
Interventions: Anticoagulation

Source guidance details
Guidance: Atrial fibrillation: the management of atrial fibrillation (CG180)
Published date: June 2014
Paragraph number: 1.4.4
Page number: 13
Alternatives to oral anticoagulation
Aspirin use discouraged in guidelines as it isn’t effective at reducing thromboembolic stroke

BAFTA tells us that in the elderly, severe bleeding is as common with aspirin as with warfarin

Chinese Registry tells us ICH rates with aspirin are higher than no therapy and similar to that of well-controlled warfarin (although dabigatran better)
Do Not Do Recommendation

Do not offer aspirin monotherapy solely for stroke prevention to people with atrial fibrillation.

Do Not Do Recommendation Details

Recommended: Do not offer aspirin monotherapy solely for stroke prevention to people with atrial fibrillation.

Interventions: aspirin monotherapy

Source guidance details

- Guidance: Atrial fibrillation: the management of atrial fibrillation (CG180)
- Published date: June 2014
- Paragraph number: 1.5.15
- Page number: 17
**ACTIVE trial**  *N Engl J Med 2009;360:2066-78*  
Clopidogrel and aspirin had fewer strokes than aspirin alone (2.4% vs 3.3% pa) and fewer ischaemic strokes (1.9% vs 2.8%) at the expense of higher severe bleeding (2.0% vs 1.3% pa)

**ACTIVE-W trial**  *Lancet 2006; 367: 1903-12*  
Clopidogrel and aspirin combination not as effective as warfarin at reducing stroke. Similar amounts of severe and fatal bleeding, although fewer haemorrhagic strokes with DAP
Steering between Scylla and Charybdis
If only there was another way
The left atrial appendage is the source of thromboembolic stroke in >90% of “non-valvar” AFib patients (i.e. who do not have rheumatic mitral valve disease or MV surgery)
The rationale for LAA closure

AFib leads to LAA thrombus that causes thromboembolic stroke

Oral anticoagulants are a **systemic solution** that reduce stroke risk by up to 2/3

Oral anticoagulants, increase the risk of serious bleeding complications. All drugs require compliance

LAAO is a **focused solution**, with a much lower long-term bleeding risk
What does LAA closure involve?

General anaesthetic (in most cases), single femoral vein puncture, 60-90 minutes
What does LAA closure involve?

Before

After
How safe is it?

- 1021 patients
- Mean age 73
- Mean CHA$_2$DS$_2$VASc = 4.5
- 62% contraindications to OAC, half due to history of major severe bleeding
Efficacy and safety of left atrial appendage closure with WATCHMAN in patients with or without contraindication to oral anticoagulation: 1-Year follow-up outcome data of the EWOLUTION trial

Lucas V. Boersma, MD, PhD, FESC,† Huseyin Ince, MD,‡ Stephan Kische, MD,† Evgeny Pokushalov, MD, PhD,† Thomas Schmitz, MD,‡ Boris Schmidt, MD,† Tommaso Gor, MD,§ Felix Meincke, MD, ** Alexey Vladimir Protopopov, MD, PhD, † Timothy Betts, MD,∥ David Foley, MD, PhD, FRCPI, FACA, FACC, FESC,‡‡ Horst Sievert, MD,∥∥ Patrizio Mazzotta, MD,∥∥ Tom De Potter, MD,∥∥∥ Elisa Wreca, MS,∥∥∥ Kenneth Stein, MD, FHRs,∥∥∥ Martin W. Bergmann, MD, PhD, FESC, † for the EWOLUTION Investigators

Heart Rhythm 2017;14:1302-1308
How effective is it?

**Percutaneous Left Atrial Appendage Occlusion**
**Using Different Technologies in the United Kingdom: A Multicenter Registry**

- 343 implants (2/3 Watchman, 1/3 ACP)
- 82.5% contraindications to OAC
- 24.7 ± 16.2 months FU
- 2 haemorrhagic strokes (0.28% per year)
  - 1 at day 21 whilst patient taking warfarin
  - 1 at 15 months after implant

<table>
<thead>
<tr>
<th></th>
<th>Predicted</th>
<th>Observed</th>
<th>RRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/TIA/SE</td>
<td>5.6</td>
<td>1.0</td>
<td>82%</td>
</tr>
<tr>
<td>(CHA_{2}DS_{2}-VASc)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>5.9*</td>
<td>1.3</td>
<td>82%</td>
</tr>
<tr>
<td>(HAS-BLED)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Had patients been taking warfarin
Price MJ et al *JACC-Int* 2015

It’s the anticoagulants that make the Watchman patients bleed
The intensive warfarin and antiplatelet regimen used in the RCTs is not necessary and in “bleeders” is rarely used.
But don’t they need warfarin and DAPT?

**EWOLUTION: LAA occlusion in the real world AHA 2015**

<table>
<thead>
<tr>
<th>Anticoagulation</th>
<th>Pre-implant (% patients)</th>
<th>Post-implant (% patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nothing</td>
<td>26.7%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Single APT</td>
<td>20.7%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Dual APT</td>
<td>21.7%</td>
<td>59.4%</td>
</tr>
<tr>
<td>OAT</td>
<td>30.9%</td>
<td>27.0%</td>
</tr>
</tbody>
</table>

No difference in thromboembolism or device thrombus rate
So, who to refer for LAAO?
2012 focused update of the ESC Guidelines for the management of atrial fibrillation

An update of the 2010 ESC Guidelines for the management of atrial fibrillation

Developed with the special contribution of the European Heart Rhythm Association

Authors/Task Force Members: A. John Camm (Chairperson) (UK)*, Gregory Y.H. Lip (UK), Raffaele De Caterina (Italy), Irene Savelieva (UK), Dan Atar (Norway), Stefan H. Hohloser (Germany), Gerhard Hindricks (Germany), Paulus Kirchhof (UK)

Recommendations for LAA closure/occlusion/excision

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class*</th>
<th>Levelb</th>
<th>Refc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.</td>
<td>IIb</td>
<td>B</td>
<td>115, 118</td>
</tr>
<tr>
<td>Surgical excision of the LAA may be considered in patients undergoing open heart surgery.</td>
<td>IIb</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

LAA = left atrial appendage.
*Class of recommendation.
*bLevel of evidence.
*cReferences.

“High risk” means CHA₂DS₂-VASc > 2
Patient with AF suffering from an intracranial bleed on OAC
If acute event: establish intensity of anticoagulation (see bleeding flow chart)

Contra-indication for OAC

Consider further information to allow informed judgement

Factors supporting withholding of OAC:
- Bleeding occurred on adequately dosed NOAC or in setting of treatment interruption or underdosing
- Older age
- Uncontrolled hypertension
- Cortical bleed
- Severe intracranial bleed
- Multiple microbleeds (e.g., >10)
- Cause of bleed cannot be removed or treated
- Chronic alcohol abuse
- Need for dual antiplatelet therapy after PCI

Factors supporting reinitiation of OAC:
- Bleeding occurred on VKA or in setting of overdose
- Traumatic or treatable cause
- Younger age
- Well controlled hypertension
- Basal ganglia bleed
- No or mild white matter lesions
- Surgical removal of subdural haematoma
- Subarachnoid bleed: aneurysm clipped or coiled
- High-risk of ischaemic stroke

Patient or next of kin choice informed by multidisciplinary team advice

Initiate or resume OAC, choosing an agent with low intracranial bleeding risk, after 4–8 weeks (IIbB)

No stroke protection (no evidence)

LAA occlusion (IIbC)
Figure 5  Algorithm of stroke protection in atrial fibrillation. LAA, left atrial appendage; NOAC, novel (non-Vitamin K antagonist) oral anticoagu- lant; OAC, oral anticoagulant.
New recommendations:

For patients with non-valvular AF, CHA2DS2-VASc ≥ 2 and acceptably low risk of hemorrhagic complications, (N)OACs are recommended (Class I)

Closure of the LAA may be considered for high-risk patients with AF who are deemed unsuitable for anticoagulation if performed at a center with low rates of periprocedural complications and the patient can tolerate the risk of at least 45 days of postprocedural anticoagulation.

Class IIb; Level of Evidence B
# Decision aids

## Anticoagulation Therapy Table

<table>
<thead>
<tr>
<th>Points</th>
<th>Risk Factors</th>
<th>CHADS2-VASc Score</th>
<th>Annual Stroke Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Congestive Heart Failurea</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>1</td>
<td>Hypertension</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>1</td>
<td>Age ≥75y</td>
<td>1</td>
<td>2.2</td>
</tr>
<tr>
<td>1</td>
<td>Diabetes</td>
<td>2</td>
<td>3.2</td>
</tr>
<tr>
<td>1</td>
<td>Vascular Diseaseb</td>
<td>4</td>
<td>4.0</td>
</tr>
<tr>
<td>1</td>
<td>Age 85-74y</td>
<td>5</td>
<td>6.7</td>
</tr>
<tr>
<td>1</td>
<td>Sex category = female</td>
<td>6</td>
<td>8.8</td>
</tr>
<tr>
<td>1</td>
<td>Recent cardiac failure or moderate-severe LVSD (LVEF&lt;40%)</td>
<td>7</td>
<td>9.6</td>
</tr>
<tr>
<td>1</td>
<td>Including US complex atrial or AV nodal ablation</td>
<td>8</td>
<td>8.7</td>
</tr>
<tr>
<td>1</td>
<td>Revascularisation or amputation</td>
<td>9</td>
<td>15.2</td>
</tr>
</tbody>
</table>

### BLOOD RISK [HAS-BLED]

- Hypertension defined as systolic blood pressure >160 mmHg
- Abnormal kidney function defined as the presence of chronic dialysis or renal transplantation, or serum creatinine >200 μmol/L
- Abnormal liver function defined as chronic hepatitis disease (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement (e.g. bilirubin >2 x ULN in association with AST/ALT >3 x ULN)
- Stroke
- Bleeding refers to previous bleeding history and/or predisposition to bleeding, e.g. bleeding disorders, anemia, etc.
- Labile INRs refers to unstable/high INR s or poor time in therapeutic range (e.g. TTR<60%)
- Elderly (>65y)
- Drug/alcohol use refers to concomitant use of drugs, such as antiplatelet agents, NSAIDs, or alcohol abuse (>8/week)
The LAAO MDT and referral pathway

AF stroke prevention team that includes LAAO

- Neurology / Neurosurgery
- GI Medicine
- ENT
- Elderly Care
- Haematology
- Urology
- Renal
- General Cardiology
- Emergency Medicine
- Primary Care

AF stroke prevention team that includes LAAO
The risks of OAC, relative to the benefits, often lead to inappropriate withdrawal or withholding of therapy.

Some bleeders risks may be reduced, particularly with GI bleeds.

Patient and physician perceptions play a major role.

OAC compliance is poor.

LAAO if an effective treatment to reduce stroke risk.

It’s an individualised choice and requires information from relevant experts to guide advice.
Who is suitable for LAAO?

A “lifestyle” choice available to all with CHA$_2$DS$_2$-VASc $\geq 1$

95% of $\geq 65$s with AFib have a CHA$_2$DS$_2$-VASc $\geq 2$

When medication is an inconvenience, or there is a theoretical environmental risk

OAC is the default, standard choice but LAAO is readily available

There is a “relative” contraindication or poor tolerance of warfarin and NOACs

OAC is the default, LAAO is available if HAS-BLED $\geq 3$ or there is a history of bleeding, high risk of trauma

There is an “absolute” contraindication

OAC is the default, LAAO is available if life-threatening bleed with no OAC or when in therapeutic range
Access to LAAO in UK

Currently patients have to self-fund or use insurance

Oxford will be participating

The Assessment of the Watchman Device in Patients Unsuitable for Oral Anticoagulation (ASAP-TOO) trial

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Martin W. Bregmann, MD, a Boris Schmidt, MD, a and Jacqueline Saw, MD, FRCP, a Rochester, Minneapolis, MN; New York, NY; Stanford, CA; Hamburg, Frankfurt, Germany; and British Columbia, Canada

Background Oral anticoagulants (OACs) reduce stroke risks with nonvalvular atrial fibrillation (AF); however, they are underused because of absolute or relative contraindications due to real or perceived risk of bleeding. Although left atrial appendage occlusion is increasingly performed in OAC-ineligible patients, this has not been studied in a randomized controlled trial.

Study objectives The ASAP-TOO study is designed to establish the safety and effectiveness of the Watchman left atrial appendage closure device in patients with nonvalvular AF who are deemed ineligible for OAC. The primary effectiveness end point is the time to first occurrence of ischemic stroke or systemic embolism. The primary safety end point includes all-cause death, ischemic stroke, systemic embolism, or device- or procedural-related event requiring open cardiac surgery or major endovascular intervention.

Study design This is a multinational, multicenter prospective randomized trial. Patients meeting the inclusion criteria with CHA₂DS₂-VASc score ≥ 2 and who are deemed by 2 study physicians to be unsuitable for OAC will be randomized in a 2:1 allocation ratio to Watchman versus control. Control patients will be prescribed single antplatelet therapy or no therapy at the discretion of the study physician. Up to 888 randomized subjects will be enrolled from up to 100 global investigational sites. Both device group and control patients will have follow-up visits at 3, 6, and 12 months and then every 6 months through 60 months.

Summary This trial will assess the safety and efficacy of Watchman in this challenging population of high-stroke risk AF patients. [Am Heart J 2017;189:68-74]