Oral anticoagulation for AF-related stroke prevention: 2018 Update

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Andrew C.T. Ha, MD, MSc, FRCPC
Cardiac Electrophysiology
University Health Network
Presenter Disclosure

• Presenter: Andrew C.T. Ha, MD

• Relationships with commercial interests:
  – Speakers Bureau/Honoraria: Bayer; BMS/Pfizer, Servier.
  – Advisory board: Servier, Bayer, Novartis.
  – Research support: Bayer.

• Dr. Andrew C. T. Ha has received honoraria from organizations whose product(s) are being discussed in this program.
  
  Company                        Product
  BMS/Pfizer                     Apixaban
  Servier                        Edoxaban
  Bayer                          Rivaroxaban

• Dr. Andrew C.T. Ha will discuss off-label use of approved medications in this presentation.
Objectives

1) Review the use of oral anticoagulation for AF-related stroke prevention, with emphasis on non-vitamin K oral anticoagulants (NOAC).

2) Updated review of the new Canadian Cardiovascular Society AF guidelines on cardioversion, with emphasis on peri-procedural anticoagulation.
### Terminology: NOAC or DOAC?

<table>
<thead>
<tr>
<th>NOAC</th>
<th>“Novel / New oral anticoagulant” or “Non-vitamin K oral anticoagulant”</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOAC</td>
<td>“Direct oral anticoagulant”</td>
</tr>
</tbody>
</table>

Both terms are commonly and interchangeably used in clinical practice and research publications.
Oral anticoagulation for stroke prevention for AF patients: Data from randomized controlled trials
Efficacy of oral anticoagulant in stroke prevention for patients with clinical AF: Randomized data

Adjusted-dose warfarin vs. placebo/control

AFASAK I, 1989;1990
SPAF 1, 1991
BAATAF, 1990
CAFA, 1991
SPINAF, 1992
EAFT, 1993

All trials (n=6)
Relative risk reduction: 64% (95% CI 49-74%)

Relative risk reduction
(with 95% confidence intervals)

Adjusted-dose warfarin resulted in a 64% relative risk reduction (95% CI: 49% to 74%) for ischemic and hemorrhagic stroke when compared to placebo/no treatment.

The relationship between INR levels and stroke / bleeding risk

From: ACC/AHA/ESC 2006 AF guidelines.

The more time spent in therapeutic range (TTR), the better.
“Real-world” time in therapeutic range in the United States: Results from 86,177 patients

- INR results from 86,177 patients treated with warfarin for ≥6 months (median # of INR tests per year: 17.9 (IQR 14.4, 23.6)).

- The mean TTR was 57.5% (SD 19.5%).

- Assuming a bell curve distribution, ≈33 and ≈25% of this patient cohort would have TTRs of ≥66% and ≥70%, respectively.

Mechanism of action of clinically approved NOAC agents

Steps in Coagulation

Initiation

Propagation

Fibrin formation

Pathway

Drugs

Initiation

Propagation

Fibrin formation

TF/VIIa

IX

IXa

VIIa

Va

II

IIa

Xa

Rivaroxaban

Apixaban

Edoxaban

Dabigatran

Fibrinogen

Fibrin

Pivotal randomized controlled trials comparing NOAC agents to warfarin

Dabigatran (Pradaxa®) (RE-LY)
Rivaroxaban (Xarelto®) (ROCKET-AF)
Apixaban (Eliquis®) (ARISTOTLE)
Edoxaban (Lixiana®) (ENGAGE AF – TIMI 48)

Time in therapeutic range (TTR) in warfarin-treated patients in NOAC vs. Warfarin RCTs

<table>
<thead>
<tr>
<th></th>
<th>RE-LY</th>
<th>ROCKET AF</th>
<th>ARISTOTLE</th>
<th>ENGAGE AF-TIMI 48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median TTR</strong></td>
<td>67%</td>
<td>58%</td>
<td>66%</td>
<td>68%</td>
</tr>
</tbody>
</table>

Key Phase III NOAC Trials: Efficacy and Safety vs. Warfarin

**Stroke or systemic embolic events**

<table>
<thead>
<tr>
<th>Trial</th>
<th>RR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY (dabigatran 150 mg twice daily)</td>
<td>0.66 (0.53-0.82)</td>
<td>0.0001</td>
</tr>
<tr>
<td>ROCKET AF (rivaroxaban 20 mg once daily)</td>
<td>0.88 (0.75-1.03)</td>
<td>0.12</td>
</tr>
<tr>
<td>ARISTOTLE (apixaban 5 mg twice daily)</td>
<td>0.80 (0.67-0.95)</td>
<td>0.012</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 (edoxaban 60 mg once daily)</td>
<td>0.88 (0.75-1.02)</td>
<td>0.10</td>
</tr>
<tr>
<td>Combined (random effects)</td>
<td>0.81 (0.73-0.91)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Major bleeding**

<table>
<thead>
<tr>
<th>Trial</th>
<th>RR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY (dabigatran 150 mg twice daily)</td>
<td>0.94 (0.82-1.07)</td>
<td>0.34</td>
</tr>
<tr>
<td>ROCKET AF (rivaroxaban 20 mg once daily)</td>
<td>1.03 (0.90-1.18)</td>
<td>0.72</td>
</tr>
<tr>
<td>ARISTOTLE (apixaban 5 mg twice daily)</td>
<td>0.71 (0.61-0.81)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 (edoxaban 60 mg once daily)</td>
<td>0.80 (0.71-0.90)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Combined (random effects)</td>
<td>0.86 (0.73-1.00)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

### All NOACs: Efficacy and Safety

#### Benefits vs. Warfarin


<table>
<thead>
<tr>
<th></th>
<th>Pooled NOAC (events)</th>
<th>Pooled warfarin (events)</th>
<th>RR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>665/29292</td>
<td>724/29221</td>
<td>0.92 (0.83–1.02)</td>
<td>0.10</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>130/29292</td>
<td>263/29221</td>
<td>0.49 (0.38–0.64)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>413/29292</td>
<td>432/29221</td>
<td>0.97 (0.78–1.20)</td>
<td>0.77</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>2022/29292</td>
<td>2245/29221</td>
<td>0.90 (0.85–0.95)</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>204/29287</td>
<td>425/29211</td>
<td>0.48 (0.39–0.59)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>751/29287</td>
<td>591/29211</td>
<td>1.25 (1.01–1.55)</td>
<td>0.043</td>
</tr>
</tbody>
</table>

Data are n/N, unless otherwise indicated. Heterogeneity: ischemic stroke $\chi^2=32\%$, p=0.22; hemorrhagic stroke $\chi^2=34\%$, p=0.21; myocardial infarction $\chi^2=48\%$, p=0.13; all-cause mortality $\chi^2=0\%$, p=0.81; intracranial hemorrhage $\chi^2=32\%$, p=0.22; gastrointestinal bleeding $\chi^2=74\%$, p=0.009.

NOAC=non–vitamin K antagonist oral anticoagulants. RR=risk ratio

Oral anticoagulation for AF-related stroke prevention: Relative and absolute risk reduction

AF patients at risk for stroke

- 64% Warfarin

CHADS$_2$=$2$

(≈4% annual stroke risk)

4.0% / year

- 19% NOAC

1.4% / year

1.1% / year
What are the benefits / risks of NOAC vs. warfarin for stroke prevention among AF patients?

Pooled analysis from 3 RCTs: ARISTOTLE, ROCKET-AF, RE-LY

- If you treat 1000 AF patients with NOAC agents instead of warfarin, you will prevent, on average, 7 strokes or systemic embolic events.

- If you treat 1000 AF patients with NOAC agents instead of warfarin, you will prevent, on average, 4 intracranial bleeds.

For which patients is the use of NOAC contra-indicated, “off-label”, or supported by paucity of data?

<table>
<thead>
<tr>
<th>Patient factor</th>
<th>NOAC use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical heart valves</td>
<td>Contra-indicated</td>
</tr>
<tr>
<td>Rheumatic mitral stenosis (especially moderate or severe)</td>
<td>Contra-indicated</td>
</tr>
<tr>
<td>Severe kidney disease (e.g. dialysis, CrCl &lt;15 mL/min)</td>
<td>Contra-indicated / off-label</td>
</tr>
<tr>
<td>Pregnancy / breast-feeding</td>
<td>Contra-indicated</td>
</tr>
<tr>
<td>Use of strong P-glycoprotein inhibitors or inducers (e.g. azoles, protease inhibitors, phenytoin)</td>
<td>Contra-indicated</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>Few prospective data</td>
</tr>
<tr>
<td>Markedly elevated BMI (e.g. ≥40)</td>
<td>Few prospective data</td>
</tr>
</tbody>
</table>
Oral anticoagulation for AF-related stroke prevention: Summary statements

1) NOAC agents are at least as effective and safe as warfarin in preventing AF-related thromboembolism.

2) In particular, RCTs have shown that patients treated with NOACs have lower rates of hemorrhagic stroke and intracranial bleeding when compared to warfarin (50% relative risk reduction).

3) Important contra-indications to NOAC agents include: (i) mechanical heart valves, (ii) moderate or severe rheumatic mitral stenosis, (iii) end-stage renal disease, (iv) pregnancy, (v) use of drugs which strongly interact with P-glycoprotein.
Peri-procedural anticoagulation for patients undergoing cardioversion for acute AF (< 48 hours): 2018 update
Case study:

- 60 year-old male.
- Presents to the ER at 7:00 PM with palpitations and shortness of breath.
- Symptoms began suddenly after shower yesterday morning (7:00 AM) (36 hours ago)
- No known history of heart disease and on no medications.
- No obvious triggers for AF were identified on history (e.g. Excessive alcohol intake).
- Heart rate = 120 bpm (irregular) and blood pressure = 135/82 mm Hg.
- Cardiovascular examination is otherwise unremarkable.
- ECG = AF with ventricular rates of 120 bpm, otherwise unremarkable.
Periprocedural anticoagulation for cardioversion of acute (<48 hours) atrial fibrillation

Cardioversion is contemplated. Will you consider anticoagulation for this patient (CHADS$_2$=0) and if so, what will you recommend?

(A) Rate-control and delay cardioversion until after 3 weeks of therapeutic oral anticoagulation (OAC).

(B) Cardioversion with no anticoagulation.

(C) Cardioversion preceded by low molecular weight heparin.

(D) Cardioversion followed by immediate institution of OAC therapy.

(E) Perform a transesophageal echocardiogram first, then decide on whether to cardiovert or not.
Cardioversion is successfully performed and the patient will be discharged ($\text{CHADS}_2=0$). Post-discharge, will you anticoagulate this patient and if so, what will you recommend?

(A) No ongoing anticoagulation or anti-platelet therapy is required.

(B) Aspirin indefinitely.

(C) Oral anticoagulant for 4 weeks.

(D) Oral anticoagulant indefinitely.

(E) Trans-esophageal echocardiogram to decide.
What are the contemporary rates of thromboembolism for anticoagulated patients who undergo cardioversion?

Irrespective of CV

4 trials
1088 events
n=71,381 pts

>48h CV Warfarin
>48h CV NOAC

From 4 NOAC pivotal trials

Within 30 days after CV

7 trials
34 events
N=8,564 pts

>48h CV Warfarin
>48h CV NOAC

From 4 NOAC pivotal trials and 3 NOAC CV RCTs

↑ 329%
↑ 258%
↓ 14%
↓ 33%

What are the contemporary rates of major bleeding for anticoagulated patients who undergo cardioversion?

Irrespective of CV

- 4 trials
- 1088 events
- n=71,381 pts

- Warfarin monthly event rate (%)
  - 0.28
- NOAC monthly event rate (%)
  - 0.23

↑ 239%

Within 30 days after CV

- 7 trials
- 34 events
- N=8,564 pts

- Warfarin monthly event rate (%)
  - 0.67
- NOAC monthly event rate (%)
  - 0.58

↑ 252%

↓ 12%

↓ 13%

From 4 NOAC pivotal trials and 3 NOAC CV RCTs

Relationship between oral anticoagulation and thromboembolic risk after cardioversion


Key points:
1) After cardioversion, patients treated with OAC had lower risk of thromboembolism relative to those who were not anticoagulated.
2) Between the 2 groups, the risk of thromboembolism was highest within the first month after cardioversion (Hazard ratio 2.25, 95% CI 1.43-3.53).
Case study:

- 60 year-old male.
- Presents to the ER at 7:00 PM with palpitations and shortness of breath.
- Symptoms began suddenly after shower yesterday morning (7:00 AM) (36 hours ago)
- No known history of heart disease and on no medications.
- No obvious triggers for AF were identified on history (e.g. Excessive alcohol intake).
- Heart rate = 120 bpm (irregular) and blood pressure = 135/82 mm Hg.
- Cardiovascular examination is otherwise unremarkable.
- ECG = AF with ventricular rates of 120 bpm, otherwise unremarkable.

36 hours of AF; CHADS$_2$=0; not anticoagulated
Relationship between oral anticoagulation and thromboembolic risk after cardioversion for acute AF (<48 hours)

Retrospective analysis of 3,143 consecutive patients who underwent 7,660 cardioversions in 3 centers in Finland between 2003-2010 (FinCV study).

3 hospitals
41 events
7,660 pts

monthly event rate (%)

0.71
0.13

<48h CV no AC
<48h CV AC

82%
Cardioversion for acute AF (<48 hours): Is it safe?

- In a case series of 366 consecutive patients with AF lasting for <48 hours who underwent transesophageal echocardiography, left atrial thrombi was detected in 1.4% of all patients (63% of whom were anticoagulated with warfarin).
- Among patients who were not anticoagulated, the prevalence of left atrial thrombi was 4%.
- “Atrial stunning” can occur immediately after cardioversion for patients with AF lasting <48 hours – this may be responsible for clot formation.

Cardioversion for acute AF (<48 hours): Is it safe?

Retrospective analysis of 2,481 consecutive patients who underwent 5,116 cardioversions in 3 centers in Finland between 2003-2010 (FinCV study).

Among unanticoagulated patients, the risk of thromboembolism within 30 days after cardioversion was 0.7%.

<table>
<thead>
<tr>
<th>Risk factors associated with thromboembolism after CV for acute AF</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to cardioversion (hours)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-24h vs. &lt;12h</td>
<td>4.0 (1.8-9.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>24-48h vs. &lt;12h</td>
<td>3.3 (1.3-8.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Age (per year increase)</td>
<td>1.06 (1.03-1.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>2.1 (1.1-4.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Heart failure</td>
<td>3.5 (1.4-8.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.7 (1.3-5.8)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Impact of oral anticoagulation on thromboembolic risk among patients with acute AF (<48 hours) who underwent cardioversion

A CHA$_2$DS$_2$-VASc score of >2 was associated with an increased risk of thromboembolism among unanticoagulated patients who underwent cardioversion for acute AF. The use of OAC appeared to be protective in this higher risk subgroup (0.2% vs. 1.1%, p=0.001)
Cardioversion for acute AF (<48 hours): Is it safe?

Based on available data, there appears to be 3 important factors which may influence the risk of thromboembolism of patients with acute AF (<48 hours) undergoing cardioversion.

- Duration of AF (<12 vs. 12-48 hours)
- CHA$_2$DS$_2$-VASc score (<2 vs. ≥2)
- Anticoagulation status (yes vs. no)
We suggest that pharmacological or electrical cardioversion of symptomatic AF or AFL without at least 3 weeks of therapeutic anticoagulation be reserved for patients with the following characteristics: *(Weak Recommendation, Low Quality Evidence)*

- patients with non-valvular AF presenting with a clear AF-onset <12 hours in the absence of recent stroke or TIA (within 6 months)

  or

- patients with non-valvular AF and a CHADS$_2$ score < 2 presenting ≥12 hours but within 48 hours of AF onset
2018 CCS AF guidelines: Anticoagulation for cardioversion in acute AF

We suggest that, in the absence of a strong contraindication, all patients undergoing cardioversion of AF/AFL receive at least 4 weeks of therapeutic anticoagulation (adjusted-dose warfarin or a NOAC) after cardioversion. *(Weak recommendation, Low Quality Evidence)*

When a decision has been reached that a patient will be undergoing unplanned cardioversion of AF/AFL, we suggest that anticoagulation therapy be initiated immediately (preferably before cardioversion). *(Weak recommendation, Low Quality Evidence)*
2018 CCS AF guidelines: Anticoagulation prior to cardioversion for patients with non-valvular AF

- **PT UNSTABLE 2º AF/AFL (↓BP, ACS, PUL EDEMA)**
  - YES → **CARDIOVERSION**
  - NO

- **ON THERAPEUTIC OAC FOR ≥3 WEEKS**
  - YES → **CARDIOVERSION**
  - NO

- **AF/AFL < 12 HRS NO STROKE OR TIA (6 MO)**
  - YES → **CARDIOVERSION**
  - NO

- **AF/AFL 12-48 HRS**
  - YES → **CARDIOVERSION**
  - NO → **CHADS₂ < 2**
    - YES → **CARDIOVERSION**
    - NO → **3 WEEKS THERAPEUTIC OAC THEN CARDIOVERSION**

- **AF/AFL >48 HRS**
  - YES → **3 WEEKS THERAPEUTIC OAC THEN CARDIOVERSION**

Periprocedural anticoagulation for cardioversion of acute (<48 hours) atrial fibrillation

Cardioversion is contemplated. Would you consider anticoagulation for this patient (CHADS$_2$=0) and if so, what would you recommend?

(A) Rate-control and delay cardioversion until after 3 weeks of therapeutic oral anticoagulation (OAC).

(B) Cardioversion with no anticoagulation.

(C) Cardioversion preceded by low molecular weight heparin.

(D) Cardioversion followed by immediate institution of OAC therapy.

(E) Perform a transesophageal echocardiogram first, then decide on whether to cardiovert or not.
Safety and efficacy of NOAC vs. warfarin among patients undergoing cardioversion: Pooled 30-day outcomes

A properly powered trial to test for non-inferiority will require 40,000-60,000 patients. Total number of patients in the 7 studies = \approx 8,500.

Practical tip: When oral anticoagulation is to be used for only a short period (<2 months) current evidence does not substantiate either an efficacy or safety advantage for use of a NOAC over adjusted dose warfarin. Nevertheless, the convenience of use of a NOAC over adjusted-dose warfarin in the peri-cardioversion period is substantial and the onset of therapeutic anticoagulation is nearly immediate with a NOAC while being delayed in the case of adjusted-dose warfarin. Accordingly, it is reasonable to use NOAC therapy in the peri-cardioversion period.
2018 CCS AF guidelines: Anticoagulation for patients undergoing cardioversion

- We suggest that, in the absence of a strong contraindication, all patients undergoing cardioversion of AF/AFL receive at least 4 weeks of therapeutic anticoagulation (adjusted-dose warfarin or NOAC) after cardioversion. *(Weak recommendation, Low Quality Evidence)*

- Thereafter, we recommend that the need for ongoing antithrombotic therapy should be based upon the risk of stroke as determined by the CCS algorithm (“CHADS-65”). *(Strong Recommendation, Moderate Quality Evidence)*
2018 CCS AF guidelines: Anticoagulation after cardioversion for patients with non-valvular AF

- **CARDIOVERSION PERFORMED**
  - YES → **OAC FOR 4 WEEKS**

- **CONSIDER LONG-TERM OAC**
  - YES → **AGE ≥65 YEARS**
    - NO
  - YES → **CHF, HTN, DIABETES, CVA**
    - NO

- **ANTIPLATELET THERAPY**
  - YES → **VASCULAR DISEASE**
    - NO

- **NO ANTI-TROMBOTHETIC THERAPY**
  - YES → **NO THROMBOEMBOLIC RISK FACTORS**

Cardioversion is successfully performed and the patient will be discharged ($CHADS_2=0$). Post-discharge, will you anticoagulate this patient and if so, what will you recommend?

(A) No ongoing anticoagulation or anti-platelet therapy is required.

(B) Aspirin indefinitely.

(C) Oral anticoagulant for 4 weeks.

(D) Oral anticoagulant indefinitely.

(E) Trans-esophageal echocardiogram to decide.
CCS guideline 2018: Anticoagulation pathway for cardioversion of atrial fibrillation or flutter

What is the definition of non-valvular AF?

2014 Canadian Cardiovascular Society AF Guidelines:

Non-valvular AF refers to AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.
## PK/PD of 4 NOACs in AF

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target</strong></td>
<td>IIa (thrombin)</td>
<td>Xa</td>
<td>Xa</td>
<td>Xa</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>BID</td>
<td>QD</td>
<td>BID</td>
<td>QD</td>
</tr>
<tr>
<td><strong>Bioavailability</strong></td>
<td>7%</td>
<td>80%*</td>
<td>66%</td>
<td>62%</td>
</tr>
<tr>
<td><strong>Hours to C_{max}</strong></td>
<td>2</td>
<td>2-4</td>
<td>1-3</td>
<td>1-2</td>
</tr>
<tr>
<td><strong>Transporters</strong></td>
<td>P-gp</td>
<td>P-gp</td>
<td>P-gp</td>
<td>P-gp</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>12-14h</td>
<td>9-13h</td>
<td>8-15h</td>
<td>10-14h</td>
</tr>
<tr>
<td><strong>Renal elimination</strong></td>
<td>80%</td>
<td>33%†</td>
<td>27%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>CYP metabolism</strong></td>
<td>None</td>
<td>18-32%</td>
<td>15-25%</td>
<td>&lt;4%</td>
</tr>
<tr>
<td><strong>Protein binding</strong></td>
<td>35%</td>
<td>&gt;90%</td>
<td>87%</td>
<td>55%</td>
</tr>
</tbody>
</table>

* Nearly 100% if taken with food
† Another 33% is excreted unchanged in the urine
CYP = cytochrome P450; NR = not reported; P-gp = P-glycoprotein
Periprocedural anticoagulation for patients undergoing cardioversion: Summary statements

1) Cardioversion (electrical or chemical) is associated with an increased risk of thromboembolism, particularly within the first few days afterwards.

2) Cardioversion of patients with acute AF (<48 hours) is associated with a small but definite risk of thromboembolism (≈0.7% within 30 days). Duration of AF (<12 vs. 12-48 hours), CHA₂DS₂-VASc score (<2 vs. ≥2), and anticoagulation use appeared to be important determinants of this risk.

3) The 2018 CCS AF guidelines recommend that all patients who undergo cardioversion be treated with at least 4 weeks of oral anticoagulant afterwards. Use of OAC may be indefinite if the patient has stroke risk factors (CHADS₂≥1 or age ≥65 years).

4) If an AF patient is being considered for cardioversion but has risk factors for thromboembolism (e.g. AF lasting >48 hours; AF within 12-48 hours but CHADS₂≥2; AF lasting <12 hours but had stroke or TIA within 6 months; valvular AF), the 2018 CCS AF guidelines recommend that cardioversion be delayed so OAC therapy can be prescribed for at least 3 weeks. (weak recommendation, low quality evidence)

5) NOAC agents are preferred over warfarin for AF-related stroke prevention, provided that there are no contra-indications to NOAC use.
Thank you for your attention

andrew.ha@uhn.ca