A novel Heparin Infusion Regimen for maintenance of stable ACT values during EP procedures
Neurological events in EP

- Current guidelines recommend administration of heparin to ACT > 300 secs
- Risk of stroke quoted at 0.25 – 0.5 %
- Silent Cerebral Ischaemia (SCI) as high as 40 -50 %

  - Gaita et al, Circulation 2010
  - Haeusler et al, J Card Electr 2013
Stroke, Cognitive decline, Dementia, Depression
ERACE Study (Verma et al, 2013)

- Low incidence of SCI when multifactorial procedural changes applied (1.7 %, 1/60 pt)

- Amongst these, maintenance of ACT >350s

- However: 1. large SD of mean ACT (405+-116) and first ACT (368 ++192);
  2. Exclusion of patients on NOACs;
  3. No control group
Current practice at Oxford University Hospitals

- Initial heparin bolus (100u/kg if on Warfarin; 150 u/kg if on NOAC) followed by an infusion fixed at 1000 u/hr via irrigation catheter; if ACT below target, intermittent top-up boluses.

- No data on efficacy. Subjective impression is that top-up boluses are frequent.

- To avoid a see-saw effect, optimizing the infusion regimen would be desirable.
Questions

- How many times do we achieve/maintain our target ACT with standard practice? How many times do we have to top-up?

- Can we improve our success rate by using an optimal post-initial bolus heparin infusion?

- Once a satisfactory initial target ACT is achieved, how much do subsequent ACTs vary from baseline? What is the % of variation when we compare a standard heparin bolus technique with an optimized infusion?
What Heparin infusion?

1. Based on patient’s weight.

Group from South Korea, JACC June 2016. 332 patients needed to show modest improvement over intermittent bolus technique. (64% vs 58%). Convoluted administration nomogram. *We did not use this method*.

2. Based on initial effective heparin dose.

Washington Uni St Louis, USA, approach. Studies on volunteers led to linear regression equation: 

\[ T_{1/2} \text{ heparin (min)} = \text{initial bolus dose (U/kg)} \times 0.3 + 33 \]

Modified in practice so to administer 1/3 of initial effective bolus dose in hourly terms, i.e. if bolus 15000U, infusion to follow at 5000U/hr.

Used on cardiac bypass cases for many years. *Subject of this project.*
15000 U
Methods

- 84 patients; 51 hep infusion (*Infusion group*) vs 33 standard management (*Control group*).
- 1 excluded (bolus overshoot), some other missing data
RESULTS

- No difference in age (63 v 60 y p=0.14), weight (88 v 89 kg p=0.8).

- No difference in 1\textsuperscript{st} heparin bolus dose (10787 v 10980U p=0.81), 1\textsuperscript{st} target ACT (346 v 347 p=0.9), mean number of ACT samples per patient (4.0 v 4.7 p=0.2)
Timing of 1st ACT measurement

- Standard practice at Oxford University Hospitals is to wait for 20-30 mins before measuring the first ACT.

- In total, 21 out of 84 initial ACTs were unsatisfactory (25%) (equally distributed, 8 of 33 bolus group, 13 of 51 infusion, p = 0.54).

- In the first 30 mins, up to 30% pts may be inadequately anticoagulated. Earlier 1st ACT measurement recommended.
Results

Counting from 1st effective ACT (included), overall 337 samples. **Target ACT** achieved:

180/194 (heparin infusion) v 97/143 (standard)

P < 0.001, χ²

Good ACTs 92.8% (infusion) v 70.7% (standard)

Boluses needed per patient:

0.3 (infusion) v 1.4 (standard), P < 0.001
How stable were subsequent ACTs?

- Mean +SD+ 95% Confidence intervals of all ACTs in both groups (from 1<sup>st</sup> good ACT included)
  - Bolus standard: 341 (46), 333 - 348
  - Heparin Infusion: 357 (27), 353 - 361

P < 0.001

- Mean % variation from initial target ACT
  - Bolus standard: -9.2% (11.7), -13.4 / -5.0
  - Infusion: 0.68% (6.2), -1.0 / 2.4

P < 0.001
Mean % variation from first target ACT

BOLUS group (n=33)  INFUSION group (n=51)
White dots: Standard Management
Black dots: Heparin infusion

Mean percentage variation from target baseline ACT
Conclusion

- Heparin infused at 1/3 of initial adequate bolus dose (in u/hr) is more effective than standard management at maintaining target ACT

- It produces extremely stable ACT values and avoids fluctuations in anticoagulation

- It requires elementary calculations and very simple set-up and it is not associated with side-effects or complications other than standard

- It could help decreasing the incidence of silent cerebral ischemia.
Thank you
What now?

- Implementation in our Department
- Prospective randomized study
- Assessment of response to NOACs if stopped / continued
- Impact on Silent Cerebral Ischaemia
- Any other ideas?
## Anticoagulation stopped or not

### Standard Bolus, n 18

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<tbody>
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<td>2</td>
</tr>
<tr>
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<td>1</td>
</tr>
<tr>
<td>APIXABAN</td>
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<tr>
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<td>7</td>
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### Heparin infusion, n 35

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Bolus/sample ratio
Control group, anticoagulation NOT stopped

- Rivaroxaban 2 / 11
- Apixaban  7 / 16
- Dobigatran 3 / 8
- Warfarin  9 / 32

21 / 67  (32/109 total in the group)
Mechanism of action

- Rivaroxaban  Anti Xa
- Apixaban     Anti Xa
- Dabigatran  Anti IIa (Antithrombin)
Scatter graphs

- Scatter graph 1: % Variation from 1st target ACT vs WEIGHT
- Scatter graph 2: % Variation from 1st target ACT vs AGE

Legend:
- Standard Bolus group
- Heparin Infusion