ACT Testing: When there’s no room for doubt

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The results shown in the studies are specific to the associated health care facilities and may differ from those achieved by other institutions.
Anaesthesia is an acute specialty!

- Not many parameters
  - metabolic state
  - coagulation
  - Hb
- Reliable results
- Fast results
Anaesthesia is an acute specialty!
Anaesthesia is an acute specialty!

Metabolic assessment:
- Blood gasses: $O_2$, $CO_2$, $SaO_2$, $HCO_3^-$, $BE$, $pH$, might need to be temperature corrected
- Electrolytes: $K^+$, $Na^{++}$, $Ca^{++}$, Lactate
- Blood Sugar
- Haematology: $Hb$, $Hct$

Coagulation Assessment:
- ACT
- INR, PT
- APTT, TT
- TEG, ROTEM, functional fibrinogen
- CBC
Cardiac Anaesthesia – slightly special

• Operations follow the same pattern:
  – pre – CPB*
  – CPB
  – post – CPB

* CPB – Cardiopulmonary Bypass
Cardiac Anaesthesia – slightly special

• Operations follow the same pattern:
  – pre – CPB
  – CPB
  – post – CPB
  OR
  – pre – anticoagulation
  – anticoagulated
  – post - anticoagulation
Cardiac Anaesthesia – slightly special

• Diagnostics during procedures
  – pre – CPB
    • ABG on induction, ACT on induction, Baseline coagulation profile, ABG before CPB, ACT before cannulation
  – CPB
    • ABG and ACT every 20 – 30 min, Assess coagulopathy
  – post – CPB
    • ABG after weaning form CPB, ACT after Protamine, Coagulation assessment
Anticoagulation

- Anticoagulation mandatory before CPB

- Heparin worldwide preferred agent
  - cheap, rapid onset, easily reversible
  - easy to test
  - Bivalirudin, Argatroban, Ancrod, Lepirudin, Prostacyclins have been reported

- ACT ubiquitous in CVORs worldwide
Anticoagulation
Anticoagulation

Cardiopulmonary Bypass
SECOND EDITION

Edited by:
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Anticoagulation

• Necessary due to
  – Blood stasis
  – Activation, inflammation
  – Clot in CPB circuit generally leads to fatal consequences
(Anti)coagulation

• Protamine
  – cheap, predictable, easy to titrate

• 1mg Protamine / 100U Heparin

• Protamine not benign

• Too little protamine can lead to unnecessary transfusion
Heparin monitoring – Once upon a time…

1918  Discovery of heparin.

1930s  Optimising for safe clinical use.

1939  Use in animal CPB

1953  Use in human CPB
Coagulation cascade

TF + FVIIa → FXa + FIIa

FIIa → FVa

FXa + FVIII → FXI

FIXa + FXII → aPTT

PT
Coagulation cascade - ANTIcoagulation

**Reagents:**
- TF + FVIIa
- PT
- FVa
- FIXa
- FXI
- FIXa + FVIII
- FXII

**Anticoagulants:**
- Rivaroxaban
- Fondaparinux
- Apixaban
- Unfractionated Heparin
- LMWH
- Bivalirudin
- Dabigatran
- Argatroban
- Vitamin K agonists: IX, X, VII and II (1972)

**Tests:**
- aPTT
- PT
Heparin monitoring – Once upon a time…

1918  Discovery of heparin.
1930s Perfectioning for safe clinical use.
1939  Used in animal CPB
1953  Used in human CPB
      Proliferation of heparin protocols after near disaster during first successful operation on CPB
1966  Hattersley first describes ACT
1974  Hill first describes use of ACT during CPB
      Bull’s work helps ACT evolve from virtually non-existent to widespread during next 5 years.
The Heparin Monitoring Dilemma
Which test and/or value gives best representation of anticoagulation level?

- Anti Xa
- TEG/TEM
- APTT
- TT
- HMS
- ACT

- Unclottable at higher heparin concentrations

- Specialized testing
- Bleeding patients
ACT - Today

- Hemochron Response
- Hemochron *Signature* Elite
- Medtronics ACT Plus
- Medtronics HMS+
- Helena Actalyke XL / Mini
- Gem PCL
- Abbott i-STAT
ACT - Detection systems

Mechanical

- magnet
- clotting times

Photo-optical

- optical sensor
- clotting times
ACT – i-STAT

- Chemical detection of thrombin formation
- Electrochemical sensor measures specific substrate conversion
- Immediate amperometrical detection of electroactive substance

Gly-Pip-Arg-NH$_2^-$ -OCH$_3$

Gly-Pip-ArgOH

NH$_2^-$

NH$_2^-$-NH$_2^-$-OCH$_3$

For in vitro diagnostics use only
For intended use please see intended use section
Laboratory Guidelines


- Procedures for selection and use of POCT are under supervision of the laboratory.
- Adequate training programs
- POCT linking with LIS, certificating en re-certification
Laboratory Guidelines


• Tests should be performed according to manufacturer’s directions

• No “standard” ACT, need to establish normal and therapeutic ranges for each system and activator used.

• Select appropriate system for clinical application and heparin ranges.

• Be aware of (pre)analytical variables
  • Platelet count and function
  • Hypothermia and/or haemodilution
  • Coagulation abnormalities
  • Different detection systems
Recommendations

• Recommend ACT to monitor heparin dose during cardiac surgery

ELSO(2014):
• ACT most commonly used test to dictate UFH dosage. However, potential shortcomings of ACT alone might require complementing with more elaborate tests like anti Xa.

European Society of Cardiology: Guidelines on myocardial revascularization (2014):
• No role for ACT during PCI

STS/SCA/AmSECT (2018):
• ACT gold standard – but prone to numerous influences, min value of 400 or 480 sec (depending on test used) reasonable
• 300 – 400 U / kg Heparin
• Institutional safe number

Laboratory test interpretation

Accurate Precise

Not Accurate Precise

Accurate Not Precise

Not Accurate Not Precise
ACT / anti Xa

<table>
<thead>
<tr>
<th>Anti-Xa Level (U/mL)</th>
<th>hACT Mean (95% CI)</th>
<th>iACT Mean (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>147.4 (132.5-163.8)</td>
<td>147.7 (138.8-157.1)</td>
<td>0.9328</td>
</tr>
<tr>
<td>0.5</td>
<td>165.3 (149.6-182.7)</td>
<td>160.5 (150.8-170.7)</td>
<td>0.2097</td>
</tr>
<tr>
<td>0.75</td>
<td>190.9 (173.4-210.2)</td>
<td>178.0 (166.4-190.5)</td>
<td>0.0058</td>
</tr>
<tr>
<td>1</td>
<td>220.5 (200.1-242.9)</td>
<td>197.5 (182.7-213.5)</td>
<td>0.0005</td>
</tr>
<tr>
<td>2</td>
<td>392.0 (341.8-449.6)</td>
<td>299.1 (259.4-345.0)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

• Very good correlation between i-STAT and other methods
  • i-STAT trending to read higher
  • Emerging evidence for higher accuracy of the chemical method compared to the mechanical
ACT

- 121 duplicate samples on Medtronic and i-STAT
  - cardiology and CVOR

- Up to 15% of duplicate Medtronic samples were outside 12% tolerance between samples

<table>
<thead>
<tr>
<th></th>
<th>i-STAT</th>
<th>Medtronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range difference (mean)</td>
<td>0 – 17% (3.5%)</td>
<td>0 – 29% (4.9%)</td>
</tr>
</tbody>
</table>
ACT

- Multicenter trial, 3 centers in 2 continents
- Elective and urgent patients, CABG +/- valve
- i-STAT and 1 mechanical ACT device
  - 2 tests per device per sampling point
- 400 cardiac surgical patients, up to 7 ACT measurements
  - ≈ 2500 ACT
  - up to 10,000 data points

Falter F, Razzaq N, Martin J, Fassl J, Maurer M, Ewing S, Hofmeyr R, Clinical evaluation of measuring the ACT during elective cardiac surgery with two different devices, JECT, 2018; 50: 38-43
Intra-device % Change @ standard measuring points

Coefficient of Variation @ standard measuring points

Falter F, Razzaq N, Martin J, Fassl J, Maurer M, Ewing S, Hofmeyr R, Clinical evaluation of measuring the ACT during elective cardiac surgery with two different devices, JECT, 2018; 50: 38-43
Falter F, Razzaq N, Martin J, Fassl J, Maurer M, Ewing S, Hofmeyr R, Clinical evaluation of measuring the ACT during elective cardiac surgery with two different devices, JECT, 2018; 50: 38-43
Time to ACT!

When anyone asks me how I can best describe my experiences of nearly 40 years at sea I merely say uneventful. Of course, there have been winter gales and storms and fog and the like, but in all my experience I have never been in an accident of any sort worth speaking of. I have seen but one vessel in distress… I never saw a wreck and have never been wrecked, nor was ever in any predicament that threatened to end in disaster of any sort.

I cannot conceive of any vital disaster happening to this vessel. Modern shipbuilding has gone beyond that.

Captain EJ Smith
Titanic
Southampton, 09.4.1912
• The i-STAT Kaolin Activated Clotting Time ($^{\text{Kaolin}}$ACT) test is an \textit{in vitro} diagnostic test that uses fresh, whole blood, and is used to monitor high-dose heparin anticoagulation frequently associated with cardiovascular surgery.

• The i-STAT Celite Activated Clotting Time ($^{\text{Celite}}$ACT) test is an \textit{in vitro} diagnostic test that uses fresh, whole blood, and is useful for monitoring patients receiving heparin for treatment of pulmonary embolism or venous thrombosis, and for monitoring anticoagulation therapy in patients undergoing medical procedures such as catheterization, cardiac surgery, surgery, organ transplant, and dialysis.
THANK YOU