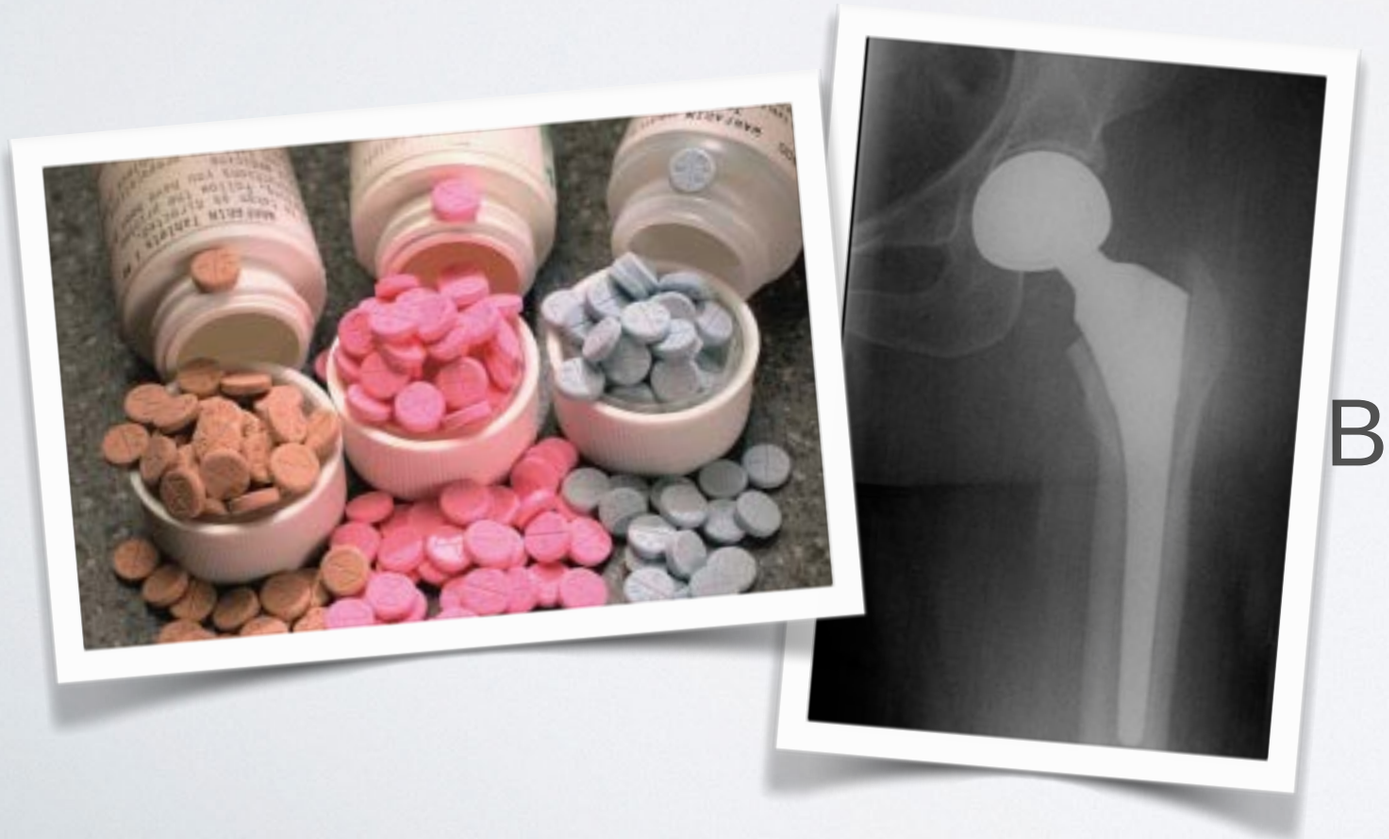
ANTICOAGULANTS

AND

HIP FRACTURE SURGERY



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- Anticoagulation is common amongst the hip fracture patient population (6-10%)
- Anticoagulation signifies co-morbidity
  - AF >> thromboembolism > valve prosthesis (Ashouri ISRN hematol 2011)
  - Cardiovascular disease present in >35% (Madsen Acta Orthop 2016)
- Guidelines exist for management of anticoagulants in both elective surgery and haemorrhage but not for hip fracture

ANTICOAGULATION DELAYS SURGERY

<u>Warfarin therapy delays surgery</u>

- 65% patients on warfarin delayed past 48h because of anticoagulation
  (Al-Rashid/Parker Injury 2005)
- Time to surgery 47 hours vs. 29 hours (Cohn J Orthop Trauma 2017)
- SHFA found that surgery was delayed in 3.4% of all hip fracture patients because of coagulation issues, equivalent to 400 bed-days PA (2008)
- Delay is associated with complications and poorer outcomes
  - LOS 8.6 days vs 5.5 days

HOW GOOD DOES THE COAGULATION HAVE TO BE?

ARE OUR FEARS FOUNDED?

- Wide range of minor surgery now performed without interrupting warfarin

- Hernia surgery on warfarinised patients - haematoma in 3/49 (Sanders, Hernia 2008)

    - Risk only increased if INR >3

- Continued warfarin therapy reduced risk of haematoma following pacemaker insertion when compared with pre-op cessation and bridging anticoagulation (3.5% vs 16%) - Birnie NEJM 2013

INR TARGETS FOR HIP FRACTURE

- Traditional INR target for surgery = 1.5 (BOA/BGS Blue Book) however risks and benefits of this target are not known

- AAGBI suggests target INR 2.0 for surgery (but 1.5 for neuraxial anaesthesia), NICE and SIGN do not stipulate coagulation targets

- INR 1.77 did not increase bleeding or transfusions compared with INR 1.25 or controls (Cohn J Orth Trauma 2017)

  - BUT higher INR target reduced time to theatre (33h vs. 54h)

- Many units now use INR target of 1.7

ANTICOAGULATION MANAGEMENT PROTOCOLS REDUCE TIME TO SURGERY

- Tayside - warfarin management protocol
  (Faulkner, Reidy)
  - reduced time to theatre 45 -> 29h
  - cancellations 43% -> 26%

- Protocolised management of anticoagulation vs. standard management reduced admission-to-surgery time from 73h to 37h
  (Ahmed J Orth Traum 2014)

IT’S ALL ABOUT THE DETAIL

- Most (70%) trauma units employ a protocol for management of warfarin (2009 survey)

  Starks J Trauma Emerg Surg 2009

- However of these, the preferred strategy was to simply withhold warfarin in 70%

- Others included FFP (16%) and vitamin K (37%)

WHAT ARE OUR OPTIONS FOR CORRECTING WARFARIN?

1. ‘Spontaneous’ reversal
2. Vitamin K
3. FFP
4. Prothrombin Complex Concentrate

SPONTANEOUS REVERSAL

- Perception that this is ‘gentler’, however in fact leaves the patient under-anticoagulated for longer, increasing thrombosis risk

- Bridging anticoagulation to cover this period greatly increases major bleeding risk (OR 3.6) Siegal NEJM 2015

SPONTANEOUS REVERSAL

- INR 2-3 takes 4-5 days to return spontaneously to 1.2 *in well patients* (White J Thromb thrombolysis 2000)

- Unwell patients receiving antibiotics etc. may increase INR and spontaneous reversal can be prolonged, or INR may even increase (Ashouri, ISRN hematology 2011)

- This significant delay to surgery increases mortality and worsens outcomes

VITAMIN K

- Recommended by SIGN & AAGBI for warfarin reversal in hip fracture patients

- Vitamin K 1mg IV reduced INR to1.5 in mean 38h (15-64h)
  Bhatia Ann R Coll Surg Eng 2010

  - At this dose, repeat dosing is usually required (2 doses in 60%, 3 doses in 16%) (Ahmed, J Orthop Traum 2014)

- Vitamin K 5mg IV reversed 11 of 12 patients with a single dose

VITAMIN K

- IV administration is much faster acting than oral (4-6h vs. 12-24h)
- IV has small risk of anaphylactoid reactions (3:10,000) which may be reduced by giving as slow infusion
- IM and SC routes are not recommended

<u>BSH recommendation for emergency surgery:</u>

- ‘If surgery can wait 4-6h then 5mg IV vitamin K can restore coagulation factors’

FRESH FROZEN PLASMA

- Contains all coagulation factors and is used to correct factor deficiency

- Dose is 12-15ml/kg, = 4 units for 70kg patient (NHSBT 2010)

- However exposes patient to risks of transfusion, infusion rate is slow and INR reversal is slow, and is rarely indicated (SIGN 111)

PROTHROMBIN COMPLEX CONCENTRATE

- E.g. Beriplex/Octaplex
- 4 factor concentrate, dose 25IU/kg for INR 2.0-3.9
- Completely reverses warfarin within 20 min, vitamin K must be given concurrently
- Significant cost (£500 per dose) HOWEVER:
  - Cost modelling favours use in hip fracture - £1250 per patient (Letter, Francis et al, Anaesthesia, 2014)

1. **‘Spontaneous’ reversal**

2. **Vitamin K**

3. **FFP**

4. **Prothrombin Complex Concentrate**

Where PCC would allow on-the-day surgery

Rivaroxaban

Dabigatran

DIRECT ORAL ANTICOAGULANTS

Edoxaban

Apixaban

DOACS

- Recommended by NICE for the treatment of atrial fibrillation, DVT and PE
- Oral Xa inhibitor
- Provides more stable anticoagulation than warfarin in some patients
- Effect not measurable through standard lab coagulation tests

DOACS

- Guidelines for elective surgery are variable
- Evidence for emergency surgery non-existent
- Delay of 2 elimination half lives before surgery is desirable (Ferrandis, Thromb Haem 2013)
- Elimination half life 8-13h (slightly longer than LMWH)
  - This is increased by renal failure

DOACS:
MANAGEMENT FOR HIP FRACTURE SURGERY (TAKEN FROM BSH)

	Normal renal function	**Creatinine clearance <30**	**High bleeding risk**
Apixaban	**24h**	**48h**	**Add 24h**
Rivaroxaban	**24h**	**48h**	**Add 24h**
Edoxaban	**24h**	**48h**	**Add 24h**
Dabigatran	**24h**	**CrCl 50-80: 24-48h** **CrCl 30-50: 48-72h**	**Add 24h**

REVERSAL OF DOACS

- Dabigatran: Idarucizumab (£6500 per treatment)

- -aban drugs: Andexanet Alfa (not available yet)

- Fresh frozen plasma

- 4 factor PCC

- Activated factor VII

ANTIPLATELETS

CLOPIDOGREL

- n=1381 Collyer BJA 2013
- Withheld in 98% (2d to surgery and 3d after)
- Blood transfusion OR 2.31. But only 1 unit!
- Post-op ACS in 20% (OR 6.7)
- Little pharmacological sense in withholding
  - Effect persists 7 days
  - At 75mg onset of action = 3-5 days
- T1/2 4h so effect virtually zero at 24h

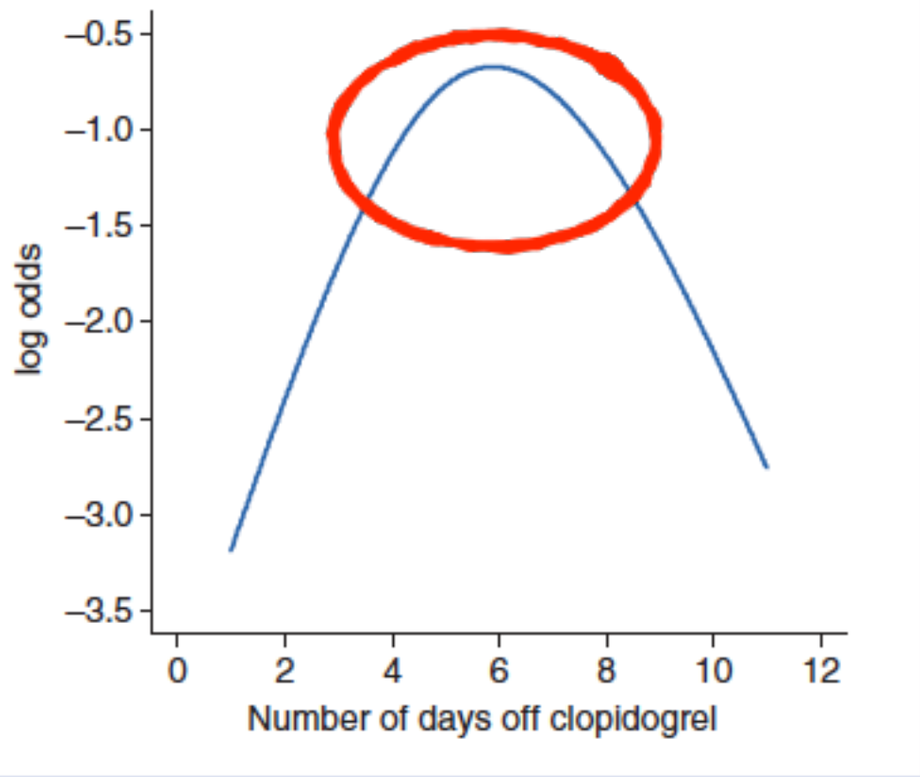

Fig 1 Estimated spline transformation showing the log odds for an ACS plotted against number of perioperative days clopidogrel was withheld. The relative odds peak at days 4–8 off clopidogrel therapy.

Risk of ACS vs. time off clopidogrel

CLOPIDOGREL

- SIGN suggest proceed without interrupting
- No need for prophylactic platelet transfusion
- May wish to withhold for 24h if high bleeding risk
- Dual antiplatelets:
  - BSH suggests: continue aspirin and withhold clopidogrel for 24 h

GENERAL POINTS

- **Do not delay surgery because of anticoagulation**
- Enact a plan for anticoagulation from patient admission
- Do not stop clopidogrel
- Think about patient thrombosis risk AND bleeding risk
- Avoid regional anaesthesia unless you are certain anticoagulation is reversed
- Tranexamic acid is very effective in reducing bleeding
- Restart 24h-48h post-op

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bjh guideline

Peri-operative management of anticoagulation and antiplatelet therapy

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