Appendix S1 Suggested management of hip fracture patients taking anticoagulant or antiplatelet medication

Antiplatelet medication
Any single antiplatelet medication (including aspirin, clopidogrel, ticagrelor, prasugrel) is not a contraindication to spinal anaesthesia for acute hip fracture surgery, if this is the best option for an individual patient. This should be discussed with the patient.

Whilst dual antiplatelet therapy (e.g. aspirin and clopidogrel) is not an absolute contraindication to central neuraxial block in the context of acute hip fracture surgery, there would need to be good reason not to proceed with a general anaesthetic on a risk/benefit basis.

All high-risk patients should be monitored for signs of vertebral canal haematoma in the postoperative period (back pain, numbness, motor weakness, bladder/bowel incontinence).

Warfarin
Admission and pre-operative
- If administered for uncomplicated atrial fibrillation, deep vein thrombosis or pulmonary embolism, stop warfarin, check INR and administer vitamin K (5mg i.v.) as soon as possible in the emergency department.
- Recheck INR after 4-6 h:
    - If ≤ 1.5, proceed with surgery
    - If > 1.5 consider either further vitamin K (5 mg i.v.) or prothrombin concentrate complex, in accordance with local hospital guidelines

Surgery and anaesthesia
- Proceed with surgery if INR is ≤ 1.8
- Proceed with neuraxial anaesthesia if INR ≤ 1.5
- Restart warfarin 12–24 h postoperatively (assuming no active bleeding). In the context of deep vein thrombosis or pulmonary embolism, treatment dose low molecular weight heparin should be considered until INR has returned to therapeutic range.

If anticoagulated for another reason (e.g. metallic valves, especially mitral), a more considered approach +/- bridging anticoagulation should be guided by discussions with a haematologist.

DOACS – direct oral anticoagulant drugs (formally NOACs)
The direct oral anticoagulant drugs (apixaban, edoxaban, rivaroxaban, dabigatran) pose a different challenge to warfarin, especially in terms of prompt time to theatre.

In broad terms, the elimination of the drug is dependent on renal function. Dabigatran is 80% cleared by the kidneys, compared to 50% for edoxaban, 33% for rivaroxaban, and 25% for apixaban.

Standard coagulation screens (INR, aPTT) are not a reliable indicator of the effects of DOACs. The thrombin time (TT) is very sensitive to dabigatran. A normal TT rules out any effect of dabigatran. Anti-factor Xa chromogenic assays can accurately measure DOAC concentrations in plasma, but are not available at all hospitals.

A specific reversal agent exists for dabigatran (idarucizumab (Praxbind)), and for apixaban and rivaroxaban in life-threatening or uncontrolled bleeding (andexanet alfa). Acute reversal increases the risk of thrombotic events. Local policies should be reviewed in conjunction with the haematology department for up-to-date advice on monitoring and new and emerging reversal techniques.

The half-lives of DOACs guide surgical and neuraxial anaesthesia timing. In general, waiting two half-lives (approximate residual anticoagulant effect of around 25%) between the last dose and surgery/anaesthesia provides an appropriate compromise between risk (avoidance of surgical haemorrhage, 'anaesthetic' vertebral canal haematoma, thromboembolism) and benefit (timely surgery). This approach is supported by Association of Anaesthetists' guidance on regional anaesthesia in patients with abnormalities of clotting.

Half-lives: dabigatran approximately 15 h (in healthy elderly volunteers), apixaban 12 h, edoxaban 12 h, rivaroxaban approximately 12 h (in elderly patients).

In the case of significant intra-operative haemorrhage, anaesthetists should follow an agreed hospital management policy.

It is safe to restart a DOAC 12–24 h postoperatively (assuming no active bleeding).

A pragmatic approach that balances these risks (accounting for renal function) is described below. Local policies may differ.

Xa inhibitors (apixaban, edoxaban, rivaroxaban)

- Stop the drug on admission to hospital
- Confirm and document time of last dose
- If estimated glomerular filtration rate (eGFR) $\geq$ 60 ml.min.1.73m^2 (creatinine clearance $\geq$ 30 ml.min^{-1}), proceed with surgery after two half lives (24 h) since the last dose, under general anaesthesia (or spinal anaesthesia if indicated)
- If eGFR < 60ml.min.1.73m^2 (creatinine clearance < 30 ml.min^{-1}), proceed with surgery after four half lives (48 h) since the last dose (i.e. the next afternoon), under general anaesthesia (or spinal anaesthesia if indicated)
- Alternatively, in those with poor renal function and if available, measure specific anti-factor Xa levels by chromogenic assay at 8 am on day of surgery. Proceed with surgery and anaesthesia (including spinal anaesthesia if indicated) if assay $\leq$ 50 ng.ml^{-1}. Discuss reversal options with haematologists if > 50 ng.ml^{-1}
- There is no need to perform an assay for people taking the above Xa-inhibitors if CrCl $\geq$ 30 ml.min^{-1} or eGFR $\geq$ 60ml.min.1.73m^2. In this instance, proceed with surgery after two half-lives (24 h) since the last dose, under general anaesthesia (or spinal anaesthesia if indicated).

Thrombin inhibitors (dabigatran)

- Stop the drug on admission to hospital
- Confirm and document time of last dose
- Plan surgery for the afternoon of the next day
- At 8 am on day of surgery, send venous blood for TT or assay
- If TT is normal, proceed with anaesthesia and surgery as planned
- If TT is prolonged, contact haematology for advice and to consider reversal with idarucizumab
- If a dabigatran assay is used, discuss with haematology for advice about patient management +/- reversal of the drug (> 50ng.ml^{-1}*).

* There is a lack of evidence or consensus about what the acceptable plasma DOAC level is for urgent surgery. Some hospitals are able to perform such tests. Currently, however, the interpretation of results requires extrapolation from elective practice; $\leq$ 50 ng.ml^{-1} may be considered "safe" when making decisions about urgent surgery. This threshold may require further modification as future data becomes available. Thrombin time is a suitable alternative to a dabigatran assay.

An A4 sized summary of this guidance is available below, and can be usefully displayed in relevant anaesthetic rooms or addended to institutional hip fracture care pathway proformas.

People with hip fracture on antiplatelet or anticoagulant medication

The Association of Anaesthetists has produced useful guidelines for regional anaesthesia in patients with abnormalities of coagulation that gives advice about when it would be considered safe to proceed with a spinal anaesthetic.

For many, general anaesthesia is an acceptable alternative and surgery should proceed when the surgical bleeding risk is felt to be acceptable. For some, the risks of vertebral canal haematoma may be (considerably) less than the risk of general anaesthesia. The Association of Anaesthetists' guidelines recognise this balancing of risks and benefits, as do recommendations made by the European Society of Anaesthesiology.

The risks of delaying surgery and/or thromboembolism usually greatly outweigh the risks of vertebral canal haematoma and/or of peri-operative bleeding.

The INR and aPTT are uninterpretable in the context of DOACS.

Drug	**Elimination half-life**	**Management**	**Acceptable to proceed with spinal**
Aspirin	Irreversible effect on platelets	Proceed with surgery	Continue
Clopidogrel	Irreversible effect on platelets	Proceed with surgery under GA Monitor blood loss Consider platelet transfusion if concerns regarding bleeding	Yes, if GA poses greater risk to patient
Ticagrelor	8–12 h	Proceed with surgery with GA Monitor for blood loss Consider platelet transfusion if concerned about risk of bleeding	Yes, if GA poses greater risk to patient
Unfractionated i.v. heparin	1–2 h	Stop i.v. heparin 2–4 h pre-op	4 h
Low molecular weight heparin subcutaneous prophylactic dose	3–7 h	Last dose 12 h pre-op	12 h
Low molecular weight heparin subcutaneous treatment dose	3–7 h	Last dose 12–24 h pre-op. Monitor blood loss	24 h
Warfarin	4–5 days	5 mg vitamin K i.v. and repeat INR after 4 h Consider repeating. Consider prothrombin complex for immediate reversal	If INR < 1.5
Dabigatran	15–17 h	Consider surgery 24–48 h after last dose Review renal function Consider idarucizumab for immediate reversal	24–36 h if TT or anti-Xa assay normal. If abnormal, give idarucizumab and proceed.
Rivaroxiban Apixaban Edoxaban	12 h	May be partially reversed with prothrombin complex Consider surgery 12–24 h after last dose Review renal function	24 h if eGFR > 60 48 h if eGFR < 60 Proceed Xa ≤ 50 $ng.ml^{-1}$ Reverse Xa > 50 $ng.ml^{-1}$

GA, general anaesthesia; i.v., intravenous; TT, thrombin time; eGFR, estimated glomerular filtration rate

Post-anaesthesia care unit (PACU) discharge criteria

The Working Party is aware of anecdotal evidence showing improvements in the continuity of peri-operative care back to ward orthogeriatric or critical care when a PACU discharge proforma is used. A specimen document is included below, and may be reproduced for attachment to anaesthetic charts in readers' institutions.

PACU discharge criteria after hip fracture surgery		
Patient name		
Procedure		
Surgeon		
Anaesthetist		
Intra-operative care (anaesthetist to complete)	Y/N/value	Patient specific factors
General anaesthesia?		
Spinal anaesthesia?		
Nerve block?		
Sedation administered?		
Starting blood pressure?		
Lowest recorded blood pressure?		
Bone cement used?		
Fluid balance +/- ml		
Deep vein thrombosis prophylaxis prescribed?		
Postop analgesia prescribed?		
Analgesia adjusted for renal function?		
Ondansetron prescribed?		
Delirium risk (high/low)?		
Postoperative care (PACU staff to complete)		
Bedside blood glucose level (if diabetic)		
Bedside [haemoglobin] level		
Pain score/10 at rest		
Pain score/10 on movement		
Leaving PACU (PACU staff to complete)		
Temperature?		
Blood pressure?		
Heart rate?		
Heart rhythm?		
Oxygen saturation?		
Inspired oxygen %?		
Sitting up?		
Intravenous fluids discontinued?		
Tolerating oral fluids?		
Other issues (anaesthetists, PACU staff to complete)		

Standardised hip anaesthesia routine protocol (SHARP)

Similarly, the Working Party is aware of anecdotal evidence showing improvements in the provision of peri-operative care when a standardised hip anaesthesia routine protocol (SHARP) document is used. A specimen SHARP document is included below, and may be reproduced and laminated for display in appropriate anaesthetic rooms/operating theatres in readers' institutions.

Standardised hip anaesthesia routine protocol (SHARP)

PRE-OPERATIVE

Analgesia
- paracetamol 1g qds (15 mg/kg < 50 kg)
- fascia iliaca block (FIB) in A+E
- (opioid protocol, NB renal function)

Minimise pre-operative fasting
- NBM 4 hours solids
- NBM 2 hours clear fluids
- forearm i.v. access + fluids

Risk stratify Nottingham hip fracture score

Determine appropriate level of postop care

Identify/treat reversible comorbidities according to agreed institutional protocol

Determine mental capacity, DNACPR, (Proxy) consent

Aim for surgery within 36 hours of admission

Discuss and confirm peri-operative plan at multidisciplinary pre-operative meeting

INTRA-OPERATIVE

Appropriately experienced surgeon/anaesthetist

Ensure antibiotics, normothermia

Spinal anaesthesia
- lower doses (< 2 ml 0.5% bupivacaine)
- avoid opioids (nerve block administered)
- sedation – avoid/propofol only (bolus/ TCI)

Blood pressure control
- NIBP 2 min cycle, consider invasive
- target MAP > 70 mmHg
- 1(-2)L crystalloid, vasoconstrictor infusion > boluses

General anaesthesia
- age-adjusted depth (TCI, MAC, BIS/Entropy)

Bone cement implantation syndrome
- follow hospital protocol if cement is used

Nerve block
- ultrasound-guided FIB (30-40 ml)

Tranexamic acid
- according to hospital protocol

Aim to facilitate:
- **Remobilisation** - analgesia
  - blood pressure
  - cognition
- **Re-enablement** - + bowel and bladder function
- **Rehabilitation** - + minimising cardiac, respiratory, neuro, renal complications

POSTOPERATIVE

Complete agreed PACU discharge criteria

Reconsider appropriate level of postop care

Review peri-operative mortality and morbidity at monthly multidisciplinary meetings

Implement continuous audit/quality improvement cycles

www.hipfractureanaesthesia.co

Research recommendations

Much of the guidance on the anaesthetic management of hip fractures is based on small amounts of historical, poor quality data, and there has been a lack of focus on improving this situation in the last decade.

The Working Party recommends that the following 10 research questions are among the most important that remain to be answered in this area, and encourage researchers to undertake large randomised controlled trials or observational studies to answer these, using these recommendations as evidence of necessity when submitting applications for funding. The order of the recommendations relates to the patient's inpatient journey, rather than their relevant importance.

In developing these recommendations, the Working Party has taken into account the research priorities identified by the 2018 James Lind Alliance Priority Setting Partnership into *Broken bones in older people – musculoskeletal injury: fragility fracture of the lower limb and pelvis* [http://www.jla.nihr.ac.uk/priority-setting-partnerships/broken-bones-in-older-people (accessed 07/07/2020)].

The Working Party supports the use of the standardised set of outcome measures determined by Delphi consensus alluded to in the main guideline document ([18]).

Questions

1. What is the best pain relief, including non-drug therapies and alternatives to reduce morphine or opioid use, for patients with hip fracture at hospital admission?
2. What is the best way of administering spinal anaesthesia to patients with hip fracture?
3. What is the best way of administering general anaesthesia to patients with hip fracture?
4. How do the best ways of administering spinal and general anaesthesia compare in relation to mortality, early postoperative morbidity and day 1 remobilisation?
5. What is the optimal peri-operative management of blood pressure for hip fracture surgery?
6. What is the optimal peri-operative management of blood transfusion for hip fracture surgery?
7. Do hip fracture benefits benefit from targeted admission to higher dependency units after hip fracture surgery, compared to ward-based care?
8. How can anaesthetists provide the best pain relief for patients after hip fracture?
9. What is the best method of assessing static and dynamic pain in hip fracture patients with and without cognitive impairment?
10. What are the best anaesthetic interventions to prevent and treat confusion and delirium after surgery for hip fracture?

Quality assurance/quality improvement (QA/QI) toolkit

The GMC states that *"for the purposes of revalidation, doctors will have to demonstrate that they regularly participate in activities that review and evaluate the quality of their work. Quality improvement activities should be robust, systematic and relevant to doctors' work. They should include an element of evaluation and action, and where possible, demonstrate an outcome or change"*.

The QA/QI toolkit aims to help anaesthetists undertake quality improvement activities both to improve the quality and safety of care that they/their department deliver to patients, and to fulfil the GMC criteria for revalidation.

There are three standardised domains:

1. Advice for the responsible lead anaesthetist
2. Advice for individual anaesthetists
3. Advice for departmental quality improvement projects.

Advice for the responsible lead anaesthetist
Your anaesthetic department should identify a consultant anaesthetist responsible for implementing this guideline.

Having read the guideline carefully, the lead anaesthetist should:

- identify and inform other anaesthetic colleagues who need to read and implement the guidelines;
- identify whether further training is needed for colleagues on the guideline topic;
- prepare and deliver a departmental meeting about the guideline topic within every 5-year guideline renewal cycle;
- inquire about guideline improvements suggested by colleagues, and feed these back to the Working Party Chairperson;
- inquire about problems that colleagues have implementing guidelines, and feed these back to the Working Party Chairperson;
- identify what problems anaesthetists have following recommendations.

Advice for individual anaesthetist
You should record:

- when you read this guideline;
- details of any improvements to or problems following the recommendations in this guideline, that you have discussed with your responsible lead anaesthetist;
- details of any quality improvement activity you have undertaken related to these guidelines, specifically: what recommendation did you look at, what did you measure, what did you find and how did you change things?

Advice for departmental QA/QI projects
A core value of Association of Anaesthetist guidelines is that they should advance and improve patient care and safety in anaesthesia.

The Royal College of Anaesthetists' *Quality improvement in anaesthesia (2012)* [https://www.rcoa.ac.uk/sites/default/files/documents/2019-09/CSQ-ARB-2012_0.pdf] provides

detailed theoretical and practical advice about how to undertake a quality improvement project.

The Working Party suggests the following QA/QI projects based on these guidelines. These have been chosen either because they ensure a basic minimum standard of patient care and safety, and/or they enable the greatest improvement in patient care and safety using the fewest resources. Failure to reach the suggested outcome targets should stimulate further root cause analysis and practice change.

QA project 1 – Training
Recommendation: all eligible anaesthetists at your hospital should receive training on how to manage people with hip fracture undergoing surgery

Suggested measurable outcomes: self-reported departmental log of training, collated by lead anaesthetist, detailing (1) attendance at departmental training session, or (2) review of educational material from that session (co-ordinated with lead anaesthetist for quality and safety).

What outcome target should your department aim for? 100% of anaesthetists should report having received training once every 5 years of practice

QA project 2 – Peri-operative nerve blocks
Recommendation: all patients undergoing surgery for hip fracture should receive peri-operative analgesic nerve blockade

Suggested measurable outcomes: proportion of patients undergoing surgery for hip fracture should receive peri-operative analgesic nerve blockade (co-ordinated with lead anaesthetist for acute pain management)

What outcome target should your department aim for? 100% of eligible patients

QA project 3 – Delays to surgery
Recommendation: all older surgical patients with hip fracture should undergo surgery within 36 h of hospital admission

Suggested measurable outcomes: proportion of older surgical patients with hip fracture undergoing surgery within 36 h of hospital admission (co-ordinated with lead orthogeriatrician)

What outcome target should your department aim for? 100% of eligible patients

QI project 4 – Intra-operative blood pressure control
Recommendation: all older surgical patients with hip fracture should have their intra-operative mean arterial pressure maintained above 70mmHg

Suggested measurable outcomes: (1) proportion of older surgical patients with hip fracture whose lowest intra-operative mean arterial pressure remains above 70 mmHg (2) proportion of older surgical patients with hip fracture in whom total duration of intra-operative MAP < 70 mmHg is < 5 min (co-ordinated with departmental Quality Audit and Research Co-ordinator (QuARC)).

What outcome target should your department aim for? (1) and (2) 100% of eligible patients

QI project 5 – day 1 postoperative remobilisation
Recommendation: all older surgical patients with hip fracture should be remobilised fully weight bearing the day after surgery

Suggested measurable outcomes: proportion of older surgical patients with hip fracture remobilised fully weight bearing the day after surgery (co-ordinated with the lead orthogeriatrician and responsible physiotherapist).

What outcome target should your department aim for? 100% of eligible patients