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International Fragility Fracture Network Delphi consensus statement on the principles of anaesthesia for patients with hip fracture.

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Running title: Consensus guidelines in hip fracture anaesthesia.

Consensus principles of anaesthesia for hip fracture surgery

1. Anaesthesia is integral to the multidisciplinary care of hip fracture patients.
2. Anaesthesia (and surgery) for hip fracture surgery should be undertaken by an appropriately experienced anaesthetist (and surgeon).
3. Anaesthetists should participate in developing formal institutional hip fracture care pathways, particularly with regard to preparation for theatre and pain management.
4. Anaesthetists should facilitate surgery within 48 hours of hip fracture.
5. Anaesthesia should be administered according to agreed standards at each hospital, using age-appropriate doses, with the aims of facilitating early patient remobilisation, re-enablement and rehabilitation.
6. Anaesthetists should routinely participate in standardised perioperative data collection about hip fracture patients, focussing on commonly agreed outcomes in the early (<5d) postoperative period.
7. All junior anaesthetists should receive specific training on how to administer anaesthesia to hip fracture patients.

Why was this consensus statement developed?

Globally, the number of hip fractures is expected to double from ~2.2 million to ~4.5 million between 2017 and 2050 [1]. For the purposes of analgesia and remobilisation, ~ 99% of hip fractures should be fixed surgically, requiring anaesthesia. Whereas surgery for hip fracture has become increasingly standardised, but peri-operative medical and anaesthetic care varies considerably. Perioperative morbidity and mortality remain high. Guidelines concerning the anaesthetic management of patients with hip fracture exist [2-7], but are (Western) nation/healthcare system specific. As no other international guidelines exist, this consensus statement advises basic standards of anaesthetic care that hip fracture patient should expect to receive in any country, regardless of resources.

How was this consensus statement developed?

Established in 2011, the Fragility Fracture Network (FFN) is an international organisation of multidisciplinary practitioners interested in improving and disseminating standards of care worldwide for fragility fractures (ie minimal force fractures of osteoporotic bone, mainly affecting older people); 'Anaesthesia' is a Working Group within this organisation. On behalf of the FFN, the current convenor of the Anaesthesia Working Group (SW) invited internationally recognised experts in hip fracture anaesthesia and national professional leaders

to contribute to a Consensus Committee; invitation was based on previous important publication authorship, current trial participation or identification of expertise by national anaesthesia organisations. Opinion was sought from all five continents; participation provided global representation with the exception of Japan, Russia, Pakistan or Turkey. Invitations were sent in November 2016, and acceptances completed by March 2017.

A three-stage Delphi process was used to reach consensus. During February and March, 2017 (stage 1), the 28 Committee members were asked to contribute by e-mail ~10-15 'broad' 'principles that every hospital anaesthetic service worldwide should aim to provide for patients undergoing surgery for hip fracture'. Four hundred and fifty-seven principles were received, which were categorized (by SW) according to 'phase' of anaesthesia (seven: pre-operative/intra-operative/postoperative/peri-operative/organizational/research/training) and 'theme' (eg 'anaesthesia type', 'patient communication' etc); 33 themes were identified. Each principle was allocated to a theme, unless it didn't relate to either any aspect of anaesthesia care or anaesthesia specifically for hip fracture.

In April, 2017 (stage 2), 47 statements were formulated from the 33 themes. To distinguish consensus in 3 contentious areas (within what time horizon should surgery take place after fracture, what type of anaesthetic modality (spinal/general) should be preferred for hip fracture surgery, should preoperative laboratory tests be ordered by protocol or patient examination), more than one statement was formulated. A similar rationale was used to formulate a multichoice statement determining expert consensus about acceptable intraoperative blood pressure thresholds [8]. A small subcommittee of the Consensus Committee (SW, MMcB, MC, RG, NF, IM) deliberated the exact wording of each statement; 6 further statements were added to clarify consensus. A total of 53 statements were digitalized using an electronic survey platform (SurveyHero, enuvo GmbH, Zurich, Switzerland), and sent to the whole Committee in June, 2017, inviting completion. All statements were formulated to elicit binary 'yes/no' responses; if more than one variable was included in a statement, a 'yes' response was sought explicitly from Committee members only if they agreed with all the variables included. Throughout this process, Committee members were welcome to review the source principles and formulation process, and were reminded that their opinion 'should be based in part on what (they thought were) desirable and achievable principles of hip fracture anaesthesia in (their) country/geographical region'.

All 28 committee members responded to all statements. 'Consensus' was denoted by the same response from 21/28 (75% [9]) Committee members to binary questions (n=41/44 (93%), table 1), and by the most popular response to the four types of anaesthesia/time

horizon/blood pressure threshold/laboratory tests questions. These responses were grouped into 7 principles of anaesthesia for hip fracture, based on the 7 'phases' of anaesthesia identified in stage 1 of the process. This process enabled development of the first draft of this paper (Delphi stage 3), describing a narrative, sequential timeline of anaesthetists' involvement with hip fracture patients, rather than a ranked, non-contextual description of the consensus principles. Importantly, contemporary references were added to the paper to guide readers towards further reading, rather than to provide exhaustive documentation of the available evidence. The first draft of the paper was sent to Committee members in early August, inviting comments about the structure of the statements, their wording and further important references that should be included. One Committee member withdrew at this stage, to retain equipoise leading a trial they were conducting, but assented to continued use of their Delphi round 2 responses.

(Insert table 1 near here)

The Consensus statements were edited accordingly, and presented (by SW) at the 4th session ('Optimising peri-operative outcome') of the 6th Fragility Fractures Network conference in Malmo, Sweden on the 24th August, 2017. Committee members were invited to attend this session and make further comments, along with other delegates. Accordingly, the Consensus statements were edited further, before being redistributed to Committee members for final comments/approval. The draft was tabled during and approved by a Board meeting of the Fragility Fractures Network in October, 2017, and then submitted to *Anaesthesia*.

The Consensus principles

1. Anaesthesia is integral to the multidisciplinary care of hip fracture patients.

Committee members unanimously agreed that anaesthesia is integral to the multidisciplinary care of hip fracture patients, and overwhelmingly (93%) agreed that multidisciplinary care should be provided for all hip fracture patients, statements that are in line with professional guidance produced by the Association of Anaesthetists of Great Britain and Ireland (AAGBI) [2]. In fact, research needs to be undertaken to quantify the specific contribution of anaesthesia and anaesthetists to hip fracture patient outcome, in a similar way to that recently undertaken in cardiac surgery in the UK [10]. Compared to the impacts of surgery/trauma and orthogeriatric/rehabilitation [11-13], the contribution of anaesthesia *per se* might possibly be small, but the contribution of the anaesthetist as perioperative physician, responsible for

continuing the physiological/amalgesic support of older, frail, cognitively impaired hip fracture patients with co-morbidities and polypharmacy undergoing major, urgent surgery, is likely to be significant.

2. Anaesthesia (and surgery) for hip fracture surgery should be undertaken by an appropriately experienced anaesthetist (and surgeon).

Related to the first principle, the Committee recognised that appropriately experienced clinicians (rather than senior clinicians, necessarily) should determine hip fracture patient management, in line with other guidance [2, 3]. The Committee made no attempt to define 'experience', as this is inevitably dependent on the local context and available resources.

Although (again) confirmatory research is required, appropriately experienced anaesthetists are more likely to expedite surgery, recognise and manage appropriately the increased risk of surgery and anaesthesia for hip fracture patients, and tailor intra-operative and postoperative care towards patient recovery and rehabilitation, compared to less experienced anaesthetists who only occasionally administer anaesthesia for hip fracture surgery. Experienced anaesthetists, as patient representatives in the peri-operative period, can help ensure that surgical expertise is appropriate for the surgery undertaken, and that anaesthesia and surgery training occur during suitable cases only.

3. Anaesthetists should participate in developing formal institutional hip fracture care pathways, particularly with regard to preparation for theatre and pain management.

While fully respecting each hip fracture patient as an individual, the Committee recognised that much of the medical and surgical care necessary for recovery after hip fracture can be administered in a relatively standardised manner, individualised at an institutional level according to the personnel and facilities available. As members of the multidisciplinary care team, experienced anaesthetists should participate in developing specific hospital protocols within a formal, documented integrated care pathway, particularly those into which they have an input. Far from threatening professional autonomy or ignoring patient individuality, standardisation of care reduces the avoidable, unwarranted variations in care that hip fracture patients receive, improving safety and outcome [14].

Specific, anaesthesia-related protocols can be developed for all peri-operative phases of care. Pre-operatively, patients should be evaluated for other injuries (particularly head and chest injuries, and other fractures that may limit surgical positioning), and have their frailty and cognitive status assessed. These are associated with early postoperative complications,

such as delirium and poor remobilisation, leading to poorer outcome. The Committee favoured ordering further pre-operative tests on the basis of clinical examination (70%) rather than according to protocol (57%), although further research needs to be done to determine the clinical and financial impact of each approach. There was greater consensus about the need for rapid (<24 hour) access to echocardiography, although this test may not be available worldwide and it remains unclear as to its clinical benefit in hip fracture patients [15, 16].

Intra-operatively, a written protocol for the prevention, recognition and management of Bone Cement Implantation Syndrome should be used at every hospital using cemented hip prostheses [17, 18].

Postoperatively, nutritional supplementation should be encouraged as necessary after surgery, in response to the catabolic stress of hip trauma, surgery and recovery, in patients who may chronically malnourished and frail. Anaesthetists can facilitate this process by using drug therapy protocols and interventions to minimise postoperative nausea, vomiting, constipation and delirium [19, 20]. Nutritional supplementation should occur in addition to a patient's normal food and fluid intake.

Peri-operatively, anaesthetists should be involved in designing and implementing written hospital protocols for blood replacement. Hip fracture patients may be chronically anaemic, anticoagulated, lose blood through traumatic and surgical haemorrhage, and/or become haemodiluted if over-administered intravenous fluids. On average, hip fracture patients' [haemoglobin] falls by 25 $g.l^{-1}$ between sustaining the fracture and their first postoperative measurement (more so after total hip replacement). Specific protocols need to be in place for managing anticoagulation (including Novel Oral Anticoagulants (NOACs - dabigatran, rivaroxaban and apixaban), blood products and intravenous fluids, based on current guidelines [21]. Anaesthetists should ensure that [haemoglobin] is routinely measured in the first 24 hours after surgery, although there was no consensus among the Committee (50%) for measuring [haemoglobin] in the recovery room after anaesthesia.

Perhaps of greatest importance to patients, the Committee recommend that anaesthetists develop and implement a comprehensive analgesia protocol, incorporating regular paracetamol (acetaminophen) administration [22], nerve blockade [23] and the minimisation of intravenous opioids, to be followed from the time of injury to the time of discharge. Although pain itself promotes delirium, doses of appropriate intravenous opioid analgesics should be titrated to effect with regard to the patient's age, renal function and comorbidities. Non-steroidal anti-inflammatory drugs (NSAIDs), tramadol, codeine, (and cyclizine and sedative premedication) should be used with extreme caution in hip fracture

patients.

Organisationally, the Committee fully endorses the involvement of patients, families and carers in treatment decisions. In relation to this, a clear decision about the patient's resuscitation status should be recorded before surgery. Such decisions should be informed by using a validated, hip fracture-specific risk stratification tool, such as the Nottingham Hip Fracture Score (NHFS, although this score requires validation in non-UK populations) [24-26]. Routine risk stratification should also be used pre-operatively to identify high-risk patients who may require critical care facilities (which should always be available at hospitals undertaking hip fracture surgery).

4. Anaesthetists should facilitate surgery within 48 hours of hip fracture.

Committee members agreed unanimously that hip fracture surgery should be delayed only if the benefits of additional medical treatment outweigh the risks of delaying surgery, with two-thirds agreeing that surgery should take place within 48 hours of admission after fracture. This is broadly in agreement with UK [2, 3, 7, 27], US [4] and Australian [5] recommendations, and supported by evidence from two large meta-analyses [28, 29]. Committee members disagreeing with a 48-hour time horizon correctly noted that this might not be achievable in countries with a relative lack of available resources.

The results of the multicentre, multinational HIP ATTACK trial [30], which aims to compare outcomes among hip fracture patients randomly allocated to receive either accelerated (<6 hour) or standard surgery, should provide further information about the timeframe within which patients can be safely be operated on.

Regardless, consensus indicated that surgery should be available 7 days a week, ideally within core working hours (although some Committee members noted again that resources might not be available to achieve this). There was strong consensus that surgical list order should prioritise older, frailer and sicker patients.

Anaesthetists have a crucial role to play in resolving the organisational and medical obstacles to timely hip fracture surgery, by allocating experienced personnel appropriately, communicating within the multidisciplinary team, developing peri-operative protocols and pre-operative information that facilitate early surgery, monitoring reasons for delay and/or cancellation, and training junior personnel.

5. Anaesthesia should be administered according to agreed standards at each hospital, using age-appropriate doses, with the aims of facilitating early patient remobilisation,

re-enablement and rehabilitation.

The actual process of anaesthesia is only one component of anaesthetists' involvement in the care of patients with hip fracture, and yet often the most controversial. Much of the limited prospective research into anaesthesia for hip fracture surgery has focussed on whether spinal or general anaesthesia promotes improved patient outcome [31, 32]. Similarly, retrospective observational research has been unable to find any consistent, significant differences in patient outcome associated with either spinal or regional anaesthesia [33-41]. There may be any number of reasons for this, including prospective research to date involving patients that are unrepresentative of the hip fracture population [14, 42], the outcomes commonly measured to date (30-day/inpatient mortality, length of hospital stay) being temporally and/or causally relatively unaffected by anaesthesia (compared to the effect of surgery, for example) and the terms 'spinal' and 'general' referring to the remarkable heterogeneity of techniques actually employed, between which it is impossible to determine 'the best' [43]. The ongoing Regional versus General Anaesthesia for promoting Independence after Hip Fracture international, pragmatic multicentre randomised controlled trial of 1600 hip fracture patients overcomes many of the methodological problems of such research, and will provide strong evidence of 'real world' comparative patient benefit between either regional or general anaesthesia [44].

The Committee's preferred recommendation, that either regional or general anaesthesia should be offered to patients, reflects current evidence, although it is worth noting that no Committee member agreed that general anaesthesia was usually preferable to regional anaesthesia. The Committee's recommendation reflects UK and US guidelines [2-4]; regional anaesthesia is recommended for most patients in Australian guidelines [5].

Committee consensus is consistent with UK, US and Australian guidelines in recommending that nerve blocks (femoral, fascia iliaca, epidural, lumbar plexus, quadratus lumborum) should be routinely administered to supplement either spinal or general anaesthesia [2-7].

There was consensus among Committee members that standards of anaesthesia should be agreed by senior anaesthetists at every hospital treating hip fracture patients [14], particularly in relation to how drugs were administered to the older, frail, hip fracture patients with co-morbidities and polypharmacy. Committee members agreed that the depth of general anaesthesia should be adjusted according to the patient's age or monitored brain activity [45, 46]. Consensus was not quite reached about recommending the same for sedation co-administered with spinal anaesthesia, where verbal contact was thought more beneficial than

monitoring brain activity (despite some evidence to the contrary [47, 48]), although Committee members agreed that supplemental oxygen should be considered for all patients undergoing regional anaesthesia with sedation.

Other standard operating procedures recommended by the Committee include the routine consideration of invasive blood pressure monitoring during anaesthesia for higher risk hip fracture patients [2], and the monitoring/maintenance of patient core temperature in the perioperative period [3].

There was overwhelming consensus that blood pressure should be carefully monitored and maintained in hip fracture patients during the perioperative period, the Committee collectively preferring relative rather than absolute thresholds above which blood pressure should be maintained intra-operatively, with ~ 50% preferring a systolic or mean arterial pressure within 20% of the pre-induction/spinal equivalent measurement. Recent evidence suggests that lower intra-operative blood pressures are associated with higher postoperative mortality in elderly patients [49] and hip fracture patients [39], possibly related to ischaemic organ dysfunction, most notably of the brain [45, 50, 51], myocardium [52] and kidneys [53-55].

Implementing these recommendations is consistent with achieving the two fundamental aims of conducting anaesthesia for hip fracture patients (that were submitted as principles and agreed by the Committee), namely the limitation of postoperative delirium (and maintaining pre-operative cognitive trajectory [56, 57]) and the facilitation of early (ie day 1) postoperative remobilisation and re-enablement, both of which are associated with reduced mortality and increased rates of rehabilitation (ie discharge to normal place of residence) [57, 58].

6. Anaesthetists should routinely participate in standardised perioperative data collection about hip fracture patients, focussing on commonly agreed outcomes in the early (<5d) postoperative period.

Quantifying improvements in hip fracture outcome brought about by standardising care in various healthcare systems has only been possible by collecting accurate, routine process and outcome data [59].

The Committee recommend that hospitals should routinely monitor outcome data for hip fracture patients and compare their data with other hospitals in their country, and internationally. Anaesthetists who routinely manage hip fracture patients should participate in data collection, as well as audit, research and quality improvement of their own and their

institutional practice [60, 61].

As alluded to above, the anaesthesia may exert its greatest effect on patient outcome in the early (<5d) postoperative period, and so the Committee agree that research into anaesthesia for hip fracture surgery should focus on commonly agreed outcomes that occur in this period, including mortality, analgesia, delirium and remobilisation. A core outcome set for peri-operative studies on hip fracture patients is currently being developed in Northern Ireland using a Delphi process among international collaborators, which should facilitate future research meta-analysis between institutions, and internationally [62].

7. All junior anaesthetists should receive specific training on how to administer anaesthesia to hip fracture patients.

Given the increased longevity of patients globally, training in geriatric anaesthesia - specifically orthogeriatric anaesthesia – requires more frequent and comprehensive future training than is offered by current curricula [63, 64]. Anaesthetists with a specialist interest should arrange specific training programmes in orthogeriatric anaesthesia, and professional bodies/institutions should arrange for trainee anaesthetists to undertake further specialist training or higher degrees in geriatric anaesthesia, focussing on the perioperative care of the high risk older patient undergoing emergent surgery, particularly anaesthetic strategies aimed at re-enabling the patient in the early postoperative period by avoiding complications such as hypotension, pain and confusion [65, 66].

The Consensus Committee accept that the recommendations above may require further resource input, but have been careful to propose changes that are mainly attitudinal or organisational, and achievable with minimal resource (re)allocation, but which have been shown to have the most cost-efficient impact on patients' care by streamlining recovery from fall to rehabilitation. We also accept that Consensus opinion forms as much a part of the recommendations above as does published evidence. Without doubt, there are many avenues for important research still to explore. The recommendations should be read as a baseline level of service provision worldwide, but one that challenges anaesthetists caring for this older, frail and vulnerable patient population to collect and publish evidence that improves future iterations of this statement.

Funding and conflicts of interest

SW is Convenor of the Anaesthesia Working Group of the Fragility Fractures Network, a member of the Association of Anaesthetists of Great Britain and Ireland (AAGBI) Hip Fracture Guidelines Working Party, sits on the Scientific and Publications Committee of the National Hip Fracture Database and the NIAA Grants Committee, and is an Editor of *Anaesthesia*. This manuscript has therefore undergone additional external review. DD is member of the REGAIN trial group, and receives funding on a recruited patient basis. NF is a member of the International Advisory Panel of *Anaesthesia*. RG chaired the AAGBI Hip Fracture Guidelines Working Party and founded the Hip Fracture Perioperative Network. He is also Honorary Secretary of the AAGBI. IMo is a member of the NICE topic expert group for Quality Standards for hip fracture, a member of the National Institute of Academic Anaesthesia (NIAA) Research Council and holds grants from the National Institute for Health Research and the Association of Anaesthetists of Great Britain & Ireland and Royal College of Anaesthetists through the NIAA for trials in hip fracture. CS's Doctoral research fellowship is funded by the National Institute for Health Research. FS is a leader of the clinical operations subcommittee for the REGAIN trial group, and receives funding on a recruited patient basis. FA, JB, BB-B, FC, MC, MD, AG, GK, J-HK, MK, P-WL, IMa, MMcB, SMcM, LMP, MP, OP, RS, AT and XX have no conflicts of interest.

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Table legend.

Table 1. Consensus committee responses to whether 52 binary ('yes/no') and 1 multiple choice statements should be included in final consensus statement. 'Consensus' was denoted by the same response from 21/28 (75%) Committee members to binary questions, and by the most popular response to the four types of anaesthesia/time horizon/blood pressure threshold/laboratory tests questions.