■ INSTRUCTIONAL REVIEW: TRAUMA

When is the ideal time to operate on a patient with a fracture of the hip?

A REVIEW OF THE AVAILABLE LITERATURE

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Fractures of the hip are common, often occurring in frail elderly patients, but also in younger fit healthy patients following trauma. They have a significant associated mortality and major social and financial implications to patients and health care providers. Many guidelines are available for the management of these patients, mostly recommending early surgery for the best outcomes. As a result, healthcare authorities now put pressure on surgical teams to 'fast track' patients with a fracture of the hip, often misquoting the available literature, which in itself can be confusing and even conflicting.

This paper has been written following an extensive review of the available literature. An attempt is made to clarify what is meant by early surgery (expeditious *versus* emergency), and we conclude with a personal view for the practical management of these patients of variable age, fitness and type of surgery performed within services that are often under considerable pressure of finance and available operating theatres and qualified staff.

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The annual incidence of fractures of the hip worldwide is about 1.3 million.[1] In the United Kingdom this incidence is about 75 000,[2] costing an estimated £2 billion,[2] with numbers projected to increase to more than 100 000 by 2020.[3]

High quality of care for patients who sustain a fracture of the hip should save both lives and money, shorten hospital stay and result in fewer patients subsequently requiring social housing.[4] Even with optimal care, however, about 10% of patients die within 30 days and one-third within 12 months of the injury.[2]

What then, is 'ideal management' and, in particular, when is the ideal time to operate on these patients?

Recently, the National Institute for Health and Care Excellence (NICE),[2] the British Orthopaedic and Geriatric Associations[5] and the Association of Anaesthetists of Great Britain and Ireland,[6] have proposed "early" intervention for patients with a fracture of the hip. Early surgery was defined as that being performed on the day or day after admission[2,5] or within 48 hours of admission).[6] Other national guidelines around the world support this 'early' approach (Table I).[2,5-13]

An early operation would seem logical for a painful condition that leads to immobility, venous stasis, thrombosis and pressure sores. However, as most fractures occur in elderly patients with significant comorbidities, a short delay would seem logical to improve reversible comordities and/or delayed until senior staff are available to operate during office hours as suggested in the United Kingdom by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD).[14,15]

This article includes an extensive review of the literature identified by Medline and Pubmed without a minimum age criteria, to clarify the ideal time to operate on a patient with a fracture of the hip. Articles were evaluated according to whether they advocated expeditions surgery, delayed surgery and then if they included national and provincial data, or were meta-analysis and systematic reviews, and randomised trials; the authors conclude with their personal interpretation of these data. This review is intended to offer the busy surgeon evidence-based reasoning for the timing of surgery for patients with a fracture of the hip.

The evidence advocating early surgery

A study from the United Kingdom in 2015 by Bretherton and Parker[16] reviewed the 30-day mortality for 6638 patients with a fracture of the hip, aged > 60 years, collected prospectively over a 24-year period. The authors concluded that the American Society of Anesthesiologists (ASA) grade was the strongest predictor of the 30-day mortality, along with increasing age and the presence of an extra capsular fracture. Delay to surgery was divided into seven categories

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Table I. National guidelines for the management of a fracture of the hip including recommended time to surgery

Country	Organisation	Date of publication or update	Recommendation
United Kingdom	National Institute for Health and Care Excellence[2]	2014	Perform surgery on the day of, or the day after admission.
United States	American Academy of Orthopaedic Surgeons[7]	2014	Moderate evidence supports that hip fracture surgery within 48 hrs of admission is associated with better outcomes.
Canada	Health Quality Ontario & Ministry of Health and long term care[8]	2013	Surgery should be performed as early as possible, not to exceed 48 hrs of initial presentation.
United Kingdom	British Orthopaedic Association and British Geriatric Society[5]	2012	Perform surgery on the day of or the day after admission on a planned trauma list.
United Kingdom and Ireland	Association of Anesthetists of Great Britain and Ireland[6]	2012	Surgical repair of hip fractures should occur within 48 hrs of hospital admission.
Canada	National Hip Fracture Toolkit[10]	2011	Ensure patients get their surgery no later than 48 hrs or 2 days after their admission to the first emergency room.
Australia & New Zealand	Australia and New Zealand Society for geriatric Medicine[11]	2011	Definitive surgery, if required, should be arranged as soon as possible (within 24 hrs). Few patients will have a medical contraindication to surgery.
Australia	The Medical Journal of Australia[12]	2010	Early surgery (within 24 to 36 hrs) is recommended for most patients once a medical assessment has been made and the patient's condition has been stabilised appropriately.
Scotland	Scottish Intercollegiate Guidelines Network[13]	2009	Surgery should be performed as soon as the medical condition of the patient allows, provided that appropriate staffing and facilities are available.
New Zealand	New Zealand Guidelines Group[14]	2003	Early operation (within 24 hrs) for people aged 65 yrs and over with hip fracture is associated with shorter hospital stay and decreased mortality/morbidity.

(less than six hours from admission, between seven and 12 hours; up to between 49 and 72 hours) but excluded patients delayed beyond 72 hours and those with correctable medical conditions as recognised within NICE guidance[2] such as anticoagulation or uncontrolled diabetes. In these relatively fit patients, surgery within 12 hours of admission significantly reduced short-term mortality ($p < 0.013$), but there remained "considerable clinical equipoise", that is, genuine uncertainty, regarding the ideal pre-operative interval.[16]

Another paper supporting this view, from 2013,[17] concluded that surgery within 12 hours reduced the early post-operative mortality. The authors analysed 2056 patients with a fracture of the hip, with a mean age of 81 years (21 to 105) with delay to surgery analysed within six 12-hour time frames up to 72 hours. A total of 100 patients underwent surgery within 12 hours of admission. The early mortality increased with age, male gender, in those who sustained their fracture whilst an inpatient and ASA grade. Furthermore, surgery undertaken in < 12 hours resulted in an early rate of mortality of 3.9 times less than in those for whom surgery was undertaken > 36 hours after admission ($p < 0.05$). In contrast to the review of Bretherton and Parker,[16] there was no minimum time to surgery which failed to confer a survival benefit up to 72 hours but for every 24 hour wait for surgery there was a 1.1-fold increase in the odds of in-hospital mortality.

In 1992, a prospective review[18] studied similar patients but with delay from injury to surgery rather than admission. From an initial cohort of 765 patients, 468 were studied, with time of surgery divided into four periods; < 24 hours, 24 to 47, 48 to 72 and > 72 hours. All were followed up for one year. There was no significant difference in outcome between the groups, but surgery within 47 hours reduced the incidence of pressure sores and showed a trend towards an increased stay in hospital and risk of pulmonary embolism. Earlier surgery increased the incidence of confusion but mortality was not significantly different.

In 2015 a 14-month prospective multicentre study from Italy evaluated 568 patients aged > 50 years[19] with low energy fractures. The authors compared results at four months and one year for early surgery (< 72 hours) with delayed surgery (> 72 hours, 43% of patients). Again, delay did not influence mortality but reduced the risk of complications and length of stay in hospital.

A prospective review from Belfast of 1780 patients admitted over a two year period, which was published in 2003,[20] attempted to identify prognostic factors for outcomes. 'Delay' was defined as surgery > 48 hours from injury. Increased mortality at 12 months was associated with male gender, increasing age, ASA grade, lower activity scores and a longer pre-operative delay. It was concluded that, by using a 'mortality score', one additional survivor could be yielded if eight medium risk or 17 high risk candidates received their surgery within 24 hours.

A retrospective study by Lefaivre et al[21] was published in 2009 and involved 607 patients aged > 65 years over a four year period. Time to surgery was divided into < 24 hours,

24 hours to 48 hours and > 48 hours from injury. Increased time to discharge was significantly related to surgical delay, comorbidity, increasing age and the type of fracture. Surgical delay however, but did not increase the risk of early mortality. Delay to surgery of > 48 hours, however, doubled the risk of the development of major complications and pressure sores.

In 2003, another retrospective review evaluated 651 consecutive patients with a fracture of the hip, aged > 60 years, admitted over a three-year period.[22] Significantly, 123 patients died during the first post-operative year, 54 with operations undertaken < 48 hours of injury and 69 after this time. This difference was significant (p = 0.00035) with delay beyond 48 hours being a significant risk for one-year mortality (p = 0.012). Unlike the study by Lefaivre et al,[21] there was no association between the development of major complications and delay to surgery. Survival curves from 12 to 24 months were similar in those patients operated on before and after 48 hours. Despite this, they concluded that every effort should be made to operate within 48 hours of admission.

Finally two further studies purported to show an advantage for operation within two days of admission.[23,24] The first from Zuckerman et al,[23] reported a three-year prospective review of 367 patients aged > 65 years. Surgery performed 'three calendar days or more' after admission was considered delayed and occurred in 100 patients (27%). At 12 months, of 355 patients, 51 died (14%) and delay beyond two days doubled the risk of mortality at one year (p = 0.05).

The second paper published in 2011,[24] retrospectively estimated the effect of delay on 30-day mortality following fracture of the hip. This review identified 1320 patients with a mean age of 83 years. A total of 746 underwent surgery within two days of admission (defined as early) and the overall 30-day mortality was 3.5% compared with surgery undertaken after two days which resulted in a two-fold increase in 30-day mortality (2.4% *versus* 4.9%).

Delayed surgery- the evidence

Although few surgeons would tolerate an unnecessary delay to surgery, all patients require pre-operative assessment and the management of risk factors, and the timing of surgery depends on the availability of an appropriate operating theatre and personnel. Furthermore, total hip arthroplasty (THA) is gaining popularity in the management of some fractures and the wait for a specialist surgeon might also cause a delay. A number of authors have also published studies suggesting that a short delay prior to surgery does not cause harm and may in fact be of benefit to the patient.

One such paper involved 2660 patients with a mean age of 80 years, who underwent surgery for a fracture of the hip, over a four year period.[25] A total of 2148 were declared "fit" for surgery on admission. Those who underwent surgery within 48 hours had a 30-day mortality of 8.7%, those whose surgery was delayed by between one and four days due to the lack of an operating theatre had a mortality of 7.3% (p = 0.51). In 28 patients, in whom surgery was delayed beyond four days, mortality increased to 10.7% (p = 0.001) and remained elevated at 90 days and one year follow-up. Those patients with an acute medical problem who were deemed unfit for surgery on admission, requiring delay, had an increased 30-day mortality of 17.5%, which persisted to one year (43% *versus* 28%). Within this sub-group there was no relationship between the timing of surgery and mortality at one, three or 12 months suggesting there was no optimal time to operate. A total of 294 patients who presented more than one day after injury had a significantly increased risk of mortality. It was concluded that although delay should be avoided, a delay of up to four days did not significantly increase morbidity or mortality in patients who did not have significant medical comorbidity.

Another study in 2004[26] failed to identify reduced mortality for surgery undertaken within 24 hours. Here, 1206 patients from four North American hospitals over a 29-month period were reviewed. Early surgery (< 24 hours) resulted in fewer days of severe pain and a shorter length of stay in hospital (two days) but did not alter mortality.

These conclusions were supported by a prospective review of 3628 patients admitted over a 15-year period.[27] In this article, patients aged < 60 years and those requiring a delay for medical reasons were excluded. The rate of mortality for those treated within 48 hours was 6.9% and beyond 48 hours 13.8%. After adjusting for ASA, mental score and mobility score, no influence could be identified on the rate of mortality or the destination of discharge.

Similar conclusions were recorded in a prospective review of 222 patients, aged > 50 years admitted to an Australian hospital.[28] A total of 120 planned operations were cancelled; this involved 84 patients, due to an operating theatre not being available (58%) and patients being unfit (33%). The overall 30-day mortality was 7.2%. The rate of mortality was 5.8% for those whose operation was undertaken within two days and 9.4% for those with a delay beyond this time. Although this difference was not statistically significant (p = 0.3), increasing ASA score and fractures treated with arthroplasty (80 hemiarthroplasty, two THAs) were found to be significant predictors of 30-day mortality.

Another retrospective study of 8383 patients with a fracture of the hip again found no association between surgery undertaken between 24 and 48 hours compared with surgery undertaken > 96 hours after admission, with adjusted short- and long-term mortality (up to 18 years).[29] The risk of the development of a pressure sore was, however, increased when surgery was delayed.

An unusual Spanish study reviewed patients with delayed surgery of more than one week due to fire damage to their hospital (n = 109).[30] This group of patients was compared with a prospectively studied group undergoing surgery within 48 hours or as soon as medically stabilised

(n = 79). Higher rates of pressure sores, urinary tract infections and deep vein thromboses and longer stays in hospital were identified in the delayed group but there was no significant difference in the rate of mortality at either three months or one-year follow-up.

A retrospective review from the Netherlands of 229 patients studied for two years[31] failed to identify an increased rate of mortality at one year with delay to surgery beyond one day. However, subgroup analysis of patients with ASA scores of 1 or 2 had a significantly increased rate of mortality at one year but delays for patients with ASA scores of 3 or 4 allowed optimisation and appeared to counterbalance any deleterious effect of such delays.

A further two frequently referenced papers warrant mention. Kenzora et al[32] and Mullen and Mullen[33] have suggested potential harm in proceeding with surgery within 24 hours of admission. Kenzora et al[32] published a six year retrospective analysis of 406 patients with a fracture of the hip with a minimum follow-up of one year or death. A total of 96 patients underwent surgery within 24 hours of admission with a rate of mortality at one year of 34%, whereas those undergoing surgery between two and five days after admission, showed a rate of mortality of 5.8%. Even removing all patients with four or more medical comorbidities revealed persistent significant differences in the rate of mortality: 28% and 4% respectively. Similarly Mullen and Mullen[33] reviewed 400 consecutive patients with a fracture of the hip. In total, 60 were deemed acutely ill on admission. The rate of mortality at one year for those patients undergoing surgery within 24 hours was 88% (7 of 8), and between 24 hours and 72 hours was 52% (21 of 40), and there were no deaths in those with a delay beyond three days (0 of 12). Thus, both of these reviews advocate a period of medical stabilisation prior to surgery.

The evidence from large national data sets

A Canadian seven-year review[34] of 57 315 patients identified an increased rate of mortality whilst in hospital with delayed surgery. The authors reported a 13% increase in the risk of mortality for every day of delay. Interestingly, this relationship was greatest for patients aged < 70 years without comorbidities.

Similarly, a three-year study from the United Kingdom reviewed 129 522 patients with a fracture of the hip and identified a similar increased risk of mortality for each day of delay.[35] Inclusion criteria were patients aged > 65 years, who were admitted from home. The unadjusted rate of mortality was 39% greater for those whose surgery was delayed beyond one day and 60% if it was delayed by more than two days. Not surprisingly, the worst rate of mortality was for those patients for whom 'no operation' was recorded.

A Scottish Hip Fracture Audit from 2008, included 18 817 patients and examined mortality at 30 and 120 days.[36] Case mix and management variables including time between injury and surgery and the grade of surgical and anaesthetic staff, were analysed. Of the latter, only the grade of anaesthetist appeared to have any significant association with the rate of mortality. Neither the time between the injury and surgery nor the time between admission and surgery significantly affected the rate of early post-operative mortality. Further review of the data was published in 2010.[37] For an 11-month period, in addition to core data, information about the delay of surgery was collected. It was found that, for 4284 patients, a major comorbidity was associated with an operating delay and lower unadjusted 30-day survival, but after case-mix adjustment time to operation was not associated with an increased 30-day mortality. Furthermore, postponement of surgery without correction of a medical abnormality resulted in a higher post-operative rate of mortality at 30-days ($p = 0.006$) compared with postponement with correction, which improved the adjusted 30-day survival, although this did not reach significance ($p = 0.10$).

A review from the United States in 2014[38] studied 9286 fractures with a rate of mortality whilst an inpatient of 4.5%, and 12.5% of patients suffering at least one complication. A total of 17.5% of those who had at least one complication subsequently died. A delay of two days to operation was identified as an independent risk factor for developing a complication and this, potentially modifiable, delay had a two-fold increase in odds for the development of a major complication including renal, venous thromboembolic disease and infection.

In a 'pseudo-randomisation' study from the United States involving 18 209 Medicare patients,[39] it was found that those admitted on the weekend were more prone to delay than those admitted during the week. This delay was used as an independent variable and analysed with techniques traditionally used by economists. Patients admitted on Sunday and Monday had a 15% increased rate of 30-day mortality compared with those admitted on other days. The authors accepted the limitations of this study as issues beyond delayed surgery confounded 'weekend admissions'.

These retrospective reviews using large national and regional datasets have identified some benefit for early surgery. Conclusions, however, need to be viewed with caution as they frequently contain limited information particularly regarding the characteristics of the patients and the reasons for delay. They also ultimately rely on the data from individual hospitals, which are recognised to be of variable quality.[40] Increased mortality with surgical delay may merely reflect the fact that patients whose general health is poor, require optimisation before surgery. Large datasets seldom contain all the relevant confounding factors.[41,42]

The evidence from systematic reviews and meta-analysis

A Canadian meta-analysis of 16 prospective observational studies including 13 478 patients concluded that earlier surgery, undertaken between 24 hours and 72 hours after either injury or admission, was associated with a significant

reduction in mortality, pressure sores and pneumonia.[43] The delay was recorded as the time from injury to surgery in five studies, and the time from admission to surgery in the remaining 11 studies. The reason for delay was available in only eight studies, and included unavailability of operating facilities or surgeon and/or medical optimisation. With unadjusted crude data, early surgery resulted in a reduction of the rate of mortality of 45% at one year. However, removing a single study evaluating only the medically ill patient, resulted in a significant improvement in the rate of mortality at both three and six months. Adjustment for age, gender and ASA score was possible in only five papers (n = 4208) with early surgery (between 24 hours and 72 hours) associated with a 19% risk reduction in all cause mortality irrespective of time of assessment at 30 days, six months or one year. The authors conceded that further prospective studies are required, particularly to identify differences between medically fit and unfit patients.

Khan et al[44] reviewed 52 studies including 291 413 patients with a fracture of the hip and concluded that early surgery was associated with a reduced stay in hospital but there were conflicting results for mortality and morbidity with delay to surgery. Although the definition of 'early' varied between studies, usually being between one and two days, there were no adverse outcomes following early surgery. It was concluded that although delay might not affect the rate of mortality, it did appear to increase morbidity, particularly bed sores, and the stay in hospital.

A meta-analysis published in 2008[45] involved 16 retrospective and prospective observational studies and included 257 367 patients. The authors concluded that surgery which was delayed beyond 48 hours increased the rate of mortality by 41% at 30 days and 32% at one year. Early surgery benefited younger low risk patients. Lastly, patients with comorbidities were more likely to require investigation and optimisation before surgery, and these patients were more likely to die.

Another meta-analysis, from 2012[46] involved 35 prospective and retrospective studies including 191 873 patients and showed a lower risk of mortality if surgery was performed within 24 hours to 48 hours of admission. Delay significantly increased the risk of mortality and pressure sores. The authors accepted that the studies which were included were widely diverse and their conclusions were to be seen as 'strongly suggestive', not conclusive. Furthermore, as elsewhere, the definition of 'early'/'optimum' surgery varied widely, from six hours to up to 72 hours, with healthy patients referred 'without hesitation' for surgery. The authors concluded that administrative delays were unjustifiable but that there should not be a 'race against time' and most patients should be operated on within one to two days.

A further two systematic reviews are worthy of reference, despite the fact that they did not directly evaluate the time to surgery but examined variables that may influence the rate of mortality.[47,48] Both studies concluded that increasing mortality was related to the increased age of the patient, male gender and reduced pre-fracture function and cognitive impairment. Interestingly, the timing of surgery was not identified as a major predictor or included within the reported seven factors offering moderate evidence or 12 factors offering limited evidence of being a predictor of mortality.

Randomised trials – the evidence

A major criticism for the above meta-analyses and systematic reviews is the heterogeneity of the studies and the paucity of high quality prospective data, particularly randomised controlled studies. Almost all patients with a fracture of the hip require surgery to survive, thus randomised studies are impossible to justify particularly if it prolongs pain and suffering. A total of two such studies have, however, been published and addressed this issue by offering expeditious surgery *versus* standard care.[49,50]

The first, by Swanson et al in 1998,[49] involving 71 patients, aimed to determine if intervention (early surgery, minimal narcotic agents and intense daily therapy with a multidisciplinary approach) within 48 hours *versus* 'routine hospital management' reduced the length of stay in hospital. This was achieved in 90% of the intervention group but also in 80% of the controls. Time to discharge was reduced for the 'intervention group' with median discharge of 17 days *versus* 21 days for the controls.

The second randomised trial included patients from both India and Canada.[50] Rather surprisingly, the authors modelled the timing of emergency care for patients with a fracture of the hip on the proven benefit of thrombolysis within six hours for patients with a myocardial infarction. The study therefore compared standard treatment for patients with a fracture of the hip (standard group) with surgery being undertaken within six hours of admission (accelerated group). Patients aged > 45 years were randomised on admission to undergo surgery within or beyond this period of time. There were 30 patients in each group. For practical reasons, only one patient per day could undergo 'fast track' surgery, on the next available elective operating list. The delayed elective patients would then receive surgery out of hours. At the start of the study all patients received medical clearance within two hours of admission but after the recruitment of 11 patients it became clear that this early medical clearance was accelerating care to both the treatment and control groups. The protocol was therefore amended during the trial with control patients no longer receiving accelerated medical care.

Although patients were from both India and Canada no sub-group analysis was available for these two different health services or the grade and experience of the surgeon. Despite this limitation, it was reported that a major perioperative complication occurred within 30 days for nine patients in the accelerated group and 14 patients in the control group (in whom the mean delay to surgery was 24.2 hours (11.1 to 29.5) with median length of stay in hospital being 9.5 days (interquartile range (IQR) 8 to 17) and 12 days (IQR 7 to 17) respectively.

Table II. Predictive subgroup analysis for American Society of Anesthesiologists (ASA) grade

Author	ASA	Measure of outcome	p-value/hazard ratio for death prediction
Zuckerman et al (1995)[23]	3:4	Death	< 0.001
Grimes et al (2002)[29]	4:5	Death	Hazard ratio 3.02x
Gdalvich et al (2004)[22]	3:4	Death	< 0.0001
Verbeek et al (2008)[31]	3:4	Benefit for delay	Not given
Rae et al (2007)[28]	Higher ASA	Increase 30-day mortality	< 0.008
Holt et al (2008)[36]	Higher ASA	Increased mortality	< 0.001
Carretta et al (2011)[24]	Higher ASA	Predictive for 30-day mortality	Hazard ratio 2.6x
Mariconda et al (2015)[19]	Higher ASA	Death within 12 mths	< 0.001
Elliott et al (2003)[20]	Higher ASA	Death within 12 mths	< 0.001
Bretherton and Parker (2015)[16]	Higher ASA	Mortality	< 0.001
Uzoigwe et al (2013)[17]	Higher ASA	Mortality	< 0.0001

Table III. Predictive sub-group analysis for "pre-operative co-morbidities"

Author	Comorbidity	Measure of outcome	p-value
Kenzora et al (1984)[32]	0 to 3 comorbidities, 4 to 6	11% mortality, 25% mortality	< 0.0004
Elliott et al (2003)[20]	Increased 'comorbidity score'	Hospital discharge delayed and increased mortality	Not stated
Bottle and Aylin (2006)[35]	Ischaemic heart disease and failure	Increased mortality	Not stated
Holt et al (2010)[37]	Effective optimisation, no improvement	Improved survival, increased mortality	Not stated

Detailed subgroup analysis for predictive indicators of mortality and morbidity review

Within our review of the literature there is considerable variation in practice and little evidence-based data to help the busy surgeon, often working in an environment of stretched financial budgets, to decide on the ideal time for surgery for patients with a fracture of the hip. Furthermore, from this review, a single policy dictating this period of time is an impossible objective for all these patients. Despite this, there is considerable pressure from authoritative groups to recommend early surgery for all patients, and not to do so is difficult to defend.

One paper, often quoted to support early operation (within 24 hours to 48 hours) by Perez et al,[51] examined post-mortem reports for a large series of patients who had sustained a fracture of the hip. The authors concluded that the principal causes of death were bronchopneumonia, cardiac failure, myocardial infarction and pulmonary embolism. It was noted that these deaths were significantly associated with delayed surgery. Although initially this seems to support a policy of early surgery, these are the patients who, without a delay for improvement of their comorbidities, have an even higher morbidity and rate of mortality. It seems illogical to suggest that death due to bronchopneumonia and cardiac failure are useful predictors for the rate of mortality as most patients die from these conditions and these causes of death are certainly not specific to patients who have a fracture of the hip.

In order to address this question in more detail, we have re-reviewed the papers in this study to search for indicators of significant predictive value for mortality and morbidity in these patients. The ASA score seemed appropriate particularly since 'the ASA is a global measure of health which is validated, ubiquitous and easily reproducible for different patient cohorts'.[52] It has been further validated by Uzoigwe et al[17] to be a 'potential predictor of general in hospital mortality' with a significance of $p < 0.0001$.

We found that the ASA score was often recorded in the studies included in this review, and in some its accuracy for predicting mortality and morbidity was quoted. Less frequently quoted were other pre-operative scores of morbidity of the patients. Tables II and III summarise these data and the predictive significance for the development of complications post-operatively including mortality.

Discussion

With such a large amount of complicated and variable data, when is the ideal time to operate on a patient with a fracture of the hip, in the ideal patient, within ideal hospital conditions, with staff who are optimally trained to do it and lastly not too tired to undertake the surgery? Quite obviously, there is no such patient, circumstance, hospital or staff available at all times.

The typical patient is often frail, admitted a significant time after injury, with potential pressure sores, possible underlying osteoporosis, cardiac and renal abnormalities, cognitive disorders and not infrequently on long-term anticoagulation. Furthermore, a fracture of the hip is not a single entity. It is better described as a proximal femoral fracture involving all fractures of the femur within and proximal to the sub-trochanteric region.

Despite these variations, the surgical goal is uniform, namely to achieve a painless and stable lower limb with early return of function[38] with the lowest rates of mortality and morbidity. One major challenge to a review of the literature is identifying the correct measure of 'success'. These

usually include the rate of mortality, time to discharge, rate of re-admission, return to previous residence and/or the level of requirement of social services.

A further measure of success is quality of life, even if this amounts to a limited period of terminal care in hospital before death. Ryder, Reynolds and Bannister[53] have suggested that if patients can be identified by comorbidities as likely to die in hospital soon after their fracture of the hip, such patients should be denied surgery. However, often in these patients, comorbidities can be improved and thus indirectly the rate of mortality. Kenzora et al[32] identified a reduction in the rate of mortality by delaying operation from within 24 hours of admission to between two and five days from 34% to 5.8%. Mullen and Mullen[33] found a reduction from 88% by delaying an operation in the 'unhealthy' patient from within 24 hours to 52% for an operation undertaken one or two days later, and there were no deaths in those patients classified as poor risk on admission whose operation was delayed by three days. Ryder et al[53] also suggested that if a group of patients could be identified by specific factors such as cardiac failure, dementia or bronchopneumonia as likely to die within days, such patients should receive analgesia and nursing care but no operation. They therefore tried to identify specific comorbidities predicting death but could not produce a 'robust combination of variables to achieve this aim' and concluded that it was not possible to define precise indications for refusing surgery and that most variables lacked sufficient specificity to withhold treatment.

In our opinion, unless a patient is likely to die rapidly, any patient with a fracture of the hip should undergo surgery. The patient is out of severe pain and can be nursed comfortably in a dignified fashion. To deny these patients such an operation would be unacceptable and rigid fixation of the fracture should be considered a measure of success rather than a cruel unnecessary intervention.

Another confounding variable in evaluating the literature is the definition of early surgery. Definitions vary from six hours to 72 hours. It is extremely difficult to interpret the evidence and compare studies in view of this heterogeneity and the ethical impossibility of undertaking randomised trials in this area.

The ASA score is identified as a consistent predictor of morbidity and mortality in patients with a fracture of the hip (Table II). Not unexpectedly, the higher the ASA grade the worse the outcome. Other consistent predictors of an inferior outcome are male gender and advanced age.[16,17,20,21,22,47,48] Adjustment of data using these poor prognostic factors frequently reduced or eliminated the significance of any detrimental outcome induced by a delay to surgery.[21,23,24,37] If there are significant reversible pre-operative comorbidities (Table III), as indicated above, a short delay to improve them seems valuable.[32,33,37] This is supported by several authors in large series showing that delay of 48 hours and maybe up to five days, is not associated with increased mortality.[21,25-27,29,30,32,33] Peri-operative complications may, however, be increased with surgical delay[19,20,22,30,31,39,44,45] with an associated increased length of stay[18,19,27,45] and costs.[54] What is not acceptable is delay or postponement of surgery without correction of a significant medical abnormality, as Holt et al[37] reported, a significantly increased 30-day mortality when this occurs. Conversely, in the otherwise healthy patient with a fracture of the hip, early surgery is beneficial,[34,44] not necessarily with regard to survival, but in order to reduce pain and the risk of pressure sores.[16-19,21,26,29,30,34,45] In such patients, delay by definition is a 'non-medical delay' and should be considered unjustifiable[46] aiming for surgery ideally within between 12 hours and 48 hours of admission.[16,17]

The logistics of achieving these time goals undoubtedly remains an issue for many health providers particularly when the literature and national guidelines suggest that surgery for a fracture of the hip should be provided during daytime hours.[14,15] The creation of dedicated regional units to deal with these patients might be considered. Unfortunately, the transfer of patients would again add a further inevitable delay[55,56] and potentially deleterious outcomes.[57]

One study did question whether the treatment of such patients should interrupt elective operating lists to achieve expeditious care.[50] The authors suggested that the affected elective patient should then be operated on out of hours using an emergency list. This would not be acceptable in most healthcare systems for reasons of both an ethical and medico-legal nature operating on elective patients out of hours, and would be in conflict with NCEPOD recommendations.[14,15]

Issues specific to these patients also affect the ability to determine the ideal timing of surgery. Simple issues including the fasting status of the patient might hamper ultra-fast surgery. Long-term anticoagulation, particularly when non-reversible, necessitates a minimum 24-hour delay.[58] Finally, THA is recommended for the treatment of some fractures of the hip[2,7] and this often involves delay whilst more specialised surgical and nursing staff become available.

One important means of reducing delay was inadvertently identified in the Canadian and Indian randomised trial.[50] As part of their early investigation an orthogeriatrician reviewed all patients within two hours of admission. This relatively simple step incorporated as part of a standardised multidisciplinary approach is achievable in most centres, expediting those fit for surgery and instigating early treatment for those in need of optimisation.

Is it possible to operate too early? There are two papers frequently quoted in this regard, both advocating a period of resuscitation before surgery.[32,33] The first, with small numbers of patients, reviewed only acutely unwell patients who may clearly benefit from a delay for optimisation[33] and the second was a retrospective review without adjustment of data and without excluding unfit patients.[32] Subsequent authors have failed to identify a detrimental effect of

early surgery and this is despite the more aggressive approach to early intervention during more recent years, following relevant expeditious guidelines.[2,5-13]

We found few data regarding the influence of the experience of the surgeon, anaesthetist and specialist nurses. Only one study specifically evaluated the grade of staff and failed to identify any significant association.[36] It would however, seem common sense that the operation should not be a procedure for the inexperienced surgeon and anesthetist without supervision, when patient outcomes are already poor.

In conclusion, this review suggests that an early operation is appropriate in the relatively fit patient (ASA 1 or 2) with a fracture of the hip, probably within 12 hours to 48 hours. Central pressure from government to this effect is appropriate. What is inappropriate is early surgery in patients with significant comorbidities that are correctable. In these patients the ASA score appears to be an important simple tool to predict morbidity and mortality. Those patients with an ASA score of 3 or 4, or other local comorbidity scoring systems should allow surgery to be delayed to allow the general condition of the patient to be improved and this decision should not be classed as a fault in management. A delay of up to five days from the injury appears to have no major impact on survival but does leave the patient with an increased period of pain and non-life threatening complications that include the development of pressure sores.

Lastly, multidisciplinary care is imperative for these frail patients. An early ortho-geriatric review can determine which patients would benefit from early surgery and identify those who would benefit from a limited delay for optimisation.

Take home message:

This paper endeavours to present an up-to-date review of the relevant literature in order to establish the ideal timing of surgery for fracture of the neck of femur in all age and fitness groups.

Author contributions:
P. M. Lewis: Literature review, Analysis of data, Initial and final manuscript preparation.
J. P. Waddell: Article conception, Editing and final manuscript preparation.

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