Accelerated versus standard care in hip fracture patients: does speed save lives?

Each year, millions of adults worldwide suffer a hip fracture [1, 2]. Hip fractures primarily occur in the elderly and have devastating consequences. A hip fracture initiates inflammatory, hypercoagulable, stress and catabolic states that can cause medical complications (e.g., myocardial infarction, pulmonary embolism, pneumonia, sepsis, stroke and life-threatening and major bleeding) [3, 4]. These complications can result in severe disability and death. After a hip fracture, the 30-day mortality rate is 7–10% [5–8]. Patients who survive to 30 days are at substantial risk of disability: 11% are bed-ridden [9], 16% are in a long-term care facility and 80% are using a walking aid at 1 year [10]. Despite the magnitude of this problem, little progress has occurred in improving the prognosis of patients suffering a hip fracture.

Without strong supporting evidence to the contrary, some physicians believe that delaying surgery in elderly patients with hip fracture and multiple comorbid conditions provides the opportunity to optimize patients’ medical status, thereby decreasing the risk of perioperative complications. Several observational studies have, however, demonstrated an association between delay in hip fracture surgery and poor outcomes [11–15]. Furthermore, there exists a biological rationale for how accelerated surgical treatment of a hip fracture may lower a patient’s risk of a major complication, improve their functional outcome and reduce their length of hospital stay. These postulated benefits could accrue from reducing the patient’s exposure to the inflammatory, hypercoagulable, stress and catabolic states induced by a hip fracture and accelerating their time to first mobilization.

Timing of surgery

Researchers have hypothesized that early surgical treatment of a hip fracture, which reduces the time patients are exposed to the inflammatory, hypercoagulable, stress and catabolic states, may improve outcomes [16]. Furthermore, accelerated surgical treatment may minimize the period of time a patient is immobile, and this may improve hospital length of stay and functional outcomes. A systematic review and meta-analysis of observational data evaluated the effects of early surgery on the risk of death and several postoperative complications among elderly patients with a hip fracture [16]. Based on the five studies that reported the adjusted risk of mortality (4208 patients, 721 deaths), irrespective of the cutoff defining delayed surgery (24, 48 or 72 h), earlier surgery (i.e., within the cutoff time) was associated with a significant reduction in mortality (relative risk [RR]: 0.81; 95% CI: 0.68–0.96; p = 0.01). Unadjusted data indicated that earlier surgery also reduced the risk of in-hospital pneumonia (RR: 0.59; 95% CI: 0.37–0.93; p = 0.02) and pressure sores (RR: 0.48; 95% CI: 0.34–0.69; p < 0.001). These data are observational, so residual confounding is possible. Therefore, current evidence is not sufficiently strong to justify the substantial system modifications required to facilitate accelerated surgical access for all hip fracture patients.
Conversely, the real potential of early surgery may be underestimated. The greatest impact of early surgery may occur when a hip fracture is treated much more quickly than studies have evaluated, similar to how treatment of an acute myocardial infarction or stroke within hours has the most dramatic impact [17]. If surgery could occur within 6 h of a hip fracture diagnosis, given the potential benefits of minimizing exposure to the harmful states (i.e., the inflammatory, hypercoagulable, stress and catabolic states) and earlier mobilization, the benefits might be substantially greater than were observed in the observational studies.

The two main factors that delay patients undergoing surgery are preoperative medical clearance and operating room access [18]. Both medical clearance and operating room access are potentially modifiable issues.

**Is accelerated surgery possible?**

We have undertaken the HIP ATTACK pilot trial. This randomized controlled trial (RCT) compared accelerated surgery (i.e., goal of medical assessment within 2 h and surgery within 6 h of diagnosis) to standard care in patients with a hip fracture [19]. The primary objective of this pilot RCT was to determine the feasibility of recruiting patients and obtaining rapid medical assessment and operating room access in the accelerated surgical group. We included consenting patients who were ≥45 years of age and diagnosed with a hip fracture requiring surgical repair during working hours on a weekday.

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In this pilot trial, we randomized 60 patients at two Canadian centers and one Indian center and established the feasibility of recruiting patients. We randomized 30 patients to accelerated surgery and 30 patients to standard care, and all patients completed the 30-day follow-up. Among patients randomized to accelerated care, we established the feasibility of obtaining rapid medical assessment (i.e., the median time from diagnosis to medical assessment was 1.5 h). None of the patients randomized to accelerated care had serious medical conditions that would have warranted medical optimization prior to surgery.

We also established the feasibility of accelerated surgery. The median time from diagnosis to surgery in the accelerated surgical care group was 6.0 h and in the usual care group was 24.2 h (p < 0.001). A major perioperative complication (i.e., mortality, nonfatal myocardial infarction, nonfatal myocardial injury after noncardiac surgery, nonfatal pulmonary embolism, nonfatal pneumonia, nonfatal stroke and nonfatal life-threatening and major bleeding) within 30 days of randomization occurred in nine (30%) of the patients randomized to accelerated surgery and 14 (47%) of the patients randomized to standard care (hazard ratio: 0.60; 95% CI: 0.26-1.39; p = 0.23). Patients randomized to accelerated surgery had a shorter time to first mobilization (mean difference 21 h), but this difference was not statistically significant (p = 0.37).

**Limitations of the trial**

The HIP ATTACK pilot trial is a pilot study with a small sample size. Furthermore, although the individuals who randomly assigned patients were instructed not to inform the data collectors of treatment allocation, data collectors may have deduced treatment allocation through documentation about the time of surgery. The impact of this possibility may have been mitigated because some patients assigned to accelerated care had their surgery delayed and some patients assigned to standard care underwent surgery within 6 h of receiving their diagnosis. Overall, although the HIP ATTACK pilot included only a small number of patients, these results are encouraging.

**Future research**

Given the encouraging observational data suggesting that accelerated hip surgery reduces mortality and the results of the HIP ATTACK pilot trial, we are undertaking the definitive HIP ATTACK Trial. This trial will be the first large international RCT of 1000 patients involving numerous centers in more than ten countries. It will determine the effect of accelerated medical clearance and accelerated surgery compared with standard care on the 30-day risk of a major perioperative complication (i.e., a composite of mortality, nonfatal myocardial infarction, nonfatal pulmonary embolism, nonfatal pneumonia, nonfatal sepsis, nonfatal stroke and nonfatal life-threatening and major bleeding). HIP ATTACK will also assess the impact of accelerated surgery on functional outcomes and hospital costs. Patients will receive follow-up at 30 days and at 1 year.
Notable aspects of HIP ATTACK include: this study will use an RCT design, whereas all the prior studies (excluding our pilot) have used observational data to evaluate the impact of surgical timing on health outcomes in patients with hip fractures. Moreover, many authors have suggested an RCT is not possible or would never occur [20]; however, our pilot has demonstrated that such a trial is feasible. Most interventions evaluated in RCTs only target one mechanistic state (e.g., hypercoagulable state). It is biologically plausible that accelerated surgery will impact four mechanistic states (i.e., inflammatory, hypercoagulable, stress and catabolic) and may therefore result in a larger effect size (i.e., hazard ratio: ≤0.70) than normally seen in most clinical trials (i.e., hazard ratio: ≥0.75). Simple entry criteria and recording only essential baseline and outcome data ensures feasibility and will facilitate rapid recruitment and completion. International enrolment with broad eligibility criteria will ensure widely applicable results. The trial will yield important results. If HIP ATTACK demonstrates accelerated surgery is beneficial, this will have immense public health implications given the millions of adults who suffer a hip fracture each year. If the trial demonstrates that accelerated surgery is not beneficial, it will avoid the substantial system modifications required to provide accelerated surgical access for hip fracture patients.

Conclusion
In North America, 0.8% of women and 0.4% of men over 65 years suffer a hip fracture annually [5]. Costs for hip fracture care are estimated to be over CAN$1 billion per year in Canada [10]. At the individual level, hip fractures have devastating consequences with up to 10% mortality at 30 days, a mortality of 20-30% within 1 year and with severe functional limitations in many survivors. These high rates have not improved in the last 15 years. There exist encouraging observational data suggesting that early surgery for a hip fracture reduces a patient’s risk of mortality. Moreover, the HIP ATTACK pilot trial demonstrates the feasibility of a trial comparing accelerated medical assessment and surgery versus standard care. As most patients currently wait more than 24 h to have surgery after a diagnosis of a hip fracture, the need for the large and adequately powered HIP ATTACK Trial to definitively settle this issue is compelling. Interested investigators and patients are welcome to find out more about the full HIP ATTACK Trial by contacting the HIP ATTACK Project Office at hipattack@phri.ca.

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