# HIP fracture Accelerated surgical TreaTment And Care tracK (HIP ATTACK) Trial

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Patients suffering a hip fracture are at substantial risk of serious complications and mortality. Among the patients randomized to standard care in our pilot RCT 13.3% died and 46.7% suffered a major perioperative complication within 30 days of...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Bone and joint therapeutic procedures |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON48891

**Source**
ToetsingOnline

**Brief title**
HipATTACK

### Condition

- Bone and joint therapeutic procedures

**Synonym**
broken hip, Hip fracture

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Population Health Research Institute
**Source(s) of monetary or material Support:** Population Health Research Institute;Canada

## Intervention

**Keyword:** Accelerated care, Hip Fracture

## Outcome measures

### Primary outcome

The primary outcome is to determine the effect of accelerated medical clearance and accelerated surgery compared to standard care on the 90-day risk of the following two co-primary outcomes: all-cause mortality and major perioperative complications (i.e., a composite of mortality, nonfatal myocardial infarction, nonfatal venous thromboembolism, nonfatal pneumonia, nonfatal sepsis, nonfatal stroke, and nonfatal life-threatening and major bleeding) in patients who have suffered a hip fracture.

### Secondary outcome

To determine the effect of accelerated medical clearance and accelerated surgery compared to standard care on each of the following individual secondary outcomes at 90 days after randomization:vascular mortality, non-vascular mortality, myocardial infarction, myocardial injury after randomization not meeting the third universal definition of MI 53-55, congestive heart failure, new clinically important atrial fibrillation, stroke, VTE (i.e., pulmonary embolism or proximal deep venous thrombosis), pulmonary embolism, proximal deep venous thrombosis, pneumonia, sepsis, infection, life-threatening bleeding, major bleeding, composite of life-threatening and major bleeding, new residence in a nursing home, and pressure ulcers. We will also inform the effect of accelerated medical clearance and accelerated surgery compared to standard care on delirium within 7 days after randomization.

We will also determine the impact of accelerated medical clearance and accelerated surgery compared to standard care at 1 year after randomization on all-cause mortality and separately the composite outcome of total mortality and any of the following nonfatal outcomes: myocardial infarction, VTE, pneumonia, sepsis, stroke, and life-threatening and major bleeding at 1 year after randomization. We will also determine the impact of accelerated medical clearance and accelerated surgery compared to standard care on each of the following individual secondary outcomes 1 year after randomization: vascular mortality, non-vascular mortality, myocardial infarction, congestive heart failure, new clinically important atrial fibrillation, stroke, VTE, pulmonary embolism, proximal deep venous thrombosis, pneumonia, sepsis, infection, life-threatening bleeding, major bleeding, composite of life-threatening and major bleeding, and new residence in a nursing home.

To determine the effect of accelerated surgery compared to standard care on each of the following individual tertiary outcomes at 90 days after randomization: hip re-operation, prosthetic hip dislocation, implant failure, peri-prosthetic fracture, surgical site infection, cardiac revascularization procedure (i.e., percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG] surgery), nonfatal cardiac arrest, peripheral arterial thrombosis, new acute renal failure requiring dialysis, time to first mobilization after randomization, length of hospital stay, length of critical care stay, length of rehabilitation stay, hospital readmission, mortality and institutionalization status of dependents and non-dependents. We will also

determine the impact on Functional Independence Measure (FIM*) motor domain and its mobility and locomotion sub-scores, and the SF-36 score at 30 days after randomization.

We will also determine the impact of accelerated medical clearance and accelerated surgery compared to standard care on each of the following individual tertiary outcomes 1 year after randomization: hip re-operation, prosthetic hip dislocation, implant failure, peri-prosthetic fracture, surgical site infection, cardiac revascularization procedure (i.e., percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG] surgery), nonfatal cardiac arrest, peripheral arterial thrombosis, new acute renal failure requiring dialysis, hospital readmission, mortality and institutionalization status of dependents and non-dependents. We will also determine the impact on Functional Independence Measure (FIM*) motor domain and its mobility and locomotion sub-scores, and the SF-36 score at 1 year after randomization.

# Study description

### Background summary

Each year, 35,000 Canadians and millions of adults worldwide suffer a hip fracture. Hip fractures primarily occur in the elderly and have devastating consequences. Patients suffering a hip fracture are at risk of developing cardiovascular (e.g., myocardial infarction, stroke), venous thrombosis (e.g., pulmonary embolism), infectious (e.g., pneumonia, sepsis), and bleeding (e.g., life-threatening and major) complications. These complications can result in death. After a hip fracture, the 30-day mortality rate is 7-10% and 90-day mortality is 10-20%. Patients who survive to 30 days are at substantial risk of

disability. Even among patients who were community-dwelling prior to their hip fracture 11% are bed-ridden, 16% are in a long-term care facility, and 80% are using a walking aid at 1 year. The disability adjusted life-years lost as a result of hip fractures ranks in the top 10 of all causes of disability globally. Hip fractures also result in substantial costs; the annual economic impact in Canada is estimated at over $1 billion. Despite the magnitude of this problem, little progress has occurred in improving the outcome of patients suffering a hip fracture.
A hip fracture initiates inflammatory, hypercoagulable, stress, and catabolic states that can cause medical complications. Early surgical treatment will reduce the time patients are exposed to these harmful states and therefore may reduce the risk of medical complications and mortality. Furthermore, rapid surgery may result in a shorter period of immobility, which may impact functional outcomes and hospital costs. There is preliminary evidence that suggests early surgical treatment of a hip fracture may improve patients* outcomes; however, standard care is that most patients typically wait >24 hours to have surgery. We will undertake a large international randomized controlled trial (RCT) to assess the impact of accelerated medical clearance and surgery versus standard care of hip fractures. We call this trial the HIP fracture Accelerated surgical TreaTment And Care tracK (HIP ATTACK) Trial.

**Study objective**

Patients suffering a hip fracture are at substantial risk of serious complications and mortality. Among the patients randomized to standard care in our pilot RCT 13.3% died and 46.7% suffered a major perioperative complication within 30 days of randomization. There exists a strong 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. There also exist encouraging observational data suggesting that early surgery for a hip fracture reduces a patient*s risk of mortality. Moreover, our pilot RCT demonstrates the feasibility of a trial comparing accelerated medical assessment and surgery versus standard care. Currently, most patients wait more than 24 hours to have surgery after a diagnosis of a hip fracture. The need for a large adequately powered trial to settle the issue in a clear way that will drive subsequent practice is compelling.

**Study design**

HIP ATTACK is an international RCT of 3000 patients with a hip fracture that requires a surgical intervention. This trial will determine the effect of accelerated medical clearance and accelerated surgery compared to standard care on the 90-day risk of all-cause mortality and major perioperative complications

(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).
Currently, across Canada, 80 to 90% of patients with a hip fracture undergo hip surgery within 48 hours after the diagnosis. Therefore, to minimize the variation in timing of surgery between centres, we will only include international centres that have >80% of their hip fracture patients undergo surgery within 48 hours. This will assure that the standard care group in all centres will have comparable time to surgery. In the HIP ATTACK Pilot 86.7% of the standard care patients had surgery within 48 hours of being diagnosed with a hip fracture.
Notable aspects of HIP ATTACK include: (1) this study is using 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 was not possible or would not occur; however, our pilot has demonstrated such a trial is feasible. (2) Most interventions evaluated in RCTs only target 1 mechanistic state (e.g., hypercoagulable state). It is biologically plausible that accelerated surgery will impact 4 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). (3) Simple entry criteria and recording only essential baseline and outcome data ensures feasibility and will facilitate rapid recruitment and completion. (4) International enrolment with broad eligibility criteria will ensure widely applicable results. (5) The trial will yield important results. If it demonstrates accelerated surgery is beneficial, it will have immense public health implications given the millions of adults annually who suffer a hip fracture. If the trial demonstrates accelerated surgery is not beneficial, this will avoid the substantial system modifications required to facilitate accelerated surgical access for hip fracture patients.

**Intervention**

Patients randomized to accelerated care will undergo medical clearance by a dedicated HIP ATTACK medical specialist (e.g., medical specialist would include, internal medicine specialist, geriatrician, cardiologist, anaesthetist), who will be available to quickly arrive in the emergency department for the assessment. This specialist will use their own judgement regarding management when considering any medical conditions that they identify, and they will weigh the potential benefits of delaying surgery for medical management versus the potential negative consequences of protracted exposure to the inflammatory, hypercoagulable, stress, and catabolic states associated with a hip fracture. The HIP ATTACK medical specialist will be aware of all the conditions that the trial consensus group believes are likely to benefit from medical optimization before surgery, listed in Appendix 1. After medical clearance the orthopedic surgeon and anaesthesiologist have to also agree that the patient is appropriate for surgery for the case to proceed.

Patients randomized to accelerated care (i.e., medical clearance and surgery) who are receiving therapeutic dose vitamin K antagonist anticoagulant will receive Prothrombin Complex Concentrate to target an INR <=1.5.
Patients randomized to accelerated care, after obtaining medical clearance, will move into the next orthopedic elective operating room slot (i.e., they will gain priority over scheduled elective cases). Immediately after medical clearance is obtained, research personnel will inform all the relevant stakeholders (i.e., surgical booking clerk, orthopedic surgeon, and anesthesiologist) to facilitate the exchange of the elective and the accelerated hip fracture cases. The scheduled elective cases will shift a slot forward and will occur a few hours later than originally planned, and the final scheduled elective case will occur after normal working hours.
Patients randomized to standard care will undergo medical clearance based on local standard practices. After the patient is medically cleared they will be waitlisted for surgery according to local standard care.
Surgeons* decisions around the choice of surgical implant will be left to their discretion and modern implants will be used.

**Study burden and risks**

With accelerated medical assessment there is a potential risk that the medical specialist will miss a medical condition that would benefit from medical optimization prior to surgery. This did not occur in the pilot, and we will attempt to minimize this risk through the following measures. At each site a HIP ATTACK medical specialist is designated daily who has time to rapidly get to the emergency department to perform a consult within 2 hours. Further, the anaesthesiologist and surgeon have to also approve the patient for surgery. Patients randomized to standard care are not at any increased risk as they will receive care according to usual local practices.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Age >=45 years
2. Diagnosis of hip fracture during working hours with a low-energy mechanism (i.e., falling from standing height) requiring surgery

## Exclusion criteria

1. Patients requiring emergent surgery or emergent interventions for another reason (e.g., subdural hematoma, abdominal pathology requiring urgent laparotomy, acute limb ischemia, other fractures or trauma requiring emergent surgery, necrotising fasciitis, coronary revascularization, pacemaker-implantation)
2. Open hip fracture
3. Bilateral hip fractures
4. Peri-prosthetic fracture
5. Therapeutic anticoagulation not induced by a vitamin K antagonist, unfractionated heparin (e.g., administration of therapeutic LMWH (>6,000 u/24h) in the 24 hours prior to enrolment) or intake of any other non-reversible oral anticoagulant(s) for which there is no reversing agent available
6. Patients on a therapeutic vitamin K antagonist with a history of heparin induced thrombocytopenia (HIT)
7. Patients refusing participation
8. Patients previously enrolled in the study

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 18-01-2018 |
| Enrollment: | 35 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 18-12-2017 |
| Application type: | First submission |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 23-10-2019 |
| Application type: | Amendment |
| Review commission: | METC Isala Klinieken (Zwolle) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| ClinicalTrials.gov | NCT02027896 |
| CCMO | NL61436.075.17 |