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Hip Fracture in Individuals under 60 Years of Age. A Prospective Multi-Center Study of the Epidemiology, Treatment, Outcome and Patient Satisfaction Regarding Hip Fractures.

Study protocol

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Hip fracture in individuals under 60 years of age. A prospective multi-center study of the epidemiology, treatment, outcome and patient satisfaction regarding hip fractures.

Background:

Hip fractures are rare in young and middle aged adults, but an increase in incidence is seen in women around 50 years (Borgstrom et al. 2006, Karantana et al. 2011). Elderly hip fracture patients constitute a quite homogenic group; frail, biologically aged individuals who sustain the fracture due to a low-energy trauma, and have a high risk of mortality. The group under 60 years is more heterogenic (Zetterberg et al. 1982). Some may have severe diseases, functional limitations or alcohol/drug abuse. Others appear healthy and sustain their fracture in high-energy accidents. Some studies identify risk factors for hip fractures in younger age groups; hormonal deficiency, low cognitive function, smoking and alcohol abuse (Jackson et al. 1992, Karantana et al. 2011). Still, the literature is scarce, probably mainly because of the low incidence and the variations in both patient characteristics and injury mechanisms.

Hip fractures can be divided into intracapsular and extracapsular fractures, the latter are treated with internal fixation in all patients. For intracapsular fractures, the patient's age determines the type of surgery. In "elderly", arthroplasty is the treatment of choice in displaced fractures, this can be either a total hip arthroplasty or a hemiarthroplasty. "Younger" patients are treated with internal fixation after fracture reduction. There is no consensus regarding which age limit should be used, and the assessment is complicated by the fact that "biological age" is more relevant than chronological age. In practical use, 60, 65 or 70 years are mostly used as the divide. Arthroplasty leads to fewer reoperations, and better pain relief and function (at least during the first years). Due to an assumed long life expectancy, internal fixation is used in younger individuals, as arthroplasty might lead to complications after 10-20 years. The short term risk of complications after internal fixation – 20-50% - is usually accepted, as these patients can tolerate secondary surgery with arthroplasty after failed fixation. The exact failure rate in younger patients is not known, and they may have better ability to heal their fracture than the geriatric population. Younger patients *may* have better bone quality, better blood supply to the femoral neck and head and better nutritional status, which all promotes fracture healing. On the other hand, we suspect hip fracture to be a sign of frailty, regardless of the patient's age.

Overall Aim:

The overall aim is to investigate the epidemiology of hip fractures in younger patients (regarding hormonal status, bone density and health profiles in comparison to a standard population), analyze of trauma and fracture type, fracture treatment and outcome as well as patient satisfaction during two years.

Material and Method:

The study is a prospective multi-center cohort study of young and middle-aged adults who have incurred a hip fracture; describing epidemiology of hip fracture in this age group, clinical results and

patient reported outcome during two years following the hip fracture. Patients aged 18 to 59 years, who sustain an acute non-pathological hip fracture (defined by ICD-codes S72.00, S72.10 and S72.20) and are treated within four weeks at any of the participating hospitals, are invited to participate in the study. All patients are invited, regardless of medical, cognitive and functional pre-fracture status. The patients' informed consent is to be obtained before inclusion in the study.

Participating hospitals and approximate annual number of hip fractures in patients under 60 years:

- Skåne University Hospital (Malmö and Lund, Sweden) - 45
- Hvidovre Hospital (Copenhagen, Denmark) - 50
- Odense University Hospital (Odense and Svendborg, Denmark) - 50
- Kolding Hospital – part of Lillebælt Hospital (Kolding, Denmark) - 50

The projected number of included patients in the study is 200 to 300 individuals, which would require inclusion during one and a half to two years at all units, depending on the degree of patients accepting inclusion in the study. The study is mainly descriptive, wherefore power calculations are not considered feasible.

Patients are treated according to the department's standard rationale. In addition, the study will comprise interview and written enquires, blood tests regarding medical, hormonal and nutritional status, bone density measurement (DEXA scans), magnetic resonance imaging (MRI) and follow-up visits with x-ray and functional assessment. The x-ray controls are standardized to follow the standard guidelines of Hvidovre Hospital and Skåne University Hospital, which at most means three more x-rays for some patients (in total approximately 1mSv with minimal life time risk of cancer). In patients accepting study participation, the researchers are allowed to read hospital files regarding pre- and postoperative health status. Patients will be followed for two years after inclusion. Analysis of hormonal status, health profile and bone density are compared to a standard population. Risk factor analysis will be performed, regarding the risk of sustaining a hip fracture per se as well as the risk of complications and re-operations after hip fracture treatment.

As a collaborating but separate study with a separate study protocol, bone biopsies taken intra-operatively at participating Danish departments will be analyzed regarding the micro- and ultra architecture of trabecular and cortical bone by means of nano-CT and micro-CT imaging techniques.

Study inclusion and informed consent

The patient will, during admission, be invited to participate in the study by a medical doctor, nurse or physiotherapist associated to the study who will provide information regarding the study orally and in written form. The patients are usually bedridden so the interview is planned at the ward in a private room or by closed curtains. The patient can choose to have a relative or other person of choice present if so wanted. Informed consent to participate in study 5 shall be obtained prior to surgery. For study 1 to 4, informed consent given post-operatively will be accepted for inclusion if not already obtained prior to surgery together with consent to participate in study 5. The patient will at most have 24 hours to review the information to be included in study 5, but at least one hour of reflection will be given for study 1 to 5.

Follow-up scheme

	Pre-operatively	Surgery	Day 1-10	6 weeks	4 months	1 year	2 years
	Hospital			Letter or phone call****	Visit	Visit	Visit
Study inclusion	(X)		X				
Blood tests	X*		X*				
Surgery		X					
Bone biopsy**		X					
Visit					X	X	X
PROM			X (prefracture recall)	X	X	X	X
Questionnaire/ interview			X		X	X	X
Functional tests			X		X	X	
X-ray	X		X		X	X	X
MRI (MARS), if cervical fracture***			X		X	X	
DEXA scan			X*****				X

** Standard screening blood test shall be taken as early as possible, as they may be disturbed by trauma and surgery.*

*** Bone biopsy taken at Danish departments.*

**** MRI MARS performed at Skåne University Hospital initially.*

***** Phone call to patients not responding to letter.*

****** DEXA no. 1 should be performed within the first month after trauma*

Functional assessment is to be done on the day before discharge from the ward or the 10th day postoperatively, which day shall be noted in the protocol. Functional assessment is performed in-ward, at follow-ups at 4 months and 1 year post-operatively, not at the 2-year follow-up.

MRI with metal artefact reduction technique (MRI MARS) is performed in patients with a femoral neck fracture, dislocated and non-dislocated treated with internal fixation, to assess signs of femoral head necrosis. MRI MARS is performed early postoperatively and at follow up visits at 4 and 12 months postoperatively. In Malmö, MRI MARS is performed using Siemens commercially available standard sequences (MARS + VAT) for metal reduction imaging together with intravenous gadolinium contrast.

Patients not meeting for follow-ups will be called upon three times, thereafter they are contacted by phone, to complete the interview normally performed at the visit.

Assessment of radiographs will be performed using standardized definitions, by one of the local researchers from each of the departments and SSR will co-assess all radiographs.

Recorded data

Basic demographic indicators:

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Gender
Age
Type of living (alone, together with someone else, institution, lacks permanent residence)
Extent of work (full time, part time, sick leave, disability pension, not working for other reason)

Health indicators:
BMI
Comorbidity (ASA and Charlson)
History of previous fractures – patient recall and medical files
Hospital admission during the year preceding the hip fracture
Use of particular medication during 5 years leading up to the fracture
Use of tobacco, alcohol or other recreational drugs – prefracture –AUDIT- and DUDIT-questionnaire.
Physical activity level
Bone mass density – DEXA scan
Regular menstruation
Laboratory blood tests:

Test:	**Purpose:**
- hemoglobin, leucocytes w. differential count, platelet count, erythrocyte sedimentation rate and/or C-reactive protein (a.s.a.p. after trauma)	normal blood samples and pathological
- electrolytes (Na^+, K^+), creatinine	renal function
- total calcium + albumin, parathyroid hormone (a.s.a.p. after trauma)	hypo-/hyperparathyroidism
- 25-hydroxyvitamin D	vitamin D deficiency
- alkaline phosphatase, INR	bone metabolism, liver disease
- TSH, T3, T4	thyroid disease
- testosterone (men) / estradiol (women)	hypogonadism
- tissue transglutaminase antibody	coeliac disease

Regarding the injury:
Information about the accident – mechanism of injury, other injuries apart from hip fracture.
Fracture type classification according to Garden (displaced vs. undisplaced) and AO – classified by local researcher, not surgeon.
Type of surgery and implant.

Outcome:
Patient reported outcome measure (PROM):
- EQ5D (3 level), EQ-VAS, Oxford hip score – prefracture recall, 6 wks, 4, 12 and 24 months.
- VAS-psr (pain, satisfaction, rehabilitation) – 6 wks, 4, 12 and 24 months.
- New mobility score (NMS) – prefracture recall, 4, 12 and 24 months.

Functional outcome – Timed up and go (TUG), 10 meter walking test (10MWT) and hand grip strength test (HGS) – in-ward, 4 and 12 months.
Clinical outcome, complications and reoperations.
Radiological outcome - definition of radiological outcome and complications in separate appendix.

Avascular necrosis is assessed clinically and radiologically by MRI and X-ray and findings are graded according to predefined definitions, sorting patients into one of three categories: no AVN, possible AVN, manifest AVN.

Ethical considerations

The study has been approved by ethical committees in Sweden (Regionala etikprövningsnämnden Lund (Diarienummer: 2015/28)) and Denmark (Videnskabsetisk Komité for Region Syddanmark (Projekt ID: s-20150137)), as well as permission granted to create a computer database on the subjects in accordance with the Swedish Personal Data Act (Samråd KVB, Region Skåne (Ärendenr 202-14) and the Danish Data Protection Agency (Datatilsynet for Syddanmark (Journal nr. 15/51398). Study subjects will be included in the study only after giving their informed consent to participate in the study. The study will be conducted in accordance with the Helsinki Declaration(World Medical 2013).

Data

The Danish Data Protection Agency (Datatilsynet) has been notified regarding this project and the Danish law about personal data will be met, as well as the Swedish Personal Data Act. The following data can be acquired from the patients' medical records:

- Type of living
- Work level
- BMI
- Co-morbidity – ASA and Charlson
- History of previous fractures – patient recall and medical files
- Hospital admission during the year preceding the hip fracture
- Use of particular medication – prefracture – patient recall and medical files
- Information about the accident – mechanism of injury, other injuries apart from hip fracture.
- Fracture type classification
- Type of surgery and implant
- Radiological outcome
- Complications
- All blood test results
- MR results
- DEXA results

This information as well as the information from patient interview will give a better understanding of the patients' health status.

Budget, strategy, financial support

There are no financial supports or donations for this study in Denmark, but a grant of 100.000 SEK has been given for the Swedish part by a local fund (Kockska stiftelserna) for secretary salary. Funds have been applied for to pay for costs associated to the project (e.g. project nurse, project physiotherapist, travel between involved departments, etc).

Project co-workers

Skånes Universitetssjukhus / Lunds universitet
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