Statistical analysis plan – TOO HIP

Revised by Stian Lydersen, 2 June 2017

1.Introduction

The aim of TOO HIP is to merge two of the world's largest randomized controlled trials (RCTs) in orthogeriatrics and make a larger dataset, to evaluate the effect of an orthogeriatric organization model on patients with acute hip fractures. This study is based on two previous randomized controlled trials, one in Oslo(1) and one in Trondheim(2). Protocols(3, 4) and results(1, 2, 4-8) from these studies have been previously published.

Inclusion and exclusion criteria

Oslo

Eligible patients were those admitted acutely to the Oslo University Hospital - Ullevaal, irrespective of age, for a femoral neck fracture, a trochanteric or a sub-trochanteric femoral fracture as result of a low energy trauma, defined as fall from own height or from a level not higher than 1 metre.

Patients were excluded if the hip fracture was part of multi-trauma or high energy trauma or if they were regarded as moribund at admittance (as judged by the admitting orthopaedic surgeon).

Trondheim

Eligible patients were those admitted acutely to the Emergency Department of St. Olav's Hospital with a femoral neck fracture, a trochanteric or a sub-trochanteric femoral fracture as a result of low-energy trauma, defined as a fall from own height or from a level not higher than 1 metre. Trondheim only included hip-fracture patients aged above 70 years, able to walk 10 metres before the fracture and did not live in a nursing home before the fracture.

Patients were excluded if the hip fracture was part of multi-trauma or high energy trauma or if they were regarded as moribund at admittance (as judged by the admitting orthopaedic surgeon).

Primary endpoint

The primary endpoint in the analysis of the combined dataset is The Nottingham Extended ADL Index (NEADL). Scored at 4 months postoperatively.

Secondary endpoints

- The Nottingham Extended ADL Index (NEADL). Scored at 12 months postoperatively.
- Intra-hospital mortality and cumulative mortality at 4 and 12 months postoperatively.
- New nursing home admissions, or dead, 4 and 12 months postoperatively, restricted to patients not living in nursing home before the fracture. This will be done using the composite variable "dead or at nursing home" as unfavourable outcome.
- The Barthel ADL Index score, 4 and 12 months postoperatively.

2. Primary endpoint analysis

The main analysis will be a linear mixed model with NEADL as dependent variable, patient as random factor, time point (baseline, 4 months and 12 months) as fixed factor, and treatment group, site (Oslo versus Trondheim), age, sex, fracture type, dwelling at home (versus nursing home), and the interaction between time and treatment group as covariates.

3. Secondary endpoint analyses

Similar mixed model analyses will be used for Barthel ADL score as dependent variable. Dichotomous outcomes will be analysed unadjusted, comparing proportions in the two treatment groups. In addition, they will be compared using logistic regression, unadjusted, and adjusted for site, age, sex, fracture type, and dwelling at home.

4. Sub-group analyses

We will perform sub-group analysis on two levels:

a) Analyses excluding nursing home patients.
The Trondheim study excluded patients dwelling at nursing home at baseline. Separate analyses excluding such patients from the Oslo study will be carried out.

b) Stratified analysis on Barthel Activities of Daily Living (BADL) cut-off
Possibly, we will carry out separate analyses for patients with baseline BADL below and above a pre-defined cut-off. The cut-off limit will be based on the medium value for BADL of nursing home patients in Oslo.

5. Handling of missing values

Single values missing on item scales will be singly imputed using mean imputation.

Missing values for the dependent variable in mixed model analyses will not be imputed, since a mixed model analyses handles this in an appropriate way.

7. References

1. Watne LO, Torbergsen AC, Conroy S, Engedal K, Frihagen F, Hjorthaug GA, et al. The effect of a pre- and postoperative orthogeriatric service on cognitive function in patients with hip fracture: randomized controlled trial (Oslo Orthogeriatric Trial). BMC medicine. 2014;12:63.
2. Prestmo A, Hagen G, Sletvold O, Helbostad JL, Thingstad P, Taraldsen K, et al. Comprehensive geriatric care for patients with hip fractures: a prospective, randomised, controlled trial. Lancet (London, England). 2015;385(9978):1623-33.
3. Wyller TB, Watne LO, Torbergsen A, Engedal K, Frihagen F, Juliebo V, et al. The effect of a pre- and post-operative orthogeriatric service on cognitive function in patients with hip fracture. The protocol of the Oslo Orthogeriatrics Trial. BMC geriatrics. 2012;12:36.
4. Sletvold O, Helbostad JL, Thingstad P, Taraldsen K, Prestmo A, Lamb SE, et al. Effect of in-hospital comprehensive geriatric assessment (CGA) in older people with hip fracture. The protocol of the Trondheim Hip Fracture trial. BMC geriatrics. 2011;11:18.
5. Taraldsen K, Thingstad P, Sletvold O, Saltvedt I, Lydersen S, Granat MH, et al. The long-term effect of being treated in a geriatric ward compared to an orthopaedic ward on six measures of free-living physical behavior 4 and 12 months after a hip fracture - a randomised controlled trial. BMC geriatrics. 2015;15:160.
6. Thingstad P, Taraldsen K, Saltvedt I, Sletvold O, Vereijken B, Lamb SE, et al. The long-term effect of comprehensive geriatric care on gait after hip fracture: the Trondheim Hip Fracture Trial--a randomised controlled trial. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2016;27(3):933-42.
7. Watne LO, Idland AV, Fekkes D, Raeder J, Frihagen F, Ranhoff AH, et al. Increased CSF levels of aromatic amino acids in hip fracture patients with delirium suggests higher monoaminergic activity. BMC geriatrics. 2016;16:149.
8. Prestmo A, Saltvedt I, Helbostad JL, Taraldsen K, Thingstad P, Lydersen S, et al. Who benefits from orthogeriatric treatment? Results from the Trondheim hip-fracture trial. BMC geriatrics. 2016;16:49.

6. Signatures

We hereby vouch for the fidelity of the study to this statistical analysis plan.

Oslo and Trondheim, November 20th 2019.

Shams Dakhil
Project administrator
University of Oslo

Leiv Otto Watne
Principal investigator
Univeristy of Oslo

Torgeir Bruun Wyller
Principal investigator
Univeristy of Oslo

Stian Lydersen
Professor of Medical Statistics
Regional Centre for Child and Youth Mental Health and Child Welfare, Department of Mental Health, Norwegian University of Science and Technology (NTNU), Trondheim, Norway