

Predictors of bone fragility in older women

Associations in older women between risk medications and measurements of physical function, bone microstructure and fracture risk

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i Mölndalsaulan, Mölndals sjukhus, SU/M, Göteborgsvägen 31, 28 januari 2022, klockan 9.00.

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Avhandlingen baseras på följande delarbeten:

- I. **Larsson B**, Mellström D, Johansson L, Nilsson A G, Lorentzon M, Sundh D. Normal Bone Microstructure and Density But Worse Physical Function in Older Women Treated with Selective Serotonin Reuptake Inhibitors, a Cross-Sectional Population-Based Study. *Calcified Tissue International*, **2018**. Sep;103(3):278-288.
- II. **Larsson B A M**, Sundh D, Mellström D, Axelsson K F, Nilsson A G, Lorentzon M. Association Between Cortical Bone Microstructure and Statin Use in Older Women. *Journal of Clinical Endocrinology and Metabolism*, **2019**. Feb 1;104(2):250-257.
- III. **Larsson B A M**, Johansson L, Johansson H, Axelsson K F, Harvey N, Vandenput L, Magnusson P, McCloskey E, Liu E, Kanis JA, Sundh D, Lorentzon M. The timed up and go test predicts fracture risk in older women independently of clinical risk factors and bone mineral density. *Osteoporosis International*, **2021**. Jan;32(1):75-84.
- IV. **Larsson B A M**, Johansson L, Johansson H, Axelsson K F, Harvey N, Vandenput L, McCloskey E, Liu E, Kanis J A, Sundh D, Lorentzon M. One leg standing time predicts fracture risk in older women independent of clinical risk factors and BMD. *Osteoporosis International*, **2021**. Sep 8.

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Abstract

Bone fragility with fractures constitutes a growing public health concern, resulting in suffering and major health care cost.

This thesis project has been carried out by means of studies based on the SUPERB cohort of 75–80-year-old women from Gothenburg. Bone fragility has been addressed in relation to the commonly used selective serotonin reuptake inhibitors (SSRIs) and statins, as well as in relation to physical functional ability, measured using TUG (timed up and go) and OLST (one leg standing time). Bone geometry and microstructure were measured at the distal site of radius and tibia using high-resolution peripheral quantitative computed tomography (HR-pQCT). Associations between TUG, OLST and the risk of incident fractures were analysed.

Treatment with SSRIs was linked to lower physical functioning regarding grip strength, walking speed, and number of chair stand rises. Independently of covariates, treatment with SSRIs was associated with worse physical function but was without any association with skeletal microstructure or bone geometry.

In a cohort of 803 women, the use of statins was associated with better cortical bone characteristics. Statin users had lower cortical porosity, higher cortical bone density, and greater cortical area than nonusers.

Regarding physical function variables, a slow TUG >12 s and a short OLST <10 s were both associated with an increased risk of fracture independently of clinical risk factors and bone mineral density (BMD). A slow TUG (> 12 s) was associated with an increased risk of major osteoporotic (MOF) fracture and hip fracture. In a 75-year-old woman with slow TUG, the 4-year fracture probability of MOF increased by a factor of 1.5–1.9, depending on BMD.

In Cox regression analyses adjusted for age, height and weight, a one leg standing test (OLST) time of less than 10 s was associated with a threefold increase in the risk for incident hip fracture, MOF and non-vertebral fracture. In a 75-year-old woman with a low OLST (< 10 s), the 4-year fracture probability increased by a factor of 1.3–1.5, depending on BMD.

Treatment with SSRIs was associated with normal bone microstructure and density but worse physical function. The use of statins was associated with better cortical bone characteristics in older women. The physical function tests TUG and OLST have substantial impact on fracture probabilities, indicating that inclusion of these tests in patient evaluation should be considered in order to improve fracture prediction in older women.

Keywords: osteoporosis, risk prediction, fracture, risk medication, selective serotonin reuptake inhibitors, statins, physical function, timed up and go, one leg standing test.