

**TITLE:** The association between type 2 diabetes mellitus, hip fracture, and post-hip-fracture mortality: a multi-state cohort analysis.

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**PURPOSE** Recent studies have suggested an increased hip fracture risk in patients suffering from type 2 diabetes (T2DM), whilst failing to model the effect of T2DM status on subsequent post-fracture mortality. We used novel multi-state cohort analyses to estimate the association between T2DM and the transitions to hip fracture, fracture-free death, and post-hip-fracture mortality.

## METHODS

**Design and participants** Cohort including all subjects aged 65 to 80 years and with a recorded diagnosis of T2DM on 1/1/2006; and T2DM-free controls matched (up to 2:1) by year of birth, gender, and primary care practice.

**Setting** Primary care electronic medical records in the SIDIAP database ([www.sidiap.org](http://www.sidiap.org)), which contains data for >5.5 million subjects (>80% of the population) from Catalonia, Spain.

**Exposure and follow-up** primary care diagnosis of T2DM on 1/1/2006. Subjects were followed from then to study outcome (hip fracture or death) date, and then from hip fracture to death (where applicable).

**Statistical Analyses** Multi-state Cox regression models were fitted to estimate Hazard Ratios (HR) and 95% Confidence Intervals [95CI] for hip fracture, fracture-free death, and post-hip-fracture death according to T2DM status. Multivariable models were adjusted for age at T2DM diagnosis and at hip fracture respectively. All analyses were stratified by gender, which otherwise violated proportionality of hazards.

**RESULTS** A total of 44,796 T2DM and 81,221 matched controls (53% women, mean age 72 years old) were followed for a median of 8 years: 23,816 died without fracturing, and 3,308 broke a hip, of which 829 subsequently died (Figure 1). Median time to hip fracture was 4.7 years, with a median of 1.5 years from then to death. Adjusted HRs for fracture-free death were 1.40 [1.35-1.45] for men and 1.86 [1.79-1.94] for women. HRs for hip fracture were

1.30 [1.13-1.49] and 1.50 [1.38-1.62], whilst HRs for post-hip-fracture mortality were estimated at 1.30 [1.05-1.62] and 1.69 [1.42-2.01] in men and women respectively.

**CONCLUSION** T2DM patients are at a 30% (men) to 50% (women) increased risk of hip fracture, and at a 30% (men) to 70% (women) risk of dying after suffering such a hip fracture. The effect of T2DM on overall baseline (fracture-free) mortality was of a similar magnitude (40% higher for men, 85% for women) to that following a hip fracture.

*Figure 1. Stacked predicted probability of study outcomes (death, fx = hip fracture, and fracture-free survival = index) in men (top) and women (bottom) stratified by T2DM status: T2DM subjects left, T2DM-free controls right.*



