

Modelling recurrent fragility fracture events

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Background: Previous studies have shown that bone density loss increases with advancing age and fragility fractures are one of the consequences. As this type of fracture is caused by small mechanical forces rather than major trauma, the occurrence of recurrent fractures is common. However, future progression is not considered in most studies, which focus only on the initial event.

Objective: This study aims to evaluate different recurrent event models to identify risk factors of fragility fractures.

Methods: Data were obtained from the EPIC study. A cohort of subjects aged 50-85 years between 2007 and 2017, was extracted from the Catalan Information System of Development of Research in Primary Care (SIDIAP). Patients with less than one year of follow-up or less than 65 years of age on 1st January 2012 were excluded. Data from major fractures (clinical, vertebral, hip, humerus and wrist) were analysed, including data up to the third fracture. Prentice-Williams-Peterson stratified proportional hazards models were adjusted for the time between events, considering death as a competing event. Age was used as the time scale; so that we had left truncation in addition to right censoring. Cause-specific Cox models were adjusted for the three gaps time, between data entry and first fracture, between first and second fracture and between second and third fracture. Proportional hazard assumption was verified graphically by means of the Schoenfeld residuals. For the analysis, we used the package `cmprsk` of R.

Results: The analysis cohort included 804158 subjects, 52.1% were women and mean age was 75.2 years. 104539 (13.0%) had at least one fracture and 148121 (18.4%) died before the end of the study follow-up. The median time from cohort entry to first major fracture was 13 years and 10 months. Among those with a first major fracture, the median time to a second major fracture was 2 years and 8 months and 2 years to a third major fracture. Early results show that regardless of the order of the fractures, women and people with a previous fracture are at higher risk. In contrast, use of corticosteroids and diabetes are important risk factors for the first fracture, but not for subsequent fractures.

Conclusions: Recurrent fractures are studied with Prentice-Williams-Peterson models. Preliminary results suggest a different role for classic clinical risk factors depending on fracture occurrence time.

Keywords: Survival, Recurrent Events, Fragility Fractures.