Association of incident fragility fractures in patients hospitalised due to unexplained syncope and orthostatic hypotension

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Background: Fragility fractures are caused by low-energy insults such as falls from standing height or less and pose a growing health challenge as their incidence rises with increasing age. Impaired orthostatic blood pressure response and a number of cardiovascular biomarkers have been previously identified as risk factors for fractures. It is likely that severe episodes of syncope and orthostatic hypotension increase the risk of subsequent fragility fractures, however this relationship has not been thoroughly examined.

Purpose: To investigate the relationship of hospital admissions due to unexplained syncope and OH with incident fragility fractures in a middle-aged population.

Methods: We analysed a large population-based prospective cohort of 30,446 middle-aged individuals (age, 57.5 ± 7.6; men, 39.8%). We included patients hospitalised due to unexplained syncope and OH. Cox regression analysis adjusted for age, sex, prevalent fractures, body mass index (BMI) were applied to assess the impact of unexplained syncope/OH hospitalisations on subsequent incident fragility fractures. Prevalent fractures occurring before syncope/OH hospitalisation were excluded (n = 39) as well as cases with no follow-up time after the event of syncope/OH (n= 8).

Results: The mean follow-up from baseline to first incident fracture or end of follow-up was 17.8 + 6.5 years, and 8201 (27%) suffered incident fracture. The mean age of patients with unexplained syncope (n = 493) and OH patients (n = 406) at baseline was 61.5 ± 7.1 years (50.1%, male) and 62.6 ± 6.6 years (49.8% male), respectively. The mean time between baseline and first admission for syncope and OH was 12.3 ± 4.5 years, and the mean age at first hospitalisation was 74.4 ± 7.6 years. In the multivariable-adjusted Cox regression, the risk of subsequent incident fractures was increased among patients hospitalised due to unexplained syncope (HR: 1.20; 95% CI 1.03–1.40; p < 0.02) and OH (HR: 1.40; 95% CI 1.20–1.64; p < 0.001), respectively (Kaplan-Meier curves; Figure 1).

Conclusions: Patients hospitalised due to unexplained syncope and OH demonstrate increased risk of subsequent fragility fractures. We suggest that patients who are hospitalised for unexplained syncope and OH should be clinically assessed for true syncope aetiology, systematically treated against fall risk, and evaluated for additional risk factors for fragility fractures.

Abstract Figure 1. Kaplan-Meier curves

Figure 1. Kaplan-Meier curves depicting the long-term cumulative incidence of fragility fractures stratified according to precedent hospitalizations resulting from unexplained syncope (green, n=493) and orthostatic hypotension (OH; red, n=406) among 30,399 middle-aged individuals (age, 57.5±7.6; men, 39.8%).