

Abstract

Fall incidents occur frequently in older persons. Annually, about 30% of persons older than 65 years falls at least once and 15% falls at least twice. The consequences of falling may be severe: about 5% of the falls leads to a fracture and about 5% causes other serious injuries. Other consequences are loss of function and mobility, fear of falling, loss of independence leading to institutionalisation and death. These facts emphasize the necessity to study the risk factors of falls and the most effective measures to prevent falling in older persons. This thesis describes research that was done to elucidate the fall risks attributable to several classes of medication and the association between frailty and fall risk.

The use of psychotropic medication, such as benzodiazepines and tricyclic antidepressants, is also associated with increased fall risk. The widely used Screening Tool of Older Persons Prescriptions (STOPP) criteria advise against the use of long-acting benzodiazepines (LBs). We studied whether LBs are associated with a higher fall risk than short-acting benzodiazepines (SBs) (elimination half-life ≤ 10 h). We used base-line data and prospective fall follow-up from the Longitudinal Aging Study Amsterdam (LASA), a longitudinal cohort study including 1,509 community-dwelling older persons (Study 1) and from a separate fall prevention study with 564 older persons after a fall (Study 2). Both in Study 1 and Study 2 the use of SBs was associated with time to the first fall, and the use of SBs was also associated with number of falls. LBs were not significantly associated with time to first fall nor with number of falls. We concluded that the use of SBs is not associated with a lower fall risk compared with LBs.

The next study resulted from the previously reported associations between the use of proton pump inhibitors (PPI) and hip fracture that may either be due to decreased bone density or to increased risk of falling. We set out to describe the association of the use of drugs for treatment of acid induced gastrointestinal complaints, PPIs and H2 receptor antagonists (H2RA) with the risk of becoming a recurrent faller, number of falls and with (hip)fracture rate and heel bone density in older persons. In the previously described population of the LASA we measured time to the second fall within six months of the first fall during one year follow-up. And we measured all fractures and hip fractures during a six year follow-up period and broadband ultrasound attenuation (BUA) of the calcaneus on both sides. The use of H2RA was associated with ≥ 1 and ≥ 3 falls. The use of PPI was not

associated with an increased risk of recurrent falls nor with fall rate. No significant associations between PPI or H2RA use and heel bone BUA was demonstrated. The use of PPI or H2RA was not significantly associated with any fracture. We concluded that the use of H2RAs, but not of PPIs is significantly associated with increased risk of falls and advised that the package insert of H2RAs should contain an explicit warning of increased fall risk.

Falls are associated with multiple risk factors, including cognitive and mood disorders. We conducted a study to investigate the association of a concept of frailty that includes psychological and cognitive markers with falls and fractures in community-dwelling older adults and to compare its predictive ability with having a history of falls. In the previously described population of the LASA, falls and fractures were registered as described above and fall history and the prevalence of nine frailty markers, including cognitive and psychological factors were assessed. Frailty was significantly associated with time to second fall. In participants aged ≥ 75 , frailty was associated with ≥ 2 falls. Frailty was also significantly associated with ≥ 2 fractures. The area under the receiver operating characteristic curve (AUC) of frailty and risk of recurrent falls and fall rate was low (≤ 0.62). The AUCs for falls history (aged ≥ 75) ranged from 0.62 for ≥ 1 falls to 0.67 for ≥ 3 falls. We concluded that a concept of frailty including psychological and cognitive markers is associated with both multiple falls and fractures. However, frailty is not superior to falls history for the selection of old persons at increased risk of recurrent falls.

Falls occur frequently in older people and strongly affect quality of life. Guidelines recommend multifactorial, targeted fall prevention. We evaluated the effectiveness of a multifactorial intervention in older persons with a high risk of recurrent falls. We conducted a randomised controlled trial at the geriatric outpatient clinic of a university hospital and regional general practices in the Netherlands. Participants had a high risk of recurrent falls, no cognitive impairment and had visited the emergency department or their family physician after a fall. The geriatric assessment and intervention were aimed at reduction of fall risk factors. Within 1 year, 55 (51.9%) of the 106 intervention participants and 62 (55.9%) of the 111 usual care (control) participants fell at least once. No significant treatment effect was demonstrated for the time to first fall or the time to second fall. No significant results were obtained for secondary outcome measures and for per-protocol analysis. We concluded that this multifactorial fall-prevention program did not reduce falls in high-risk, cognitively intact older

persons, possibly due to simultaneous primary care interventions in the control group.

In our last randomised trial we studied the effect of withdrawal of fall risk increasing drugs (FRIDs) versus 'care as usual' on reducing falls in 612 community-dwelling older men and women who visited the Emergency Department due to a fall. In all participants a structured medication assessment was performed and in the intervention group withdrawal of FRIDs was pursued. During the 12 months follow-up, 91 (34%) of the control participants and 115 (37%) of the intervention participants experienced a fall. FRIDs withdrawal did not have a significant effect on the time to the first fall, the time to the second fall or the time to the first general practitioner consultation due to a fall. Cardiovascular FRIDs withdrawal increased the time to the first general practitioner consultation due to a fall. Per-protocol analyses did not alter the results. From these results we concluded that the risk of falls did not decrease following FRIDs withdrawal. It was especially surprising that no effect of psychotropic drug withdrawal was seen, possibly due to the group size and low compliance.

In conclusion we showed that, contrary to previous evidence, the use of short acting benzodiazepines is a risk factor for falls that is at least of similar relevance as the use of long acting benzodiazepines. Furthermore we demonstrated that the use of H2 antagonists and not of proton pump inhibitors is associated with increased fall risk. We showed that a frailty concept that includes psychological and cognitive markers is associated with increased fall risk but that the single risk factor fall history is at least as relevant. In two randomised controlled trials we could not demonstrate fall risk reduction due to a multifactorial fall risk evaluation followed by a multifactorial intervention or withdrawal of fall risk increasing drugs, respectively. Both demographical developments and dramatic individual consequences of falls call for better methods of selecting those at risk of falls and far more effective interventions than are currently available.