Fracture liaison service

CHAPTER 8

SUMMARY

In order to strive for standardized and optimal FLS-care, a systematic, preferably coordinator-based, approach for identification, enrollment, evaluation, treatment and monitoring of patients with a fracture after the age of 50 years has been proposed (*van den Bergh JP, van Geel TA, Geusens PP. Osteoporosis, frailty and fracture: implications for case finding and therapy. Nat Rev Rheumatol. 2012).* After identification of patients, a detailed evaluation of medical history, medication use, clinical risk factors, vitamin D status, dietary calcium intake, known contributors to secondary osteoporosis and fall risk should then be performed, together with assessment of BMD and VFA. Next, patients need to be further evaluated for undiagnosed contributors to secondary osteoporosis and metabolic bone disorders. Then a multifactorial intervention should follow, including lifestyle management recommendations, calcium and/or vitamin D supplementation if required, and treatment of underlying disorders. Specific anti-osteoporotic treatment should be considered in line with national guidelines with organized follow-up of patients after 3 months and annually, thereafter (*Richtlijn Osteoporose en Fractuurpreventie - Dutch Institute for Healthcare Improvement - CBO 2011).*

This dissertation consists of six studies on several aspects of secondary fracture prevention. We studied the Dutch FLS performance in Chapter 2. The hospital registration and patient-related factors that were associated with FLS attendance and non-attendance were studied in chapter 3 and in chapter 4 we further studied the reasons for non-attendance. In Chapter 5 we assessed if a Pulse Echo Ultrasound device enables identification of women with recent non-vertebral fractures at the FLS who would not need a DXA/VFA. In Chapter 6 we analyzed the daily calcium intake in FLS patients and in Chapter 7 the impact of telephone calls on one-year osteoporosis medication adherence was studied.

In ***Chapter 2*** we evaluated the implementation of the "Capture the Fracture" standards proposed by the IOF in non-university hospitals in the Netherlands by questionnaire to gather information on the selection, evaluation and treatment of patients older than 50 years with a recent fracture. All 90 Dutch non-university hospitals received the invitation to participate in this survey which resulted in 24 (27%) full responses, providing data of 24,468 consecutive patients, corresponding with 25% of fracture patients in the Netherlands in the year 2012. The data showed that all FLSs in the participating hospitals scored above 90% for the following Best

Practice Framework standards: identification of patients with a recent fracture in the hospitals, invitation for FLS, timing of assessment, identification of vertebral fractures, application of national guidelines, evaluation of secondary osteoporosis, drug initiation when indicated, communication with the general practitioner and application of follow-up strategy. Our data suggest that patients attending the Dutch FLSs were evaluated, treated and followed in high compliance with the IOF standards but with the major shortcoming that FLS's attendance rates are low and that future research should focus on identification of the causes of this low attendance rate and ways to improve it.

In ***Chapter 3*** we studied hospital registration and patient-related factors that were associated with attendance or non-attendance to the Fracture Liaison Service (FLS). During the process of this study, we found that there was an important invitation gap, indicating that 14% (278 out of 2006 consecutive patients with a fracture) was not invited at the FLS due to administrative errors. All 1288 patients that were invited at the FLS received a questionnaire. A total of 745 patients (of whom 537 attended and 208 did not attend the FLS) returned an analyzable questionnaire. Non-attendance was associated with male gender, frailty, living alone, low education, being not interested in bone strength and being unaware of increased subsequent fracture risk (with Odds Ratios (ORs) between 1.62 and 2.08). Attendance was significantly associated with information perceived by the patient (OR: 3.32). Based on this study, failures in administrative fracture entry registration as well as frailty, male gender, having low general education, living alone, and low interest in bone health and subsequent fracture risk were independent determinants for FLS non-attendance. Adequate motivation of patients by the healthcare professional shortly after the fracture, or the lack of it, was the strongest determinant associated with both FLS attendance and non-attendance. Therefore, adequate registration processes and a more personal tailored approach with adequate patient information and shared decision making may improve FLS attendance rates.

In ***Chapter 4*** we further analyzed the characteristics of patients who did not respond to an invitation for an FLS visit. Non-responders were traced and contacted by phone to consent with a home visit (HV) and to fill in a questionnaire or, if HV was refused, to receive a questionnaire by post (Q), in order to gain insight in their believes on fracture

cause and subsequent fracture risk. Of the 197 non-responders, 181 patients were traced and phoned until 50 consented with HV; 42 declined HV but consented with Q. Excluded were 8 Q-consenters to whom no choice was offered (either HV or Q) and 81patients who declined any proposition (non-HV|Q); 62% could recall the initial FLS invitation letter. Patient believes about the main causes of fracture significantly differed between HV and Q with regard to a fall (96% vs 79%), bad physical condition (36% vs 2%), dizziness or imbalance (24% vs Q 7%) and osteoporosis (16% vs 2%). Age ≥70, woman gender and major fracture were significantly associated with consent for HV compared to Q (OR 2.7, 2.5 and 2.4, respectively) and HV compared to non-HV|Q (OR 16.8, 5.3 and 6.1). This study showed that FLS non-responders consider their fracture risk to be low. Note, 50 patients (about 25%) consented with a home visit after one telephone call, mainly older women with a major fracture. This subgroup of non-responders with high subsequent fracture risk is therefore presumably still approachable for secondary fracture prevention.

In ***Chapter 5*** we evaluated whether the application of Pulse-Echo Ultrasound (P-EU) enables the identification of women with recent non-vertebral fractures at the FLS who would not need a DXA/VFA referral because they had no osteoporosis and/or subclinical vertebral fractures. In this cross-sectional study, 209 consecutive women of 50-70 years with a recent non-vertebral fracture (NVF) were studied at the Fracture Liaison Service (FLS) of one hospital. All women received DXA/VFA and P-EU (Bindex®) assessments. Various P-EU thresholds (based on the Density Index (DI, g/cm^2)) were analyzed to calculate the best balance between true negative (indeed no osteoporosis and/or subclinical VF) and false negative tests (osteoporosis and/or subclinical VF according to DXA/VFA). 83 women had osteoporosis (40%) and 17 women at least one VF (8%). Applying the manufacturer's recommended P-EU threshold (DI 0.844g/cm^2) being their proposed cut-off for not having hip osteoporosis resulted in 77 negative tests (37%, 31% true negative and 6% false negative tests). A DI of 0.896 g/cm^2 resulted in 40 negative tests (19.3%) (38 true negative (18.3%) and 2 false negative tests (1.0%)). The application of P-EU enabled the identification of a proportion of women with recent non-vertebral fractures at the FLS who would not need a DXA/VFA referral because they had no osteoporosis and/or subclinical vertebral fractures. The most conservative P-EU threshold resulted in 18.3% true negative tests verified by DXA/VFA against 1% false negative test results.

In a dairy producing country such as the Netherlands (globally the second provider of dairy and agricultural products after the USA) milk consumption has been considered healthy and indispensable in a bone supporting menu mainly for the elderly. In ***Chapter 6*** we investigated whether FLS patients complied with recommendations for daily calcium intake, and quantified the daily dairy calcium intake including milk, milk drinks, pudding, yoghurt, and cheese and compared outcomes with recent data of a healthy U.S. cohort (80% Caucasians). We collected data of 1526 female and 372 male FLS patients older than 50 years of age. On average, participants reported three dairy servings per day, independently of age, gender or population density. Median calcium intake from dairy was 790 mg/day in women and men. Based on dairy products alone, 11.3% of women and 14.2% of men complied with Dutch recommendations for calcium intake (adults ≤ 70 years: 1100 mg/day and >70 years: 1200 mg/day). After including 450 mg calcium from basic nutrition, compliance with the recommendation raised to 60.5% and 59.1%, respectively, compared to 53.2% in the U.S. cohort. While daily dairy calcium intake of Dutch fracture patients was well below the recommended dietary intake, it was comparable to intakes in a healthy U.S. cohort. These findings question recommendations for additional dairy products to preserve adult skeletal health, particularly when sufficient additional calcium is derived from adequate non-dairy nutrition.

In ***Chapter 7*** we focused on the treatment persistence in FLS patients who started with alendronate. Postmenopausal women with a recent fracture and osteoporosis who started alendronate were randomized to receive three phone calls (PC) (after 1, 4, and 12 months) or no phone calls (no PC). s-CTX and P1NP were measured at baseline and after 3, 6, 9, and 12 months. As a reference group, 30 postmenopausal osteopenic patients with a recent fracture were analyzed as well. Persistence was assessed using the Dutch National Switch Point Pharmacies-GPs database and cross-referenced with PC, no PC, and BTM changes. Cut-off values of BTMs were calculated based on least significant change (LSC) and also on underrunning median values of the untreated osteopenic postmenopausal reference group with a recent fracture. Out of 119 patients, 93 (78%) completed 12 months follow-up (45 PC and 48 no PC). Mean age was 69 years. Persistence was similar in PC and no PC participants. Using an optimal cut-off value > 29% (< 415 ng/L) as LSC of s-CTX and > 36% (< 53.1 µg/L) as LSC of P1NP, alendronate persistence after 1 year was 93 and 88% for PC and no PC, respectively. It was concluded that in this context, telephone calls did not

improve persistence. In around 90% of patients, the 1-year alendronate persistence was confirmed by levels beyond the LSC of s-CTX and P1NP at 12 months compared to baseline values.