Impaired spinal stability in fractures and metastases of the thoracolumbar spine

Impact Paragraph

This paragraph briefly outlines the potential impact of the findings of the present dissertation on a societal and academic level, in which therapeutic and prognostic aspects for decision making and management of osteoporotic fractures and metastases of the thoracolumbar spine are elaborated.

Osteoporosis and its associated fragility fractures have a major impact on health and quality of life. Fragility fractures can be life-changing events and can bring pain, social isolation and dependence. The decline in quality of life following a fragility fracture does not only impact the person who has experienced the fracture, but also their family and other (informal) caretakers. As such, fragility fractures present major medical and socioeconomic challenges, to individuals, but also to society, exemplified above all by a substantial incidence of approximately 76,000 new fragility fractures in the Netherlands per year, consisting roughly of about 13,000 hip fractures, 12,000 vertebral fractures, 12,000 forearm fractures, and 38,000 other fractures [1]. By 2025, when accounting for the demographic projections, the number of incident fractures is estimated at 107,000, representing an increase of 31,000 fractures and the associated economic burden in the Netherlands is estimated to increase by 30% to € 1069 million [2]. Osteoporosis treatment can reduce the incidence of fractures by up to a half. Nevertheless, about 50% of women and 90% of men with minimum trauma fractures are not treated with any anti-fracture medication [3-4]. A Fracture liaison service (FLS) has been recognized as the most successful approach to achieve secondary prevention and is highly supported by the International Osteoporosis Foundation (IOF), other international and national scientific organizations and authorities. FLSs are well established in the Netherlands, however, the low FLS attendance rate of patients with a recent fracture and low compliance rates for prescribed anti-osteoporosis medication considered a huge problem needing further exploration [5-6]. In this thesis we posed the question if FLS is effective in the elderly >85 years [7]. This is the first study to show, that there is no risk benefit of an FLS programme in the extreme elderly patient population. The low FLS attendance rate was also considered a substantial problem in our study. 282 patients sustained a fracture at an age > 85 years in which only 122 patients (43%) underwent post-fracture assessment by the FLS. In 160 patients (57%) aged 85 years and older no screening was performed because of dementia (32%), at the request of patients or relatives (37%), for age-related reasons ('too old') (9%), immobility (1%), other reasons (4%) and 17% did not attend their scheduled appointment without explanation. When we look at the risk factors in the elderly population of extreme ages, the risk factors for osteoporosis fractures are the highest. In our study we showed that the risk factors were multifactorial, with a high percentage (92%) of osteoporosis or osteopenia in which 45% of the patients

had a previous fracture (before the current fracture). Hence there is tremendous need for treatment to reduce subsequent risk. Besides there's need for more adherence of anti-osteoporosis medication. For the patients in which osteoporosis treatment was prescribed, we found that 63% after 1 year and 51% after 2 years were persistent to their prescribed therapy. However, screening patients at an extreme of ages (> 85 years) was associated with lower mortality risk compared to patients who did not undergo this screening and treatment protocol. The multidisciplinary approach followed in the FLS can potentially aid in the identification of health hazards and comorbidities, and therefore improve health-care for these complex patients. We conclude that more emphasis should be laid on guidance of this elderly population instead of screening.

Vertebral fractures are the hallmark of osteoporosis as they are the most common fragility fractures [8]. Besides secondary prevention of new osteoporotic fractures, it is crucial to treat pain and disability after an osteoporotic vertebral fracture (OVF) in order to regain ambulation and functional capacity as soon as possible in elderly patients. In a systematic review of the literature, we conclude that minimally invasive percutaneous cement augmentation techniques are effective in pain reduction in patients with an OVF as compared to conservative care [9]. The results of our systematic review are in contrast to the latest Cochrane guideline [10]. Minimally invasive percutaneous cement augmentation procedures can be considered in elderly patients with severely disabling vertebral fractures in the acute phase (<6 weeks). We recommend that this minimally invasive treatment option should be discussed with patients in informed decision in order to make treatment more personalized.

In many patients with bone metastases, bone mineral density (BMD) is decreased, leading to osteopenia or osteoporosis as a consequence of hormone and/or chemotherapy or osteolysis, thus increasing the risk of vertebral fractures [11]. Spine metastases affect more than 70% of terminal cancer patients [12]. Advances in medical treatment for systemic disease have improved survival rates among patients with cancer, which has contributed to an increased incidence of spinal bone metastases. Quality of life in these patients is affected considerably because of pain, loss of functional abilities and possible spinal cord injury. Bone metastases can cause skeletal- related events (SREs), defined as a pathologic fracture, spinal cord compression, necessity for radiation (for pain or impending fracture) or surgery. The occurrence of SREs contributes significantly to the cost of care [13]. Data from a large study across four major European countries showed that all types of SREs are associated with considerable health resource utilization (HRU) and costs of up to €12,082 per SRE [14]. About 30–40% of patients do not receive care based on the current scientific evidence, and about 20–25% of the care provided is unnecessary or even potentially harmful to patients [15]. In order to provide a treatment that is optimally tailored to a patient's individual

situation, it is important to estimate the remaining life expectancy as accurately as possible. This could be achieved by implementing an accurate prediction model. However, most existing prediction models have been based on cohorts treated several decades ago and lag behind the evolution in oncology, which profoundly impact care for these patients. Ours is the first study to externally validate and compare two prediction models recommended by the Dutch Guideline Database Oncoline and we found that accurate individualized prediction remains suboptimal when using those existing prediction models. Besides, we found an essential predictive impact of overall visceral and brainmetastases. Finally, we showed that breast tumor subtypes based on immunohistochemistry markers seem to be important for the prognostication of breast cancer patients with spinal bone metastases (SBM). Since cancer biology plays a dominant role in patient survival, our findings regarding tumor type-specific prognostic parameters could contribute to prognostic models' accuracy.

There is lack of an easy-to-use prediction support system essential in the clinical scenario of SBM. With the development of a digital nomogram for SBM we tried to reliably estimate the 1, 3, and 6-months overall probabilities of survival for these patients and guide personalized medicine. This nomogram is the first to include both age and sex as prognostic factors, which can make predictions at any given time point as low as half a month. Besides the survival probability, it also provides the confidence interval of the predicted survival probability and a personalized survival curve. This could serve as a good starting point for shared decision making between patients and physicians.

Furthermore in this thesis, we aimed to identify radiomics based prognostic markers for survival prediction of SBMs. As yet, we didn't find added discriminative performance of radiomics signatures. Therefore, radiomics may not be the magic bullet that solves all our decision-making dilemmas in clinical practice for our domain. Integration of all health data, will accelerate the revolution of personalised medicine in oncology as well as expand and further study the role of radiomics.

References

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