IN SILICO CLINICAL TRIAL TO PREDICT THE EFFICACY OF HIP PROTECTORS FOR PREVENTING HIP FRACTURES

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Introduction

Osteoporosis (OP) is characterized by low bone mineral density (BMD) and bone architecture deterioration, associated with increased fracture risk. Hip fractures are of particular concern given their severe impact on the patient's health. Therefore, reduction of hip fracture incidence is of major clinical importance. Hip protectors aim to reduce impact force at the hip upon falling, however different conclusions on their efficacy have been reported, which could be due to poor compliance [1]. *In Silico* trials, i.e. the use of computer modelling and simulation, with virtual patients, could improve the assessment of OP interventions. Finite element (FE) models of the femur based on Computed Tomography (CT) data have been validated for the prediction of the femur strength [2]. FE models have also been integrated in a multiscale approach to simulate side falls [3].
The aim of this work is to apply an *In Silico* trial framework to predict the efficacy of hip protectors in reducing hip fractures.

Materials and Methods

A cohort of 1044 virtual patients was generated based on a cohort of 94 postmenopausal women [4], for which CT scans of the proximal femur were available. A FE model was generated for each virtual patient [2]. Side falls were simulated using the fall model developed previously [3]. Under the assumption that elderly patients had long reaction times, the effect of muscle co-contraction on the impact was neglected. It was also assumed that patients were treated with antiresorptive drugs so that BMD did not decrease over time. A failure load map was obtained for each patient by simulating 28 impact directions [3]. The intervention group was simulated by assuming that 81% of the impact force was transmitted to the femur when patients wore the hip protector (attenuation of Hipsaver device of 19% [5]). For the placebo arm (no hip protector) attenuation provided by external devices was equal to zero.
A Markov chain workflow was implemented to predict fracture incidence in each arm. At each simulated follow up year, a Poisson distribution was randomly sampled to determine if each patient sustained one or more falls. Impact direction and force were randomly sampled from a range of possible scenarios [3]. A patient was considered fractured when impact force exceeded femur strength in the corresponding direction.
Compliance was implemented at each fall as an unbiased probability that the patient wore the device.

Results

Without hip protector, virtual patients experienced 66 proximal femur fractures in 10 years follow up, similar to the incidence reported in previous clinical studies [6]. Wearing the hip protector, fracture incidence was reduced to 35 (Fig 1). As expected, the efficacy of the device was dependent on compliance (RR=0.52-1.00).

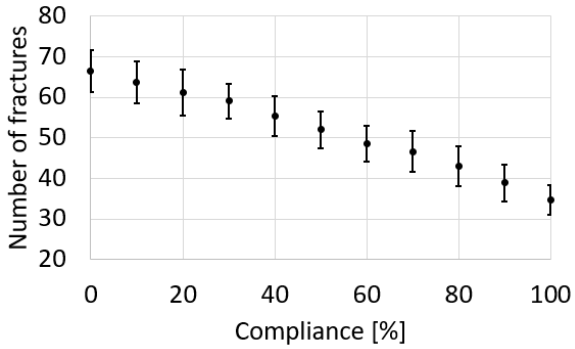

Figure 1: Incidence of hip fractures over 10 years in 1044 virtual patients as a function of compliance.

Discussion

An *In Silico* trial technology was applied to predict the efficacy of hip protectors. Previous studies reported very different conclusions on their efficacy (RR=0.14-1.49) likely due to large differences in compliance among studies (30-80%) and in the design of devices [1]. The potential of this technology includes the possibility to test and compare different interventions or combination of treatments, to optimize treatment strategies, to improve clinical trial design and drug development. Models of OP progression and pharmacological treatments are currently being developed and integrated in the methodology.

References

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