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The Garvan calculator and fragility fracture risk

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Loss of bone mass is only part of the syndrome which, in addition to densitometric osteoporosis, sarcopenia and other risk factors, eventually contributes to fragility fracture. The low sensitivity and specificity of bone mineral density (BMD) measurement in predicting fracture risk has led to the development of tools that include several known risk factors such as demographic variables, physical examination, personal and/or family history of fracture, presence of diseases or medications with influence on bone metabolism and risk factors for falls[1]. Some of these algorithms for predicting the risk of fracture have not been validated in external populations, others lack methodological deficits and only a few have been integrated into national clinical guidelines for osteoporosis.

Validation, both internal and external, is one of the keys to developing a risk calculator. In particular, external validation generalizes the scale to populations beyond those in which it was generated. The work of Reyes Domínguez et al.[2], published in this issue of the Journal of Osteoporosis and Mineral Metabolism, is the first in Spain to validate the Garvan calculator in a sample of 121 individuals without basal densitometric osteoporosis, monitored over 10 years and who had not received anti-osteoporotic treatment during that time.

Furthermore, the discriminative capacity of a predictive model or tool, that is, its ability to distinguish between subjects with or without the event (in this case, osteoporotic fracture), is usually assessed by the area under the ROC curve (AUC). Its value varies between 0 and 1, with a figure between 0.7 and 0.8 considered acceptable. Reyes Domínguez et al.[2], reported an AUC value of 0.72 for any fragility fracture, which gives the Garvan calculator an acceptable predictive capacity. These results are superimposable to those published by Langsetmo et al.[3] in a validation study of the Garvan calculator in Canada. These authors find an AUC for any brittle fracture of 0.69 in females and 0.70 in males. The AUC for hip fracture was higher (0.80 and 0.85, respectively). Only in the quintile at highest risk of fracture did the model overestimate the 10 year risk of any fragility fracture in males and hip fracture in females.

The GLOW study included 19,586 postmenopausal women 60 years of age or older without previous anti-osteoporotic treatment, recruited in 723 primary care centers in 10 countries and followed over a two-year period. Three predictive models that did not include the BMD value were evaluated; the FRAX®, the Garvan calculator, and a model that only considered the age and antecedent of a previous fracture. An AUC of 0.64 was found to predict major osteoporotic fracture and 0.76 for prediction of hip fracture. However, neither of the two models (FRAX® and Garvan) was better than the one that only included age and previous fracture, which fuels the debate about the utility of more complex risk scales[4]. Indeed, in a recent systematic review, tools that predict the risk of osteoporotic fracture and that include few risk factors, such as the Garvan calculator, often have equal or even greater discrimination capacity which include many risk factors (FRAX®, QFracture®)[5].

In general, the predicted risk with the Garvan calculator in the validated work is close to or slightly higher than the observed risk of osteoporotic fracture and better predicts the risk of hip fracture than that of any fragility fracture[1,3,4-8]. In the work of Reyes Domínguez et al.[2], the risk of hip fracture could not be analyzed because of the limited number of incident fractures in the analyzed population.

The significance of the absolute risk of fracture should be related to the threshold value of therapeutic intervention recommended in each country, to provide the patient with adequate information about their risk. In order to calculate the validity criteria of the Garvan calculator, Chen et al.[9] used the American FRAX® cut-off points (20% in the case of the major osteoporotic fracture), finding a sensitivity of 20%, a specificity of 96% and a negative predictive value of 89%. In the study of Reyes Domínguez et al.[2], the authors' optimal cut off point considers a high risk of osteoporotic fracture to be 18.5%, with a sensitivity and specificity of 67% and a negative predictive value of 86%, similar to that found by Chen et al.[9]

In summary, the work of Reyes et al.[2] has the importance of being the first to validate the Garvan calculator in Spain and, in addition, the interest of its possible use as a screening tool to identify subjects with low risk of fracture. Its greater discriminative capacity has been demonstrated with respect to the negative predictive value of any osteoporotic fracture. Its usefulness as a predictor of hip fracture has not been assessed in this study, as has already been noted.

Further validation studies of the simplest risk calculators, such as Garvan, are required, with prospective population cohorts including participants with different risk factors. Given that no predictive tool captures all the known risk factors for fragility fracture or temporal relationships, clinical judgment should remain a key factor in applying the results of these scales to an individual patient.

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