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Risk Factors for Fractures Identified in the Algorithm Developed in 5-Year Follow-Up of Postmenopausal Women From RAC-OST-POL Study

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Abstract

The aim of the study was to establish factors with an impact on fracture risk and to develop an algorithm to predict osteoporotic fracture. A total of 978 postmenopausal women from the epidemiological, population-based RAC-OST-POL study with a mean age of 65.7 ± 7.3 years were enrolled. At baseline, bone mineral density at hip and clinical risk factors for fracture were collected. Afterward, each person was asked annually on fracture incidence in the 5-year follow-up. Finally, data for complete 5-year observation were gathered for the group of 802 patients. During the follow-up, 92 osteoporotic fractures occurred in 78 women. The most common fracture site was the forearm (n = 45). The following baseline factors were found as significant for fracture incidence: femoral neck bone mineral density, prior fractures, steroid use, falls within previous 12 months, and height. Fracture risk was predicted by the following formula: $Risk\ of\ \ fracture\ incidence = \frac{1}{1+e^{-\left(\begin{array}{l}-9.899+1.077*STEROIDS+0.681\\ *PRIORFALLS+0.611*PRIORFRACTURES\\ -0.483*FN\ Tscore+0.042*HEIGHT\end{array}\right)}}$. In our current longitudinal study, an algorithm predicting fracture occurrence over a period of 5 years was developed. It may find application in daily medical practice.

Key Words: Bayesian Model Averaging; follow-up; fracture risk; logistic regression; postmenopausal women.

Introduction

Osteoporosis is one of the most important health problems in the elderly. Patients with osteoporosis do not usually have any clinical symptoms. That is why osteoporosis is also called a "silent epidemic." The most important consequences of osteoporosis are fractures that can be caused even by minimal trauma, for example, a fall from standing height. One may expect that such fracture will occur in approximately 40% of postmenopausal women *(1)*.

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According to the World Health Organization, there are a number of osteoporosis risk factors, namely, prior fractures, the level of physical activity, smoking, alcohol intake, a family history of fracture, age, and many others. Some new methods of assessing fracture risk on the basis of various factors, including those abovementioned, in the last decade, have been developed. Among them are FRAX *(2)*, the method proposed by Garvan Institute *(3,4)*, and QFracture *(5)*. These methods are dedicated to estimate an individual's risk of osteoporotic fracture occurrence over the next 5 (Garvan) or 10 years (FRAX, Garvan, QFracture). The risk given by FRAX is modified by expected life duration, and in fact it expresses fracture probability. The established fracture probability according to FRAX results is proposed as a threshold for the beginning of pharmacologic treatment *(6,7)*. However, it should be underlined that because of several reasons, a fracture risk can be different in various populations, and the model of fracture prediction derived in 1 country not necessarily expresses a risk in another country properly. Therefore, studies showing fracture risk for each society are extremely necessary.

The RAC-OST-POL is such a kind of study that was performed on Polish postmenopausal women in the year 2010. The matters of interest were, among others, nutrition *(8,9)*, functional status *(10)*, the role of education, marital status, kind of job or place of living *(11)*, and vision impairment *(12)*. In this epidemiological, population-based study, the osteoporotic fractures were observed in 28% of all women *(13)* older than 40 years. Besides, in our recent paper, fracture incidences in 4-year follow-up were analyzed in regard to fracture risk (Garvan) and probability (FRAX) *(14)*.

In the current research, we developed a model of fracture risk assessment, and the following detailed aims of the study were defined:

(1) determination of risk factors on the basis of the RAC-OST-POL study with the use of various techniques and statistical models,
(2) creation of the new model for predicting fracture risk,
(3) evaluation of the proposed model for predicting fracture risk by estimating its prediction accuracy.

Materials and Methods

The RAC-OST-POL study is an epidemiological, population-based program designed to reveal data related to postmenopausal osteoporosis. Women who make up the cohort of the RAC-OST-POL study were randomly selected from local population of the whole Racibórz district in Southern Poland *(2)*.

During the 5-year follow-up, phone calls were performed in May 2011–2015, and all fractures of nontraumatic origin were noted. Each patient was asked for confirmation of the fracture by her doctor, and only confirmed events were included in the study. The initial cohort consisted of 978 women. In the case of 176 women, data were censored because of loss of contact, as 131 women did not respond to either phone call or our letters probably because of phone number or postal address change, 40 women died, and 5 refused to cooperate. Finally, data for all 5 observation points were available on the group of 802 patients.

Table 1
Baseline Characteristics of RAC-OST-POL Subjects Enrolled to the 5-Year Longitudinal Observation, n = 802

Parameter	Mean	SD	Median
Age (y)	65.52	7.23	64.49
Height (cm)	156.32	5.73	157.00
Weight (kg)	74.58	13.80	73.00
BMI (kg/m^2)	30.53	5.44	29.71
Menarche (y)	13.97	1.67	14.00
Menopause (y)	49.25	4.88	50.00
FN T-score	–1.24	0.91	–1.30

For all study participants, various data suspected as potential osteoporosis or fracture risk factors were collected *(2)*.

Bone mineral density (BMD) for both femoral neck (FN BMD) and total hip (TH BMD) were established using Lunar DPX (GE, Madison, USA).

Baseline data of the RAC-OST-POL study sub-cohort enrolled to the longitudinal observation is presented in Table 1.

At the beginning of the RAC-OST-POL study, the information about previous 373 fractures that happened over the age of 40 years in 286 patients was collected. Meanwhile, 92 new fractures occurred (hip, 4; spine, 15; forearm, 45; arm, 6; lower leg, 10; rib, 3; foot, 5; clavicle, 4) in n = 78 women during the 5-year follow-up. We present data of all fractures noted over the period of observation, but in the statistical analyses described below, fracture prediction concerns only the first fracture incidence in follow-up.

Statistics

For all calculations, the $p < 0.05$ was taken as a cutoff point of statistical significance. The analyses and computations were performed in 3 main steps using the particular software environments and tools listed in the corresponding paragraphs.

Step 1. Analysis of Risk Factors for Osteoporosis

In our original database, each patient was initially described by nearly 200 variables, but the preliminary reduction in dimensions of source database was done for the purpose of data quality improvement. Some of the features were eliminated because they were redundant or insignificant and did not affect the existence or absence of the fracture (e.g., name, marital status, and so forth). It was accomplished with Waikato Environment for Knowledge Analysis software Weka 3.7.13, developed at the University of Waikato, New Zealand *(15)*, and software environment for statistical computing and graphics R project *(16)*.