Just One Look, and Fractures and Death Can Be Predicted in Elderly Ambulatory Women

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Key Words
Elderly ambulatory women, fractures/death - Fracture prediction - Death prediction

Abstract
Background: The chronological age is clearly the strongest risk factor for fractures or death. Age as a concept can be described exactly as chronological age. Age in relative terms can be described as biological age. Objective: We postulated that, even without taking into account known or unknown comorbidity, an immediate and totally subjective evaluation of an individual’s biological age is predictive of forthcoming fractures and death. Methods: At baseline the biological age was estimated in 1,004 randomly recruited ambulatory 75-year-old women. All women were of the same ethnic background. Two independent observers estimated the biological age within 15 s of first sight of each woman. Based on this estimation of the biological age, the women were divided into tertiles. The women were then followed prospectively for a mean of 4.6 (range 3.0–6.5) years. All retrospective fractures and prospective fractures and deaths were registered. Results: When the tertile of the biologically oldest women was compared with all other women, their odds ratio for sustaining any type of prospective fracture was 1.71 (95% confidence interval 1.22–2.39), for hip fractures 2.69 (1.42–5.11), for clinical vertebral fractures 2.83 (1.57–5.11), and for multiple fractures 3.17 (1.64–6.10). Also, when retrospectively sustained fractures were included, the predictive ability for biological age remained. The death rate amongst the tertile of biologically oldest women was increased when compared with the rest of the women (odds ratio 4.33, CI 3.62–5.17). Conclusions: In ambulatory elderly women, without specific consideration of comorbidity, a subjective estimate of the biological age is predictive of future fractures and death. Subjective estimation of the biological age, in relation to the chronological age, is a valuable indicator of health, conveying additional information that merits its use in clinical practice.

Introduction
Numerous risk factors for osteoporosis and fractures have been described. These include bone mineral density [1], balance [2], history of falls [3], fractures [4], and specific diseases [5] and drugs [6]. The risk factors can be
subgrouped as intrinsic or extrinsic, whereby intrinsic factors often are related to each other and carry different weights during different ages in life. Since osteoporosis is a multifactorial condition, as are the causes of fractures, no single risk factor can sufficiently describe the risk at the individual level. Therefore, additional instruments to increase the predictive ability are warranted, particularly a global assessment. The chronological age is clearly the strongest risk factor influencing the susceptibility to fractures. Nevertheless, the chronological age does only to a certain extent adequately describe a person.

The term ‘biological age’ or the closely linked term ‘frailty’ has often been used to describe an individual’s general health or appearance which definitely might differ from the chronological age. Assessment of the biological age is routinely, but often unconsciously, used in medical practice and is possibly, but so far without any evidence, influencing decision-making. The biological age is of importance for our perception of a person, and attempts have been made to associate more or less subjective estimates of biological age or frailty with survival rates [7–10] and time to institutionalization [9]. So far, as we know, the relationship between biological age and forthcoming fractures has not been described.

We have earlier shown that estimation of the biological age of an elderly woman within 15 s of first sight is possible and that there is a good correlation between the estimates of independent observers [11].

We hypothesized that, in ambulatory elderly women and without taking comorbidty into account, the estimation of the biological age may serve as a predictor of fractures and that this predictive ability is independent of retrospectively sustained fractures. Furthermore, we postulated that estimation of the biological age might be an indicator of premature death.

**Subjects and Methods**

**Subjects**

Within the framework of the Malmö Osteoporosis Prospective Risk Assessment (OPRA) study, 1,604 women of the same chronological age, 75 years, were randomly selected from the city files. These women represented 33% of all 75-year-old women living in the city during the study inclusion period 1995–1999. Of these, 1,044 women participated in the baseline examination. This study refers to the 1,004 women who received a biological age estimate.

**Estimation of the Biological Age**

At baseline, all women visited our osteoporosis research unit for a comprehensive 2-hour investigation, including different bone density assessments and balance tests, the results of which have been reported earlier [11]. This visit also included a subjective estimation of the biological age of each woman. According to our definition, this estimate is a subjective evaluation of an individual’s general health appearance. The specific technique used for this estimation has been described in detail in our previous study [11]. In brief, a visual estimation of the biological age or the frailty of each participant was made by two observers working independently within 15 s of first sight. Intentionally, no specific instructions were given for this visual estimation. The estimate was transferred to a scale ranging from 1 to 100 (1 representing an individual not frail at all and 100 a very frail and biologically aged individual). The observers were two physiotherapists and two research nurses, and the correlations between the assessments were satisfactory ($r = 0.51–0.59, p < 0.0001$) [11]. In 957 women two scores were given, and the mean values were used in the calculations. In 47 women only one score was given, and this score was used in the calculations.

**Registration of Prospective Fractures**

Follow-up visits were made after 1, 3, and 5 years. All fractures having occurred during the follow-period (mean 4.6, range 3–6.5 years) were verified by searching the files of the Department of Radiology at the Malmö University Hospital. This is the only hospital serving the city (260,000 inhabitants) due to the personal identification number of each Swedish citizen, retrieval of such data was possible, as was avoidance of double entrances.

**Registration of Retrospective Fractures**

Retrospective fractures include all fractures sustained throughout life and until baseline investigation in this study. All X-rays and X-ray files have been saved, since the turn of the previous century which made it possible to trace all women with fractures treated at this hospital. At baseline, each woman was asked to record the age at the time of a previous fracture and its type and whether fracture treatment had taken place elsewhere. Also, a search was done in the files of the Department of Orthopaedics, if a self-assessed fracture could not be confirmed in the X-ray files.

**Registration of Death**

From the city files, data were obtained on whether a participating women had died or not and if so on what date. Collection of these data was possible on an immediate basis. Therefore, the follow-up period of this variable lasted somewhat longer (range 3.4–6.9, mean 5.0 years).

**Statistics**

The biological age estimation was divided into tertiles. By using logistic regression, the odds ratio for sustaining a prospective fracture or death was calculated. Comparisons were made as follows: Women within the oldest tertile of biological age were compared with all other women, and they were also separately compared with women belonging to the youngest tertile of biological age. Fracture comparisons were made with women without any ‘prospective’ fracture. Kaplan-Meier survival analysis was used to demonstrate differences in death rates.
Results

The number of women prospectively sustaining fractures from baseline until follow-up was 174 out of the 1,004 study participants. The numbers of women sustaining any type of fracture, hip fractures, or clinical vertebral fractures and the numbers of women sustaining two or more ‘prospective’ fractures are presented in table 1. Ninety-seven women were dead at the time of follow-up (table 1). The distribution of the biological age is shown in figure 1.

When women who were judged to belong to the oldest tertile of biological age were compared with all other women together, the odds ratio for sustaining a fracture varied between 1.71 and 3.17, with a significant risk increase found for any fracture, hip fractures, clinical vertebral fractures, or multiple fractures (table 2). When, on the other hand, the same group of women belonging to the tertile of the biologically oldest was compared with the women in the tertile of the biologically youngest, the odds ratio varied between 1.56 and 7.98, with a significant risk

**Fig. 1.** Distribution of the biological age scores in all 1,004 women. The boundaries of tertiles of the women are indicated.

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<th>Table 1. Number of women sustaining prospective fractures and death</th>
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<td>Any fracture</td>
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<th>Table 2. Odds ratios (and 95% confidence intervals) for prospective fractures of different types and death</th>
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<td>Comparing women within the oldest tertile of biological age with all other women</td>
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<td>After correction for retrospectively sustained fractures</td>
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change for any fracture, hip fractures, clinical vertebral fractures and multiple fractures (table 2).

Before baseline investigation, 512 of the 1,004 women had sustained a fracture of any kind throughout life. Inclusion of retrospective fractures into the logistic regression analysis did not significantly alter the predictive ability of biological age for prospective fractures (table 2).

Women in the biologically oldest tertile had a four times higher death rate compared with all other women (tables 1, 2; fig. 2).

Discussion

Age as a concept can be described both exactly and in relative terms. Age as an exact term is defined as chronological age. Age in relative terms has multiple definitions, all more or less defined. For example, young and old are relative descriptions, as are psychological age and biological age. In this paper, we are discussing biological age not only as it is commonly used in daily life, but also when it has medical implications. Biological age is often used to assign an additional dimension in relation to chronological age and related to perceived appearance and health status. Even though biological age estimates are highly subjective and clearly related to ethnic and cultural factors, this type of assessment is an unverified and unspecific but valuable indicator of health. In this study, we included women all of the same age, 75 years, and of the same ethnic origin (99% were born in Sweden and 1% in other European countries), thereby allowing for a subjective estimation of biological age on equal grounds.

We have evaluated biological age as a risk factor for fractures. From this study, we report that an estimate of the biological age in ambulatory elderly Swedish women is not only a predictor of future fractures, but also of death.

The biological age estimate used was an arbitrary score between 1 and 100, but with no intention of reaching 75 as the median value of 75-year-old women, but rather a perceived biological age or frailty status. Therefore, the score for any woman should not be judged in terms of an absolute score, but only in relative figures. We chose to use, for the calculations made, the average score for two independent observers, since there was a fairly good correlation between the observers. Noticeable, the results remained (data not shown) when separate calculations were made for each observer. Each observer made up her own reference values, however, and, therefore, comparing absolute instead of relative figures of the biological age score should not be done.
The score could have been constructed otherwise, for example, with a median around the chronological age 75 years. However, such a choice would most probably not reflect an accurate estimate of the biological age, since the observers were always aware of the true chronological age (i.e., 75 years) of all women. Nevertheless, since we have in the statistical calculation divided the results into tertiles of biological age, the result would not have differed.

Others [8] have reported that a high visually estimated age (relative to chronological age) in men was associated with the death rate up to 20 years after the original investigation. That study population had a wide chronological age span (range 17–97 years), a comparably low mean age (49.9 years), and the visual age estimation was made by only one of the available examining physicians. A high biological age, or frailty, estimated from construction of scales including defined measurable factors, has also been associated with a higher mortality rate [7, 9, 10] and also a shorter time to institutionalization [9]. We have reported earlier [11] that the biological age is related to balance and mobility, and it is also related to falls during a 1-year follow-up period. It was, therefore, to be expected that such a subjective visual estimation of the biological age would correlate with fractures. However, to our knowledge, this has never been demonstrated previously. Additional studies on the validity of biological age estimates are warranted on groups of elderly, preferably using a reverse design with the chronological age unknown to the observer. Such studies would also make possible comparisons between subjectively estimated biological age and true chronological age for fractures and mortality.

Intentionally, we did not give any other instructions to the observers’ assessment of the biological age, only that scoring should be done within 15 s of their first sight. Neither of the observers were medical doctors: one was a physiotherapist and the other a research nurse. The observers had several years of experience in investigating bone mass and physical ability in patients and research participants. It is, nevertheless, possible that the predictive ability for prospective fractures or death would be even better, had the observer been a medical doctor, with experience in assessment and treatment of clinical patients with fractures. It is also important to note that the independent observers in this study had no information other than the name of the subject before their first meeting, and they did not discuss the evaluation, or their results, with each other during the study period. Knowledge of the patient’s history and comorbidity could, therefore, most probably in a clinical situation further strengthen the predictive ability for future fractures.

A prerequisite for this study was the cohort of women representing the same age, 75 years, and ethnicity. By choosing this study design, we avoided the evaluation to be blurred by differences in chronological age. We find reason to believe, however, that estimation of the biological age may be of help to predict fractures or death in both sexes, at different ages, and in different ethnical settings, as long as relative, and not absolute, comparisons are made and as long as comparisons are made within and not between the specific groups.

We did not take into account the increased death rate in the biologically oldest women when prospective fracture data were compared. Had we done so, the influence of the biological age on the fracture susceptibility would have been even more pronounced. On the other hand, when retrospectively sustained fractures were included in the model, it did not change the results. The bone mineral density is a well-known indicator of fractures. We have previously shown [11], in the same cohort, that the biological age did not correlate with the bone mineral density of either hip or spine, a finding suggesting that estimation of the biological age is a predictor of future fractures independent of the bone mass.

Concluding Remarks

The biological age, as here described as a rapid visual evaluation of general appearance and health, is predictive of future fractures in 75-year-old ambulatory women. The biological age estimate is predictive for up to 5 years and independent of fractures sustained earlier throughout life. In addition, the estimate is also predictive of death.

Acknowledgments

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References


