Letter to the Editor

PLASMA BETA-2 MICROGLOBULIN AS A MARKER OF FRAILTY IN OLDER ADULTS: A PILOT STUDY

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The first step of any efficient geriatric care relies on the early identification of frail older adults (1,2). The screening for frailty is yet limited by its difficulty of implementation in clinical practice in part due to the time consumption of standard validated tools such as the Study of Osteoporotic Fractures index (1–4). An easily accessible blood test could simplify the systematic assessment of frailty in daily practice (5,6). For instance, plasma β-2 microglobulin (β2M) concentration—a light chain of MCH-1 antigen that dissociates from nucleated cells membrane under various stimuli—has been established as a nonspecific biological marker of disease activity in malignancies (multiple myeloma), chronic renal dysfunction, autoimmune affections, and various infections (7–10). Thus, an increase in plasma β2M concentration reflects declines across multiple physiologic systems and may account for the frailty phenotype among older adults. The aim of this pilot study was to examine the association between the frailty phenotype assessed with the Study of Osteoporotic Fractures index (4) and elevated plasma β2M concentrations (ie, >2.5 μg/mL) among geriatric inpatients while taking potential confounders into account.

In December 2009, 43 participants aged 70 years and older were included in this cross-sectional study during their hospitalization in the geriatric acute care unit of Angers University Hospital, France. All included participants received a comprehensive geriatric assessment on admission to the care unit that consisted of structured health questionnaires targeting chronic diseases (ie, diseases of indefinite duration or running a course with minimal change) and a standardized clinical examination including the Study of Osteoporotic Fractures index. The Study of Osteoporotic Fractures index explores three areas of health: the unintentional weight loss of at least 4.5 kg during the past 12 months; the inability to rise from a chair five times without the help of arms or hands; and the feeling of lack of energy for at least 3 days during the previous week (4). The frailty phenotype was defined by the finding of at least one of these criteria (4). Fasting early morning venous blood was collected after rehydration from resting participants for the measurement of plasma β2M concentration (CobasCore β2M EIA; Hoffmann-La-Roche, Switzerland). Participants were separated into two groups based on plasma β2M (elevated β2M concentrations > 2.5 μg/mL). The study was conducted in accordance with the ethical standards set by Helsinki declaration (1983). The entire study protocol was approved by the local ethical committee. Univariate and multiple (ie, fully adjusted and stepwise backward methods) logistic regression analyses were performed to specify the association between elevated β2M concentrations and the frailty phenotype. Age, gender, body mass index, and the number of chronic diseases were used as potential confounders. p Values <.05 were considered as statistically significant. All statistics were performed using SPSS (version15.0; SPSS, Inc., Chicago, IL) and Dag-stat, a spreadsheet for the calculation of comprehensive statistics for the assessment of diagnostic tests (11).

Among 43 older adults included (median age = 83.1 years [interquartile range = 7.2], range: 70.8–101.5 years; 65.1% women; 100% Caucasian; median body mass index = 25.2 kg/m² [IQR = 7.0]; median number of chronic diseases = 4.0 [IQR = 3.0]), median plasma β2M concentration was 2.8 μg/mL [IQR = 2.0]. No multiple myeloma was diagnosed. Thirty-three participants (76.7% of the sample) exhibited frailty. Compared with participants with normal
The main limitation of our study was that it took place in one single acute care unit among patients with unstable health condition. Thus, the reported odds ratio of 12.5 may be overestimated compared with the 1.4 relative risk for frailty because both outcome (frailty) and exposure (elevated βM2) were very prevalent in this population.

The assessment of plasma βM2 concentration could become commonplace in care units for older adults to assess the level of frailty and, thus, the level of health care required. Further research in a variety of adult care units with a longitudinal prospective design is needed to corroborate and explain this finding.

**Conflict of Interest**

C.A. has no relevant financial interest in this manuscript. R.B. has no relevant financial interest in this manuscript. N.F. has no relevant financial interest in this manuscript. D.D. has no relevant financial interest in this manuscript. O.B. has no relevant financial interest in this manuscript.

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Author contribution: C.A. has full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

Study concept and design: C.A. and O.B.

Acquisition of data: N.F. and D.D.

Analysis and interpretation of data: C.A., N.F., D.D., and O.B.

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**References**


### Table 1. Univariate and Multiple Logistic Regressions Showing the Cross-Sectional Association Between the Frailty Phenotype* (dependant variable) and Elevated β-2 Microglobulin Concentrations† (independent variable), Adjusted for Participants’ Characteristics (n = 43)

<table>
<thead>
<tr>
<th>Frailty Phenotype*</th>
<th>Unadjusted Model</th>
<th>Fully Adjusted Model</th>
<th>Stepwise Backward Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>p Value</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Elevated β-2 microglobulin concentrations‡</td>
<td>12.50 1.21–128.66 .034</td>
<td></td>
<td>24.35 1.41–421.02 .028</td>
</tr>
<tr>
<td>Age</td>
<td>1.07 0.92–1.25</td>
<td>.365</td>
<td>1.14 0.87–1.50</td>
</tr>
<tr>
<td>Female gender</td>
<td>0.44 0.04–4.38</td>
<td>.482</td>
<td>0.07 0.01–2.44</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.09 0.89–1.34</td>
<td>.396</td>
<td>1.17 0.86–1.60</td>
</tr>
<tr>
<td>Number of chronic diseases††</td>
<td>0.94 0.63–1.41</td>
<td>.771</td>
<td>1.02 0.55–1.88</td>
</tr>
</tbody>
</table>

**Notes:** OR significant (ie, *p* < .05) is indicated in bold. CI = confidence interval; OR = odds ratio.

* Defined as Ensrud and colleagues’ Study of Osteoporotic Fractures frailty index ≥1 component.
† Plasma β-2 microglobulin concentrations >2.5 μg/mL.
‡ Obtained from a standardized health status questionnaire.
§ Diseases of indefinite duration or running a course with minimal change.

βM2 concentrations (n = 15), those with elevated βM2 concentrations (n = 28) were more often frail (96.2% vs 66.7%, *p* = .012, that is to say a relative risk for frailty of 1.4). There was no significant between-group difference for the clinical characteristics. Elevated βM2 concentrations were significantly associated with the frailty phenotype (unadjusted odds ratio = 12.5, *p* = .034; adjusted odds ratio = 24.4, *p* = .028 for fully adjusted model) and remained the only characteristic associated with frailty in the stepwise backward model (odds ratio = 12.5, *p* = .034; Table 1). Finally, we found that the sensitivity of βM2 test (ie, plasma βM2 > 2.5 μg/mL) was 75.8% for the diagnosis of frailty in the studied cohort, and its sensitivity was 80.0%. The diagnostic efficiency (ie, correct classification rate) was 76.3%.

Our results show for the first time that elevated plasma βM2 concentrations are associated with frailty among geriatric inpatients. Theses findings are in concordance with Shinkai and colleagues (10), who showed that βM2 was an independent predictor of all-cause mortality in a prospective cohort study of 1,034 initially nondisabled community dwellers aged 65 years and older (mean follow-up, 7.9 years).

In this study, elevated βM2 concentrations better predicted mortality than cystatin C or C-reactive protein (10). In addition, it has been reported that βM2 concentration may also predict disability in older adults (12). Because it seems to be difficult to fully explain the loss of functionality by βM2-related low-grade inflammation and renal dysfunction, increased βM2 concentrations were more likely to reflect the age-related morbidity burden and frailty phenotype.

The main limitation of our study was that it took place in one single acute care unit among patients with unstable health condition. Thus, the reported odds ratio of 12.5 may be overestimated compared with the 1.4 relative risk for frailty because both outcome (frailty) and exposure (elevated βM2) were very prevalent in this population.


