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

Cédric Annweiler,1,2,3 Régis Bataille,1,4 Nicolas Ferrière,1,2 Delphine Douillet,1,2 Bruno Fantino,1,2,3 and Olivier Beauchet1,2,3

1University Medical School, UNAM, Angers, France
2Department of Internal Medicine and Geriatrics, Angers University Hospital, France.
3UFRES EA 2646, University of Angers, UNAM, France.
4Regional Center of Fight against Cancer, Angers, France.

Address correspondence to Cédric Annweiler, MD, PhD, Department of Internal Medicine and Geriatrics, Angers University Hospital, 49933 Angers Cedex 9, France. Email: ceannweiler@chu-angers.fr

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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 elevated β2M concentrations and the frailty phenotype. Age, gender, body mass index, and the number of chronic diseases were used as potential confounders.

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 4.0 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 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 three 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).
β2M concentrations (n = 15), those with elevated β2M 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 β2M 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 β2M test (ie, plasma β2M > 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 β2M concentrations are associated with frailty among geriatric inpatients. Theses findings are in concordance with Shinkai and colleagues (10), who showed that β2M 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 β2M concentrations better predicted mortality than cystatin C or C-reactive protein (10). In addition, it has been reported that β2M concentration may also predict disability in older adults (12). Because it seems difficult to fully explain the loss of functionality by β2M-related low-grade inflammation and renal dysfunction, increased β2M 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 β2M) were very prevalent in this population.

The assessment of plasma β2M 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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Study concept and design: C.A. and O.B.

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

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