Hemoglobin and platelets with Bone Mineral Density

Hemoglobina e plaquetas com Densidade Mineral Óssea

DOI:10.34117/bjdv7n7-099

Recebimento dos originais: 06/06/2021
Aceitação para publicação: 06/07/2021

Mário Maciel de Lima Junior
Department of Internal Medicine, State University of Roraima, University in Boa Vista, Brazil

Maria da Conceição Lima Chaves
Federal University of Roraima, Boa Vista, Brazil

Ronaldo da Silva Cruz
Cathedral College,
Av. Luis Canuto Chaves no. 293 – Caçari, Boa Vista-RR, Brazil

Magna Bezerra Feitosa
Urologia Avançada de Roraima, Boa Vista, Brazil

ABSTRACT

Background: The primary objective of this study was to evaluate the association between hemoglobin and platelets with bone mineral density (BMD) in men between the ages of 40 and 80 in the Boa Vista, the capital of the Brazilian state of Roraima. The population study conducted in this study was based on the WHO tool [Fracture Risk Assessment Tool (FRAX®)] nomogram model proposed by the World Health Organization (WHO). Specifically, the current work focuses on (i) determining the inverse correlation between the hemoglobin and femur score and between the hemoglobin and spine score by the WHO tool (FRAX®) nomogram and by using the linear regression model, and (ii) correlating the risk factors with different categorical variables and continuous variables using statistical methods.

Methods: This cohort and cross-sectional study involve both quantitative and qualitative data obtained in the field from 272 patients. However, for this paper, only quantitative findings from screening are described.

Results: The mean Frax score and the hemoglobin level across the group were significantly different. The Frax score of the femur was significantly associated with osteopenia and osteoporosis of the spine. All the data obtained in this study were analyzed using SPSS version 21, and a p-value of ≤ 0.05 was considered as statistically significant.

Conclusions: Hemoglobin and platelets strongly associate with the BMD and the key risk factors for the association between hemoglobin and platelets with BMD includes BMI, smoking and alcohol habit, and vitamin-D and serum calcium level.

Keywords: Hemoglobin, Platelets, bone, mineral density, Boa Vista

RESUMO

Antecedentes: O principal objectivo deste estudo foi avaliar a associação entre hemoglobina e plaquetas com densidade mineral óssea (BMD) em homens com idades

compreendidas entre os 40 e 80 anos na Boa Vista, a capital do estado brasileiro de Roraima. O estudo populacional realizado neste estudo foi baseado na ferramenta da OMS [Fracture Risk Assessment Tool (FRAX®)] modelo de nomograma proposto pela Organização Mundial de Saúde (OMS). Especificamente, o trabalho actual centra-se em (i) determinar a correlação inversa entre a pontuação de hemoglobina e fémur e entre a pontuação de hemoglobina e coluna vertebral pela ferramenta da OMS (FRAX®) nomograma e usando o modelo de regressão linear, e (ii) correlacionar os factores de risco com diferentes variáveis categóricas e variáveis contínuas usando métodos estatísticos.
Métodos: Este estudo de coorte e transversal envolve dados quantitativos e qualitativos obtidos no terreno de 272 pacientes. No entanto, para este artigo, apenas são descritos resultados quantitativos do rastreio.
Resultados: A pontuação média da Frax e o nível de hemoglobina em todo o grupo foram significativamente diferentes. A pontuação Frax do fémur foi significativamente associada à osteopenia e osteoporose da coluna vertebral. Todos os dados obtidos neste estudo foram analisados utilizando SPSS versão 21, e um valor p de ≤0.05 foi considerado como estatisticamente significativo.
Conclusões: A hemoglobina e as plaquetas estão fortemente associadas à DMO e os principais factores de risco para a associação entre hemoglobina e plaquetas à DMO incluem o IMC, o tabagismo e o hábito alcoólico, e o nível de vitamina D e soro de cálcio.

Palavras-chave: hemoglobina, plaquetas, osso, densidade mineral, Boa Vista

1 INTRODUCTION

Bone mineral density (BMD) is acquired even before attaining adulthood [1]. Several different components like osteoblasts, osteocytes, osteoclasts (or the remodeling cells), a non-mineral matrix of collagen, osteoid (non-collagenous proteins) and inorganic mineral salts make up the bone mass. Throughout the lifetime the entire bone mass network undergo repeated remodeling to protect the critical and vital organs of the body [2]. Apart from protecting the vital organs, bones are the primary source of minerals, growth factors, cytokines and home to calcium homeostasis [3].

Hemoglobin is an iron-containing metalloprotein that transports oxygen in the red blood cells of all vertebrates. Deficiency in these metalloprotein or red blood cells is a medical condition defined as Anemia. Osteoporosis is a skeletal disorder caused by the compromised bone strength that eventually leads to an increased risk of fractures of different skeletal sites in the body [4].

While various genetic or constitutional factors are reported as the causal risk factors for osteoporosis, modifiable factors or the genetically determined factors play a pivotal role in the etiology of the disease [5-7]. Other factors that contribute significantly to osteoporosis include lower body weight, age and dyslipidemia among many others and can be categorized into at least five different categories; genetics, lifestyle, chronic

disease conditions, prior or current active medications and others [8]. On the same note, we would like to emphasize that adequate prevention is the key to control lower BMD. In one of their publications, the National Osteoporosis Foundation (NOF), emphasizes the requirements that cover few daily lifestyle adaptations which includes control on taking excess tobacco products (including alcohol), regular exercise and adequate intake of vitamins D and calcium [8-10]. Even though our study includes only male population, according to a survey conducted by the National Health Services in 2011, it is reported that the lack of enough red blood cells or the anemic condition is a typical disease state, prevalent in both men and women aged >12 years. During that survey, it was also found that the prevalence is more common in women (12.7%) than in men (2.4%). It was interesting to find that at old age (>70), the prevalence rate is almost equal in both men and women (~15% in men and ~18% in women). Regardless, anemia primed low hemoglobin levels itself is a known risk factor for many different kinds of diseases, e.g., Hypoxia is a risk factor for osteoporosis [9-11].

Previously, a critical study has been undertaken to reveal the exact mechanisms of bone loss using mainly either blood samples or urine samples from patients with normal or low BMD [12]. That study was insightful in understanding not only understanding the possible causes of the bone metabolism, but also differentiating osteoporosis from other osteopenic conditions such as osteomalacia (which is considered as a secondary cause of osteoporosis). According to Matkovic et al., factors that influence the formation and maintenance of bone includes but not limited to different hormones, calcium level, daily physical activities, prior history of medicine, and intoxications [13]. Also, related but different reports suggest a possible association between bone density and hemoglobin level in disease conditions such as sickle-cell anemia or chronic inflammatory condition [14-16]. Irrespective of all the available information, the association between hemoglobin and platelets with BMD is elusive and need more attention [17,18]. According to Cesari et al., BMD levels do associates with hemoglobin level both in males and females as determined in a local Italian population [17]. Also, few previous pieces of literature also suggest a direct correlation between lower hemoglobin level and bone mass density [9,16,19,20]. However, the study approach in these studies was complex, unconventional and not targeted to study in mid-age to the old age group patient population. Apart from that, in these studies, even though the authors have established an association between the hemoglobin level and BMD, they fail to differentiate between the trabecular and cortical bones, two critical components of BMD.

In this current study, we have evaluated the association between hemoglobin and platelets with BMD in men in an age range of 40 and 80, assessed by FRAX® nomogram.

2 MATERIALS AND METHODS

2.1 INCLUSION AND EXCLUSION CRITERIA

Male individuals with age group between 40 years and 80 years old, and individuals who agree to participate in the research program and signed the free and informed consent form were included in the inclusion criteria. Female individuals or males with any prior history of transplantation, or any sign of neurological disorder (stroke), or autoimmune symptoms (e.g. lupus, inflammatory disease or intestinal disease), or hematological disease (e.g. leukemia, myeloma, lymphoma), or under the treatment of osteoporosis (lack of vitamin D or calcium), or in the use of corticosteroids, or in a process of hormone replacement or a carrier of either hypo or hyperthyroidism were included under exclusion criteria.

2.2 STUDY SELECTION

Assuming 50% of the people with osteoporosis, with 5% error and 80% power, the required sample size, was estimated to be 380. The research participants were selected randomly. Also, few participants voluntarily participated upon spontaneous demand and were referred from the Coronel Mota state hospital.

2.3 DATA COLLECTION

Blood sample from each participant was collected by a group of the competent and trained laboratory team. The disposal of laboratory waste was done according to the SUS network. Collected the blood samples were used to measure serum concentration of calcium, vitamin D, hemoglobin and platelet counts. Followed by, bone densitometry exam was done for each participant. Required data was collected to calculate the probability of fractures in the WHO tool (FRAX®) nomogram. Clinical diagnosis of everyone was delivered and directed to the medical conduct by a medical professional of the Hospital Estadual Coronel Mota, as well as the necessary prescription or need for other tests. On the day of sample collection, participants were explained about the study and procedure in the local language. Following which, informed consent was sought. Only, those who agreed to participate in the study and signed the informed consent form were considered for sample collection. Besides these, information on age, marital status,

smoking and alcohol habits were collected through a questionnaire. Height and weight of each participant were measured for calculation of BMI. The tool was adapted from WHO-FRAX® fracture risk assessment instrument. The Ethics Committee approved the project with a number 50207115.7.0000.5301. The data collected only according to the guideline of IBGE (The Brazilian Institute of Geography and Statistics).

2.4 STATISTICAL ANALYSIS

Data analysis was performed using STATA (STATA corp 14, Texas). Categorical variables are presented with frequency and percentage. Mean/median and their dispersion summarize continuous variables. For analysis purpose, variables are described across the WHO tool (FRAX) femur score category (<3% no risk, ≥3% at risk) as per the Sheffield cut off criteria. Independent t-test did the univariate analysis for continuous data and categorical data; the chi-square test was done. For non-normal data, Mann-Whitney test was done to detect the significant difference. One last outlier information was removed from the analysis to make the distribution normal. A linear regression model was used to predict the association of hemoglobin with WHO tool (FRAX) score femur and spine, separately. Multivariate regression analysis was done to estimate the adjusted coefficient hemoglobin after considering for other variables. For all the analysis, statistical significance was decided at p-value <0.05.

3 RESULTS

Of the total, complete information was available for 272 participants. Mean age of the study participants were 58.38 years (SD 10.10) and were higher in the group having hip Frax score ≥ 3. Details of the descriptive characteristics are provided in Table 1.

Table 1. Descriptive statistics of continuous variables

Variables	No risk (Frax< 3) N = 185 Mean/Median (SD/IQR)	At risk (Frax ≥ 3) N = 87 Mean/Median (SD/IQR)	Total N = 272 Mean/Median (SD/IQR)	P value
Age	57.56 [9.79]	60.13 [10.57]	58.38 [10.10]	0.050
Height (m)	1.66 [0.08]	1.67 [0.08]	1.66 [0.08]	0.596
Weight (kg)	74.85 [13.36]	74.04 [11.02]	74.59 [12.64]	0.625
BMI (m/kg^2)	27.15 [5.76]	26.53 [3.40]	26.95 [5.13]	0.358
Vitamin D (ng/mL)	43.23 [10.68]	42.96 [12.28]	43.15 [11.20]	0.452
Serum calcium (mgdL)	8.92 [1.02]	8.95 [1.03]	8.93 [1.02]	0.164
Haemoglobin (g%)	12.52 [0.79]	17.95 [0.21]	14.41 [1.33]	<0.001*
Frax spine^	0.2 [0.3]	1 [1.2]	0.3 [0.5]	<0.001*$
Platelets (mm^3)^	211500 [116000]	208000 [125000]	209000 [68000]	0.251$

*P value <0.05, ^Median and IQR, $Mann Whitney test, for rest independent t-test.

Significant difference of the mean score across the group was observed for hemoglobin and Frax score of spine at p value less than 0.05. The Frax score of femur was significantly associated with osteopenia and osteoporosis of spine, decided by T-Score and provided in Table 2.

Table 2. Descriptive statistics of categorical variables

Variables	No risk (Frax<3) N=185	At risk (Frax>=3) N=87	Total N=272	Chi Square test P value
Osteopenia of spine	24.32 [18.09-30.55]	40.22 [29.82-50.64]	29.41 [23.96-34.86]	0.007*
Osteoporosis of spine	7.56 [3.72-11.40]	28.73 [19.12-38.34]	14.33 [10.14-18.52]	<0.001*
Marital status				
Single	28.64 [22.08-35.21]	28.73 [19.12-38.34]	28.67 [23.27-34.08]	0.988
Married	71.36 [64.78-77.91]	71.27 [61.65-80.87]	71.32 [65.91-76.73]	
Current smoke	5.94 [2.51-9.37]	10.34 [3.88-16.81]	7.35 [4.23-10.47]	0.195
Current alcohol	23.78 [17.60-29.96]	24.13 [15.05-33.22]	23.89 [18.79-28.99]	0.949

The inverse correlation of haemoglobin with Frax score of femur and spine are given in scatter plot distribution at Figures 1 and 2, respectively.

Figure 1. Scatter plot of Hemoglobin with Frax Femur score displaying the correlation between hemoglobin levels and the bone mineral density in study population (n=272).

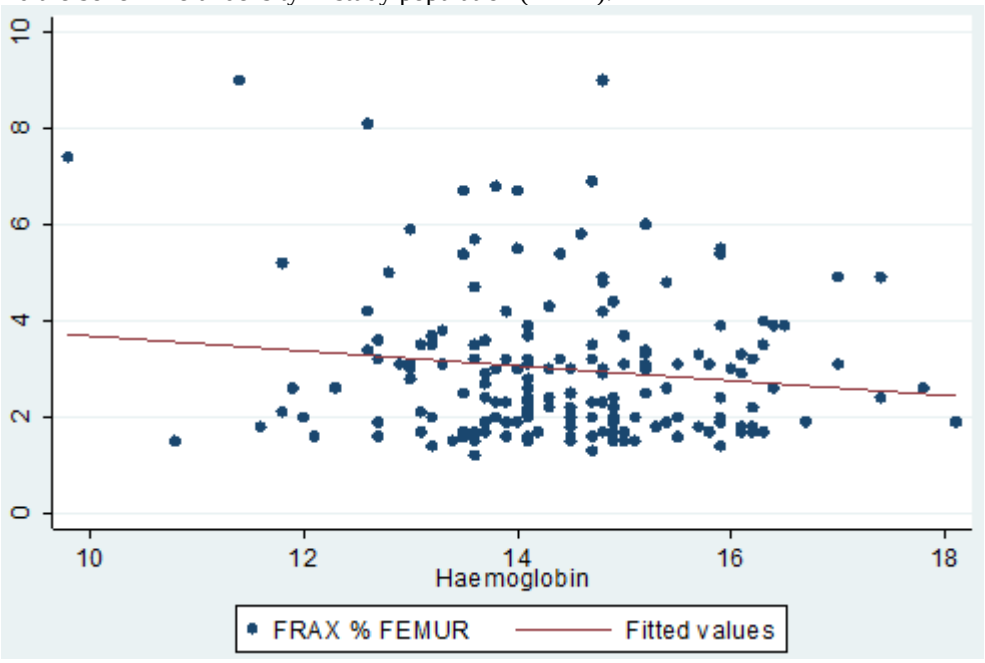
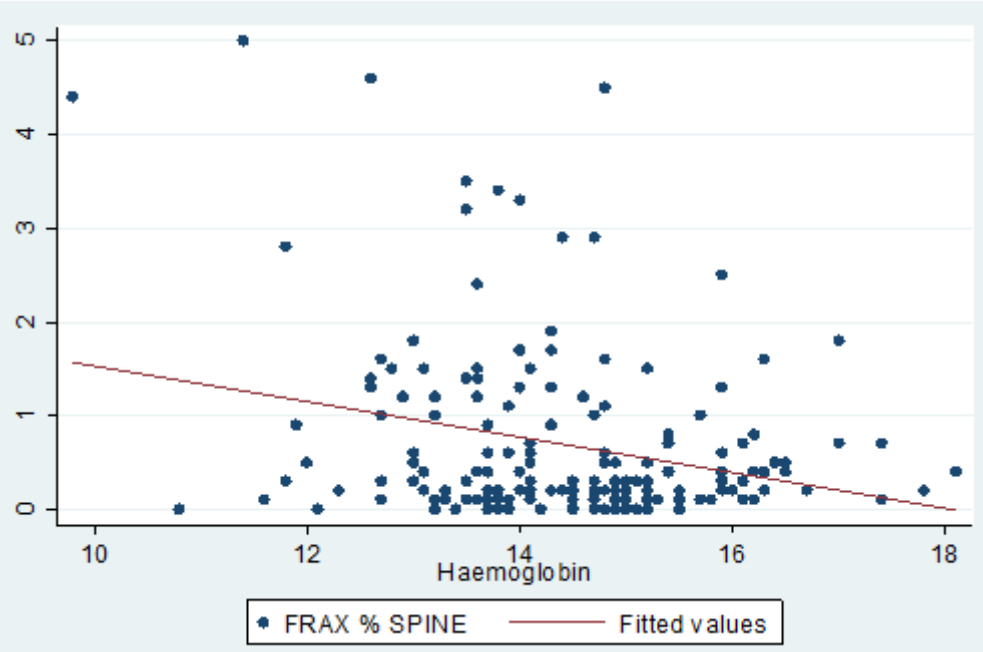


Figure 2.Scatter plot of Hemoglobin with Frax Spine score displaying the correlation between hemoglobin levels and the bone mineral density in study population (n=272).



We also performed two linear regression models, to predict the association of hemoglobin with the femur Frax score and spine Frax score, separately. The unadjusted regression coefficient for femur Frax score was -0.25 [95% CI: -0.45 to -0.04]. For every unit change in hemoglobin level (g%) there was 0.22 units reduction in femur Frax score after adjusting for age, BMI, current smoking and alcohol habit, vitamin-D and serum calcium level, which was statistically significant at the level p value <0.05 and is provided in Table 3.

Table 3. Linear regressions with femur FRAX score

Variables	Crude Coefficient [95% CI]	Adjusted Coefficient [95% CI]
Haemoglobin (g%)	-0.25 [-0.45 to -0.04]*	-0.22 [-0.42 to -0.02]*#

*P value<0.05 # adjusted for BMI, Age, current smoking habit, alcohol habit, Vitamin-D level and serum calcium level

Similar inversion relationship was seen with spine Frax score, where the adjusted coefficient was -0.24 [95% CI -0.38 to -0.10] and tabulated in Table 4.

Table 4. Linear regressions with spine FRAX score

Variables	Crude Coefficient [95% CI]	Adjusted Coefficient [95% CI]
Haemoglobin in g%	-0.28 [-0.43 to -0.14]*	-0.24 [-0.38 to -0.10]

*P value<0.05 # adjusted for BMI, Age, current smoking habit, alcohol habit, Vitamin-D level and serum calcium level

4 DISCUSSION

The current study evaluates the association between hemoglobin and platelets with BMD in men in an age range of 40 and 80 in the Boa Vista, the capital of the Brazilian state of Roraima using FRAX® nomogram. In this study, compared to healthy patients, anemic patients had significantly lower bone mass density. However, those anemic patients were older than a control group. Besides, we observed a strong and independent association of hemoglobin with the femur Frax score and spine Frax score after controlling for BMI and other potential risk factors (smoking and alcohol habit, vitamin-D and serum calcium level) in the linear regression analysis. The tight association of the hemoglobin levels to the BMD in our study is not eccentric. In fact, it is in agreement with several previous studies, where the prevalence of osteoporotic fractures is frequent in an aged population [21-23]. In contrary, evidence from epidemiological data suggests that anemia is more frequent in an older population and about more than 13% older population with the age range of 70-80 gets affected by this medical condition [23]. Not only that the anemic condition influence older population it is also regarded as one of the dominant risk factors that lead to disability in the elderly [24-26]. However, we speculate that the defect in locomotor activity may be because of weak and poor muscular strength that is a secondary effect to reduced hemoglobin level [24-28].

The medical conditions diagnosed in association with anemia may or may not directly influence the prevalence of osteoporosis [15,16,29]. However, it is possible that anemia may influence osteoporosis independently [17]. In this current work, our data suggest the following situation where the association between low hemoglobin level and BMD may be an independent event. The overall contribution of risk factors is also crucial. In corroboration with Laudisio et al., we found that different confounding factors like BMI, smoking alcohol habit, vitamin-D and serum calcium level influence the bone mineral density in the older subject significantly [30]. As described in the result section, we did utilize the power of linear regression analysis to minimize the effect of the confounders on the association between low hemoglobin level and BMD.

We observed that the overall association between the hemoglobin levels with BMD did not change even after establishing linear regressions with femur FRAX score (Table 2) and with spine FRAX score (Table 3), where the confounders are appropriately adjusted. This observation suggests a potential clinical and therapeutic intervention to low BMD, adjusting the hemoglobin level in patients. Regardless of any therapeutic intervention, our observation of an association between the hemoglobin levels with BMD

will add additional information to the existing knowledge on different risk factors in the field.

Although our findings are in agreement with previous studies, our data represents a strong association between BMD losses in general to that of hemoglobin levels and not to a specific bone. Besides, in corroboration with Laudisio et al., 2009, our data suggest that proper control of potential confounders is essential to meet the desired association between hemoglobin and BMD level. [17,18] Fail to do so; patient population with related medication may contribute to the outliers and hence misrepresentation of the data. It is noteworthy that the findings from these two studies are restricted to a particular ethnic group and may not truly applicable to other ethnic groups.

The current study is cross-sectional, and hence it is hard to speculate the origin of lower BMD; whether before or after the development of anemia. So, it did not allow us to confirm the cause-effect relationship. It would have been more impactful to gather information on potential treatment efforts where improving hemoglobin level would improve the BMD quality. We also did not include a possible investigation to test if a hormone replacement option or calcium supplements would improve the BMD quality and leave us any clue of its association with hemoglobin level.

5 CONCLUSIONS

In conclusion, our study indicates that the key risk factors for the association between hemoglobin and platelets with bone mineral density include BMI, smoking and alcohol habit, vitamin-D and serum calcium level. Also, our study also suggests that the hemoglobin and platelet levels in the given population are strongly associated with the BMD, once these confounders are tightly controlled. However, further clinical investigations are required to gain a better understanding of the overall pathophysiological pathways that connects the hemoglobin level and BMD in patients of this age group.

REFERÊNCIAS

1. K. Kouda, K. Ohara, H. Nakamura et al., "Predicting bone mineral acquisition during puberty: data from a 3-year follow-up study in Hamamatsu, Japan," *Journal of bone and mineral metabolism,* vol. 35, pp. 185–191, 2017.

2. A.L. Boskey and R. Coleman, "Aging and bone," *Journal of dental research,* vol. 89, pp. 1333-1348, 2010.

3. R.S. Taichman, "Blood and bone: two tissues whose fates are intertwined to create the hematopoietic stem cell niche" *Blood,* vol. 105, pp. 2631–2639, 2005.

4. N.E. Lane, "Epidemiology, etiology, and diagnosis of osteoporosis," *American Journal of Obstetrics and Gynecology,* vol. 194, pp. S3–S11, 2006.

5. S.A. New, "Exercise, bone and nutrition," *Proceedings of the Nutrition Society,* vol. 60, pp. 265–274, 2001.

6. M. Espallargues, L. Sampietro-Colom, M.D. Estrada, et al., "Identifying bone-mass-related risk factors for fracture to guide bone densitometry measurement: A systemic review of the literature," *Osteoporosis International,* vol. 12, pp. 811–822, 2001.

7. Y.J. Tang, W. Huey, H. Sheu, et al., "Positive associations of bone mineral density with body mass index, physical activity, and blo*od triglyceride level in men over 70 years old: A TCVGHAGE study," *Journal of bone and mineral metabolism,* vol. 25, pp. 54–59, 2007.

8. Washington, DC: Prevention: who's at risk? 2008. National Osteoporosis Foundation. Retrieved from: http://nof.org/prevention/risk.htm

9. H. Fujimoto, K. Fujimoto, A. Ueda, et al., "Hypoxemia is a risk factor for bone mass loss," *Journal of bone and mineral metabolism,* vol. 17, pp. 211–216, 1999.

10. F. Karadag, O. Cildag, Y. Yurekli, et al., "Should COPD patients be routinely evaluated for bone mineral density?" *Journal of bone and mineral metabolism,* vol. 21, pp. 242–246, 2003.

11. A. Laudisio, E. Marzetti, L. Antonica, et al., "Association of left ventricular function with bone mineral density in older women: A population-based study," *Calcified tissue international,* vol. 82, pp. 27–33, 2008.

12. X. Lin, H. Yu, C. Zhao, et al., "The peripheral blood mononuclear cell count is associated with bone health in elderly men: A cross-sectional population-based study," *Medcine, (Baltimore)* vol.95, pp. e3357, 2016.

13. V. Matkovic, "Calcium and peak bone mass," *Journal of internal medicine,* vol. 231, pp. 151–160, 1992.

14. M. Sarrai, H. Duroseau, J. D'Augustine, et al., "Bone mass density in adults with sickle cell disease," *British journal of haematology,* vol. 136, pp. 666–672, 2007.

15. C. Gasche, "Complications of inflammatory bowel disease," Hepatogastroenterology vol. 47, pp. 49–56, 2000.

16. MW. Taal, T. Masud, D. Green, et al., "Risk factors for reduced bone density in haemodialysis patients," Nephrology Dialysis Transplantation, vol. 14, pp. 1922–1928, 2007.

17. M. Cesari, M. Pahor, F. Lauretani, et al., "Bone density and hemoglobin levels in older persons: Results from the In CHIANTI study," Osteoporosis International, vol. 16, pp. 691–699, 2005.

18. A. Laudisio, E. Marzetti, F. Pagano, et al., "Haemoglobin levels are associated with bone mineral density in the elderly: A population-based study," Clinical Rheumatology, vol. 28, pp. 145-151, 2009.

19. AM. Kenny, L. Dawson, A. Kleppinger, et al., "Prevalence of sarcopenia and predictors of skeletal muscle mass in nonobese women who are long-term users of estrogen-replacement therapy," J Gerontol vol. 58, pp. M436–M440 2003.

20. EP. Vichinsky, "The morbidity of bone disease in thalassemia," *Annals of the New York Academy of Sciences,* vol. 30, pp. 344–348, 1998.

21. P. Kannus, S. Niemi, J. Parkkari, et al., "Hip fractures in Finland between 1970 and 1997 and predictions for the future," Lancet, vol. 353, pp. 802–805, 1999.

22. C. Cooper, G. Campion, L.J. Melton. Hip fractures in the elderly: A world-wide projection. Osteoporosis International, vol. 2, pp. 285–289, 1999.

23. U. S. National Center for Health Statistics.1985 Summary, National Hospital Discharge Survey; Advance Data from Vital and Health Statistics.1986. No. 127. DHHS Pub No. [PHS] 86–1250, Hyattsville, MD.

24. BW. Penninx, JM. Guralnik, G. Onder, et al., "Anemia and decline in physical performance among older persons," *The American Journal of Medicine*, vol. 115, pp. 104–110, 2003.

25. BW. Penninx, M. Pahor, M. Cesari, et al., "Anemia is associated with disability and decreased physical performance and muscle strength in the elderly," *Journal of the American Geriatrics Society*, vol. 52, pp. 719–724, 2004.

26. R. Woodman, L. Ferrucci, J. Guralnik, "Anemia in older adults," *Current Opinion in Hematology*, vol. 12, pp. 123–128, 2005.

27. JA. Kanis and CC Gluer, "An update on the diagnosis and assessment of osteoporosis with densitometry. Committee of Scientific Advisors, International Osteoporosis Foundation," Osteoporosis International, vol. 11, pp. 192–202, 2000.

28. TC. Mineo, V. Ambrogi, D. Mineo, et al., “Bone mineral density improvement after lung volume reduction surgery for severe emphysema,” Chest, vol. 127, pp. 1960–1966, 2005.

29. S. Leng, P. Chaves, K. Koenig, et al., “Serum interleukin-6 and hemoglobin as physiological correlates in the geriatric syndrome of frailty: A pilot study,” Journal of the American Geriatrics Society, vol. 50, pp. 1268–1271, 2002.

30. A. Laudisio, E. Marzetti, L. Antonica, et al., “Masticatory dysfunction is associated with osteoporosis in older men,” Journal *of Clinical Periodontology,* vol. 34, 2007.