Relationship between bone mineral density, coronary risk factors, C-reactive protein, and Insulin growth factor in frail elderly

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ABSTRACT

Objective: This study aimed to explore the relation between bone mineral density (BMD), inflammation, coronary risk factors, and Insulin growth factor (IGF) in frail elderly. Design: A case-control study. Setting: Ain Shams University Hospital Cairo, Egypt. Participants: Ninety aged 60 years and above; sixty frail (30 males and 30 females; mean age 70.03 ± 8.10) and thirty matched controls (15 males and 15 females; mean age 69.07 ± 5.93). Measurements: History, examination, comprehensive geriatric assessment, measurement of BMD, and laboratory investigations including; high sensitivity C-reactive protein (hs-CRP) glycated haemoglobin, IGF, low-density lipoprotein (LDL), high-density lipoprotein, total cholesterol, and triglycerides. Results: The frail group had significantly lower levels of triglycerides and LDL, hs-CRP and glycated haemoglobin levels were significantly higher (P < 0.001), and BMD and IGF levels were significantly lower when compared with the control group (P < 0.001, P = 0.05) respectively. We also found that BMD had a significant positive linear correlation with IGF and negative correlation with age. Conclusion: Frailty was associated with low BMD, lower triglycerides & LDL levels, and higher hs-CRP levels. A borderline significance was found between IGF levels and frailty. A positive correlation was found between BMD and IGF in frail.

KEYWORDS

Frailty; Bone Mineral Density; Coronary Risk
by two different pathways. The first explanation might be that pathological processes part of disease can lead to subclinical end organ damage, thus decreasing total physiologic reserve. The second possibility is that atherosclerosis, as a state of chronic inflammation, may result in a catabolic state with its systemic manifestations contributing to frailty [7]. The purpose of this article is to further explore the relation between bone mineral density, inflammation, IGF-1, and coronary risk factors in frail elderly Egyptians.

2. MATERIALS AND METHODS

2.1. Study Design and Setting

This was a case control study. The study sample comprised 90 participants aged 60 years and above. They were selected from Ain Shams University Hospital from inpatient wards and outpatient clinics. Cases included thirty frail elderly females and thirty frail elderly males diagnosed by Fried’s criteria [8] as applied by Avila-Funes et al. [9]. Controls included thirty healthy elderly subjects (15 males and 15 females) age matched with no apparent evidence of disease after full medical history and physical examination.

Any patient who refused to participate in the study, patients who were suffering from acute infection, and any patients who were taking drugs that have anti-inflammatory effects as steroids, statins and aspirin were excluded from this study.

2.2. Data Collection

Each patient then underwent comprehensive geriatric assessment in the form of detailed history and physical examination, cognitive function assessment by Mini-mental status examination (MMSE) [10] (The Arabic version used in this study was done by El-Okl et al. [11]), functional assessment by Activities of daily living (ADL) [12], Arabic version [13], and Instrumental activities of daily living (IADL) [14] (An Arabic version of the test was applied [15]), and Geriatric depression scale 15 items (GDS-15) [16] was used to screen for depression (the Arabic version of the test was applied by Shehta et al.) [17].

Frailty was defined according to the construct previously validated by Fried et al. in the Cardiovascular Health Study [8]. All five components from the original phenotype were retained; however, the metrics used to characterize the frailty criteria were slightly different and defined as follows [9]:

- Shrink—Recent and unintentional weight loss of ≥3 kg in the prior year was identified and body mass index calculated. Participants who answered “yes” for weight loss or had a body mass index < 21 kg/m² were considered to be frail for this component.
- Poor endurance and energy—As indicated by self-report of exhaustion, identified by two questions from the Center for Epidemiological Studies-Depression scale (CES-D) [18]: “I felt that everything I did was an effort” and “I could not get going.” Participants were asked: “How often, in the last week, did you feel this way?” 0 = rarely or none of the time; 1 = some or a little of the time; 2 = a moderate amount of the time; or 3 = most of the time. Participants answering “2” or “3” to either of these questions were considered as frail by exhaustion.
- Slowness—Meets criteria for frailty if time to walk 6 m was ≥8 seconds for height ≤ 173 cm or >7 seconds for height > 173 cm in males, and ≥8 seconds for height ≤ 159 cm or >7 seconds for height > 159 cm in females.
- Weakness—Participants answering “yes” to the following question were categorized as frail for this component: “Do you have difficulty rising from a chair?”
- Low physical activity—A single response was used to estimate physical activity. Individuals who denied doing daily leisure activities such as walking or gardening and/or denied doing some sport activity per week were categorized as physically inactive. Those who reported doing them were considered to be active.

2.3. Laboratory Investigations

Five mL whole blood was drawn from each participant after 12 hours fasting, and was divided into 2 tubes: 1 mL in EDTA-anticoagulated tube for glycated haemoglobin (HBA1C) assay, and 4 mL allowed to clotting in a plain tube. The resulting serum was used for quantitative c-reactive protein (CRP), and the remaining serum was frozen to −70°C till assay of IGF-1. HBA1c was assayed by ion-exchange chromatographic separation and colorimetric detection kit (Biosystems, SA, Barcelona, Spain). Quantitation of CRP was performed by immunoturbidimetric assay using Biosystems CRP-hs kit (Biosystems, SA, Barcelona, Spain). IGF-1 was measured by ELISA using kits supplied by DRG (DRG international, New Jersey, USA). Lipid profile was done in the central laboratory in Ain Shams University teaching hospital.

2.4. Bone Mineral Density

Measured by dual-energy x-ray absorptiometry, at the left femoral neck and lumbar spine, with the use of a Lunar DPX-L densitometer (Lunar).

2.5. Statistical Analysis

Analysis of data was performed by using the 19th version of Statistical Package of Social Science (SPSS).
Description of all data in the form of mean (M) and standard deviation (SD) for all quantitative variables. Frequency and percentage for all qualitative variables. Comparison between quantitative variables was done using t-test to compare two groups. Comparison of qualitative variables was done using Chi square test. Correlation coefficient was also done to find linear relation between different variables using Spearman’s correlation coefficient. Significant level measured according to P-value (Probability), P > 0.05 insignificant, P < 0.05 significant and P < 0.01 highly significant.

3. RESULTS

The clinical characteristics of the study sample are presented in Table 1; frail group had significantly lower levels of triglycerides and LDL. Hs-CRP level and glycated haemoglobin (HBA1C) were significantly higher among the frail group (P < 0.001). BMD and IGF-1 levels were significantly lower in frail group compared with the control group (P < 0.001*, P = 0.05) respectively.

However there is no difference between the two studied groups regarding age, smoking status, total cholesterol, HDL level and the presence of chronic diseases.

Table 2 shows the Pearson correlation analysis between BMD as measured by Femoral and Lumbar T-scores with age, BMI, lipid profile, IGF, and hs-CRP level among frail group. We also found that BMD had a significant positive linear correlation with IGF and negative correlation with age.

4. DISCUSSION

The current study assesses the relationship between bone mineral density, inflammation, IGF-1, and coronary risk factors in frail elderly. The findings of this study demonstrated that frail group had lower BMD, as measured by Femoral and Lumbar T-scores, than the control group. This finding was consistent with previous studies [19,20].

As anticipated, we found that frail participants had significantly higher levels of hs-CRP in comparison to their healthy counterparts. Studies done by Walston et al. & Hubbard et al. had comparable results [21,22]. The results of the current study showed that frail elderly had higher HBA1C levels. The results of Blaum et al. revealed that a HbA1c level of 6.5% or greater in older women was significantly associated with higher likelihood of prefrail and frail status and that BMI, inflammation, and comorbidities did not explain the association [23].

It was found that LDL and TG levels were significantly lower in the frail participants, and there was no association with total cholesterol and HDL levels. A study conducted by Walston et al. had similar results.

Table 1. Clinical characteristics of study participants.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frail group</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>70.03 ± 8.10</td>
<td>69.07 ± 5.93</td>
<td>0.41</td>
</tr>
<tr>
<td>Smoker (%)†</td>
<td>26</td>
<td>78.79</td>
<td>0.06</td>
</tr>
<tr>
<td>BMI*</td>
<td>28.92 ± 6.58</td>
<td>27.91 ± 5.64</td>
<td>0.47</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL*</td>
<td>159.4 ± 49.33</td>
<td>176.9 ± 37.3</td>
<td>0.09</td>
</tr>
<tr>
<td>LDL level, mg/dL*</td>
<td>103.12 ± 42.29</td>
<td>121.7 ± 28.64</td>
<td>0.03*</td>
</tr>
<tr>
<td>HDL level, mg/dL*</td>
<td>31.85 ± 13.45</td>
<td>35.3 ± 6.5</td>
<td>0.19</td>
</tr>
<tr>
<td>Triglycerides level, mg/dL*</td>
<td>112.22 ± 48.06</td>
<td>141.3 ± 42.5</td>
<td>0.006*</td>
</tr>
<tr>
<td>IGF-1*</td>
<td>57.21 ± 17.04</td>
<td>68.2 ± 33.28</td>
<td>0.05</td>
</tr>
<tr>
<td>Hs-CRP*</td>
<td>15.07 ± 7.46</td>
<td>5.17 ± 1.69</td>
<td>0.00*</td>
</tr>
<tr>
<td>HBA1C*</td>
<td>7.03 ± 1.63</td>
<td>5.52 ± 0.56</td>
<td>0.00*</td>
</tr>
<tr>
<td>Lumbar T-score*</td>
<td>−2.13 ± 0.9</td>
<td>−1.02 ± 1.15</td>
<td>0.00*</td>
</tr>
<tr>
<td>Femoral T-score*</td>
<td>−2.31 ± 1.06</td>
<td>−1.08 ± 1.44</td>
<td>0.00*</td>
</tr>
</tbody>
</table>

*Mean ± Standard deviation; †Number of cases (%); BMI = body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein; IGF = Insulin growth factor; hs-CRP = high sensitivity C-reactive protein.

Table 2. Correlation between lumbar & femoral T-scores in the frail group with age, BMI, lipid profile, IGF, CRP & HBA1C.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>R</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>−0.555</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BMI</td>
<td>0.083</td>
<td>0.052</td>
</tr>
<tr>
<td>TG</td>
<td>0.086</td>
<td>0.513</td>
</tr>
<tr>
<td>HDL</td>
<td>0.271</td>
<td>0.590</td>
</tr>
<tr>
<td>LDL</td>
<td>0.249</td>
<td>0.055</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.209</td>
<td>0.109</td>
</tr>
<tr>
<td>IGF</td>
<td>0.283</td>
<td>0.029*</td>
</tr>
<tr>
<td>CRP</td>
<td>0.084</td>
<td>0.522</td>
</tr>
<tr>
<td>HBA1C</td>
<td>0.087</td>
<td>0.507</td>
</tr>
</tbody>
</table>

BMI = body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein; IGF = Insulin growth factor; hs-CRP = high sensitivity C-reactive protein.

They found that low-density lipoprotein cholesterol levels were lower in the frail group (with and without diabetes or CVD), and that the relationships of mean total cholesterol, high-density lipoprotein (HDL), and triglyceride levels with frailty level were weak. This was inconsistent with traditional views of CVD risk factors, but most consistent with the lower lipid levels reflecting and associating with frailty through an inflammation mechanism [21].

The findings of this study showed that frail participants had lower IGF-1 levels; which denotes that frail elderly tend to have lower levels of anabolic hormones than similarly aged non-frail counterparts. This has also been demonstrated in several other studies [24,25]. On the other hand, VanItallie stated that there was no association between frailty and low IGF-1 levels, and sug-
gested that this maybe because it is not yet clear whether, in comparison with their non-frail counterparts, frail individuals consistently manifest larger reductions in IGF-1 [5].

The results of the current study showed a positive correlation between IGF-1 levels and BMD in the frail group. Serum IGF-1 levels were found to be independent predictors of total bone density [26]. In fact, Giustina et al. found that both Growth Hormone and IGF-1 are essential for the development and growth of the skeleton and maintenance of bone mass [27]. Conversely Van den Beld et al., found no correlation between serum IGF-1 concentrations on the one hand and measures of bone mass and body composition on the other [28].

No linear correlation between hs-CRP and other coronary risk factors with the BMD among frail elderly was found in this study. Because frailty is multifactorial and frail elderly display heterogeneous characteristics it is difficult to establish a correlation between various markers of inflammation and frail status, especially in the presence of underlying chronic inflammation.

5. CONCLUSION

This study found that frailty was significantly associated with low BMD, lower TG & LDL levels, higher CRP levels, and higher HbA1c levels. A borderline significance was found between IGF-1 levels and frailty. A positive correlation was found between bone mineral density and IGF-1 in frail. These findings may support the hypothesis that frailty is associated and overlaps with disability. The results of this study also reflect the role that inflammation has to play in the pathogenesis of frailty.

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