Frailty and Cognitive Impairment
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ABSTRACT
Background: frailty is defined as a multifactorial syndrome leading to difficulties in maintaining homeostasis, and vulnerability to stressors. Depression shares many manifestations, risk factors and consequences with frailty. Some studies included cognitive assessment as a component to evaluate frailty. Aim of the work: this study aimed to assess depression and cognition in frail elderly and to assess if depression could be an underlying link between cognitive function and frailty. Patients and methods: this case control study included 102 males and females elderly living in geriatric homes in Cairo and excluded those who were bedridden or had sensory impairment interfering with communication, stroke, Parkinsonism, severe osteoarthritis, or dyspnea on ordinary exertion. All patients were subjected to comprehensive geriatric assessment. Frailty was diagnosed using a modified version of Fried criteria. We used the physical activity metric that was constructed by Avila-Funes.
Conclusion: this study showed that cognitive impairment and depression did not differ between frail and non-frail subjects.

Keywords: frailty, cognitive impairment, depression, elderly, geriatric homes.

INTRODUCTION
Frailty in the elderly is defined as a multifactorial syndrome which occurs due to a decrease in metabolic activities and reserves, difficulties in maintaining homeostasis and vulnerability to stressors, progressing to increased risk for disabilities(1). The prevalence of frailty in community-dwelling elderly populations is approximately 11%; however; this estimate differs considerably depending on how frailty is identified with estimates ranging from 4% up to 59% (2). Depression shares many manifestations, risk factors and consequences with frailty. For example, physical inactivity and fatigue are criteria used to define both frailty and depression (3) (4). In addition, the inclusion of cognitive performance in frailty diagnosis has been discussed in some investigations and in this sense, there were studies that included cognitive assessment as a component to evaluate frailty (5-7). This study aimed to assess depression and cognition in frail elderly and to assess if depression could be an underlying link between cognitive function and frailty.

PATIENTS AND METHODS
This case control study, was conducted at elderly homes, among non-frail versus frail elderly. Inclusion criteria: males and females, 60 years and older living in geriatric homes in Cairo. Exclusion criteria: bedridden subjects or those with sensory impairment interfering with communication, stroke, Parkinsonism, severe osteoarthritis, or dyspnea on ordinary exertion.

The study was approved by local ethical committee of Faculty of Medicine, Ain Shams University. All patients were subjected to comprehensive geriatric assessment. Cognitive function was assessed by mini-mental status examination (MMSE) (8), adjusted MMSE for age and education (9) and Clock Drawing Test (CDT) was performed in those educated(10). Depression was assessed by geriatric depression scale-15 (GDS-15)(11). Cases with frailty were diagnosed with a modified version of the construct described by Fried et al.(12). The original frailty index used the short version of the Minnesota Leisure time activity questionnaire (13) to assess physical activity, while we used the physical activity metric that was constructed by Ávila-Funes(14). Nutritional status among elderly was assessed through Mini Nutritional Assessment (MNA) (15) using the Arabic version (16), functional assessment was done using activities of daily living (ADL) (17), Arabic version (18) and instrumental activities of daily living (IADL) (19). The study was approved by the Ethics Board of Ain Shams University.
Statistical methods

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric while non-parametric data were presented as median with Inter Quartile Range (IQR) and qualitative data were presented as number and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test only when the expected count in any cell was less than 5.

The comparison between two independent groups with quantitative data and parametric distribution were done using Independent t-test while data with non-parametric distribution was compared using Mann-Whitney test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:

- \( P > 0.05 \): Non significant
- \( P < 0.05 \): Significant
- \( P < 0.01 \): Highly significant

Generalized linear regression was done to assess if frailty is a significant predictor of cognitive function or depression separately, with adjustment for possible confounders.

RESULTS

This study included 102 subjects, with mean age of 69.6±6.9 years, among them 48% were females. Frail subjects were older (\( P=0.004 \)), more illiterate (\( P=0.001 \)), malnourished (\( P=0.001 \)) and dependent in ADL and IADL than non-frail subjects (\( P=0.001 \)) (Table 1).

Frail subjects had worse MMSE and CDT scores (\( P=0.001 \)), but not adjusted MMSE (\( P=0.18 \)). There was no difference in GDS-15 score between cases and controls (\( P=0.194 \)) (Table 1). Frailty was not a significant predictor of GDS-15 (\( P=0.18 \)) (data not shown). Frailty was a significant predictor of MMSE (\( P<0.001 \)), however this significance was lost after adjustment for age and education (\( P=0.14 \)) (Table 2). Among controls, 6 subjects were excluded from CDT, and 32 among cases because of educational level. However, frailty was a significant predictor of CDT (\( P=0.001 \)), and this significance was kept after adjustment for age (\( P=0.002 \)) and after adjustment for age and GDS-15 (\( P=0.003 \)) (Table 3).

### Table 1: characteristics of the study groups.

<table>
<thead>
<tr>
<th></th>
<th>Non-frail (N=34)</th>
<th>Frail (N=68)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Values</td>
<td>Values</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>66.94</td>
<td>5.881</td>
<td>70.91</td>
</tr>
<tr>
<td><strong>Male gender</strong></td>
<td>22(64.7%)</td>
<td></td>
<td>31(45.6%)</td>
</tr>
<tr>
<td><strong>Illiterate</strong></td>
<td>4 (11.8%)</td>
<td></td>
<td>32 (47.1%)</td>
</tr>
<tr>
<td><strong>MMSE</strong></td>
<td>28.57</td>
<td>2.253</td>
<td>25.44</td>
</tr>
<tr>
<td><strong>Adjusted MMSE, below cut off</strong></td>
<td>5(14.7%)</td>
<td>18 (26.5%)</td>
<td></td>
</tr>
<tr>
<td><strong>CDT</strong></td>
<td>4.09</td>
<td>1.9</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>GDS</strong></td>
<td>3.77</td>
<td>2.734</td>
<td>4.72</td>
</tr>
<tr>
<td><strong>MNA</strong></td>
<td>25.07</td>
<td>3.29</td>
<td>22.04</td>
</tr>
<tr>
<td><strong>ADL</strong></td>
<td>6.00</td>
<td>.000</td>
<td>5.42</td>
</tr>
<tr>
<td><strong>IADL</strong></td>
<td>7.83</td>
<td>.568</td>
<td>5.62</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>29.1771</td>
<td>4.62634</td>
<td>29.4620</td>
</tr>
</tbody>
</table>

### Table 2: predictors of MMSE:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>B</th>
<th>P value</th>
<th>OR</th>
<th>95% Wald Confidence Interval for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower</td>
<td>Upper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frailty</td>
<td>-3.015</td>
<td>&lt;0.001</td>
<td>.049</td>
<td>.011 .216</td>
</tr>
<tr>
<td>After adjustment for age and education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frailty</td>
<td>-1.949</td>
<td>0.14</td>
<td>.387</td>
<td>.109 1.375</td>
</tr>
</tbody>
</table>

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**DISCUSSION**

The current study showed that advancing age and low level of education were significantly higher in frail than non-frail. This opinion was supported by a systematic literature review that was done by Mello et al. (20), they showed that the prevalence of frailty was increased with advanced age and low schooling. Frailty was a significant predictor of CDT rather than MMSE, this relation was not altered after adjustment for GDS-15. Furthermore, GDS-15 score did not differ between frail and non-frail subjects. As CDT is a reliable test to screen for mild cognitive impairment (MCI) rather than MMSE (21), this highlights the potential link of frailty to MCI rather than dementia. This is not in accordance with results of Kulmala et al. and Jacobs et al., they found association between frailty and worse cognitive performance this was assessed by MMSE as shown by Arevalo-Rodriguez et al. (21) and Kulmala et al. (22). However, the age of their subjects was higher than the current subject’s age, mean age was 82 years old in Kulmala et al. (23) study, 85-90 years old in Jacobs et al. (24) study VS 69.6± 6.9years old in the current study.

On the other hand, Langlois et al. (24) did not find significant difference between frail and non-frail subjects, with mean age of 72 years old, in MMSE. However there was significant difference in executive function and processing speed. Previous reports found executive dysfunctions in MCI subjects (25,26). Raji et al. 2010 and Kim et al. found association between frailty, assessed by the modified version of the Fried and Walston frailty and the cardiovascular health study frailty index consecutively and worse MMSE (27,28). The difference between literatures may be linked to the different frailty criteria. This study showed no significance between depression screened by Geriatric Depression Scale (GDS), in non-frailty and frailty state. This is inconsistent with the findings of Feng et al. (29). In their population-based cohort study they found that the presence of frailty conferred a significant risk of new onset of depression. This can be explained by the fact that he explored the future relation regarding new onset depression in a prospective manner, while our study was a case control retrospective study. Another study reported that depression was not associated with the onset of frailty (30). These contradictory data was explained, even partly, by Lakey et al. (31). They demonstrated a link between antidepressant drugs and increased incidence of frailty in older women. Furthermore, They also declared association between depressed women on antidepressants and chronic comorbidities and poor health, suggesting that an overlap of depression and a comorbid disease could facilitate incident frailty, regardless of antidepressant use. The current study showed statistical significance between malnutrition, non frail and frailty state. This is consistent with a study done by Bonnefoy et al. (32) which concluded that poor nutritional status is one of the main risk factors for frailty. Nutritional status was assessed by the Mini-Nutritional Assessment which is the same screening test we used in the current study. This study showed statistical significance between functional dependence, non-frailty and frailty state. This is supported by a study included the Cardiovascular Health Study (CHS) by Xue et al. (33) that showed a predictive association between frailty and intermediate frailty status with worsened mobility or activities of daily living (ADL) and disability. This is inconsistent with the three cities study that was done by Ávila-Funes et al. (14) in which the association between frailty and incident IADL and ADL disability was not found to be a statistically significant predictor of incident mobility disability. This is due to the exclusion of individuals with a prior mobility disability, which led to the exclusion of the most vulnerable persons, reducing substantially the risk for disability.

**CONCLUSION**

Frailty was associated with worse performance on CDT. Furthermore, GDS-15 score did not differ between frail and non-frail subjects.
REFERENCES