The association between cognitive impairment and physical frailty and their impact on mood, nutrition, and fall risk.

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Introduction

The dramatic increase in number of elderlies worldwide affected their quality of life because of the higher risk of disease, disability, and dementia [1]. One of the major challenges facing elderly population is functional impairment. Frailty is one of these challenges which is defined as a clinical state in which there is an increased vulnerability to stressors, occur due to decreased physiological reserves. Frailty is an important contributor to functional decline and early mortality in older adults, and frailty is not part of the normal ageing process [2].

Frailty is caused by variety of diseases and medical conditions as well as certain demographic factors. Increase number of chronic comorbidities as cardiovascular disease, diabetes, and stroke is associated with increased risk of occurrence of frailty. Other risk factors that could play a role in increased risk of frailty is overweight/obesity, physical inactivity, alcohol use, female gender. Moreover, advancing age more than 85 years old is associated with increased risk. Frailty has adverse effect on general health as it increases risk of falls, disability, hospitalization, delirium, and mortality. The effect of frailty could be reversed if managed in early stages [3,4].

Another condition that occurs among elderly is cognitive impairment which is progressive loss of one or more of cognitive abilities, such as Alzheimer disease (AD) which is also associated with changes in muscle bulk and body composition, strength, and mobility, suggesting that many older persons with AD may be frail. Recently there is another suggestion that changes in the motor system including reduced strength and walking speed and changes in body composition can antedate the onset of dementia, these findings raise the possibility that physical frailty shares a common etiopathogenesis with late-life cognitive impairment [5].

The Consensus Group formed from International Academy on Nutrition and Aging (I.A.N.A) and the International Association of Gerontology and Geriatrics (I.A.G.G) introduced a new term called cognitive frailty which is a complex clinical phenotype that simultaneously captures both physical and cognitive phenotypes without a clinical diagnosis of AD or another dementia. This means that during assessment of frailty they did not concentrate on physical function only but more comprehensive assessment including assessment of cognitive function, it even extended to assess depressive symptoms to capture psychological aspect as well, this comprehensive assessment is done because all these elements together will affect health outcome. Both physical frailty and cognition together have impact on general health causing adverse health outcomes due to combined risk of both including death, disability, fall, hospitalization and incident dementia, which is more than effect of either condition alone [6].

Risk factors for cognitive frailty includes sociodemographic factors (female sex, age, lower education, and poor social support), poor nutritional status, higher total body fat and higher waist circumference, depressive mood, sleep disturbance, Sedentary behavior and lower engagement in physical activities and cognitive activities, increased number of comorbidities, and polypharmacy.

So, the current study aimed at investigating the association between cognitive impairment and physical frailty and their impact on mood, nutrition, and fall risk.

Methods

The study is a cross sectional study, data collected from patients during admission in geriatric hospital Ain shams university hospital. The study population involved 149 elderly aged 60 years or older that agreed to participate in the study. We excluded those who refused to participate in the study, patients with critical or terminal illness.

Each participant was subjected to:

History taking: (personal history, demographic data, past relevant medical history) and physical examination.

Anthropometric measures: including weight and height and BMI calculation.

Frailty assessment: (Through Fried Frailty Criteria) [7].

1. The Fried frailty criteria assesses physical frailty through five criteria: unintentional weight loss; weakness or poor handgrip strength; self-reported exhaustion; slow walking speed; and low physical activity.
2. Participants were categorized as frail if they met three or more of Fried's criteria, pre-frail if they met one or two criteria. While robust if no criteria are met.

Cognitive assessment tool used to diagnose cognitive impairment: Mini-mental state examination [8].

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1. Total score 30
2. Scores for cognitive impairment was according to age and education [9].

Mood assessment Using the Arabic version of geriatric depression scale (GDS) [10].

1. Using, the short form which contains 15 questions.
2. Scores of ≥ 5 suggests depression.

Nutritional assessment by Min nutritional assessment scale-short form [11]

1. Total score of the short form of the scale is 14.
2. Score 12-14 is normal.
3. Score 8-11 at risk of malnutrition.
4. Score 0-7 is malnourished.

Hand grip strength: (using Jamar hydraulic hand dynamometer)

1. Handgrip Strength (HGS) was measured, in kilograms (kg), using Jamar hydraulic hand dynamometer. Measurements were obtained with the participants in the seated position, elbow at 90°, and the handle adjusted to the second position. Then they applied the maximum grip strength for 3 to 5 s using the dominant hand. The procedure was performed three times with an interval of one minute between each measurement. The maximum HGS was identified considering the highest HGS value.

Assessment of risk of fall using: Time Up and Go Test (TUG)

1. Timed Up and Go (TUG) was used to assess mobility. The participants are asked to perform specific sequence of movements: getting up from the chair, walking three meters, turning around, walking back to the chair, and sitting again. Patients were allowed to use their usual walking aid, but no physical assistance is allowed.
2. The shorter time indicates better physical function. The score of ≥13.5 seconds is used as a cut-point to identify those at increased risk of falls [12-14].

Statistical Analysis

Appropriate statistical methods were used to present and analyze the data. Quantitative variables presented as mean and standard deviation. Qualitative data presented as frequency and proportion. Correlation analysis also used to measure how two variables are related. The correlation coefficient (r) tells you the strength and direction of that relationship. It is expressed as a positive or negative number between -1 and 1. The value of the number indicates the strength of the relationship: (r=0 means there is no correlation, r=1 means there is perfect positive correlation, r =-1 means there is a perfect negative correlation). Statistical Package: Data entry and statistical analysis was done on a personal computer using statistical package for social science (SPSS) version 26.0.

Results

The study included 149 participants aged 60 years or older. They were classified according to both frailty status and cognition into 17 (11.41%) cases had Cognitive frailty, 15 (24.16%) had frail but with intact cognition. While 36 (10.07%) case had cognitive impairment without frailty and 81 (54.36%) were robust without cognitive impairment.

Table 1 illustrates demographic data of the cases among each group previously mentioned. For age the oldest age group was among the cases with cognitive frailty with the mean 74.82±10.72, while cognitive impairment without frailty the mean was 69.2±5.26, frail with intact cognition the mean was 70.38±7.5. However, the youngest age group was among robust without cognitive impairment the mean was 67.6±7.05. (P-Value 0.004).

Regarding gender among the participants there were 8 (47.1%) males and 9 (52.9%) females among group with cognitive frailty. While 4 (26.7%) males and 11 (73.3%) females among those with cognitive impairment without frailty. There was 14 (38.9%) male and 22 (61.1%) female among the frail group with intact cognition, and 54 (66.7%) males and 27 (33.3%) females among robust without cognitive impairment. (P-Value 0.004) (Table 1).

Table 1: *baseline demographic and clinical data of different groups.*

		Cognitive frailty N=17	Cognitive impairment without frailty N=15	Frail with intact cognition N=36	Robust without cognitive impairment N= 81	P value
Age		74.82±10.72	69.2±5.26	70.38±7.5	67.6±7.05	0.004*
Gender	**Male**	8 (47.1%)	4 (26.7%)	14 (38.9%)	54 (66.7%)	0.004*
	Female	9 (52.9%)	11(73.3%)	22 (61.1%)	27 (33.3%)	
BMI		26.11±7.14	27.34±6.42	29.12±9.75	30.77±11.36	0.46
DM n=63		7 (11.1%)	6 (9.5%)	23 (36.5%)	27(42.9%)	0.022*
CHF n= 41		2(4.9%)	6(14.6%)	7 (17.1%)	26 (63.4%)	0.15
COPD n=44		3 (6.8%)	1(2.3%)	4(9.1%)	36 (81.8%)	<0.001*
CKD n=39		7 (17.9%)	3(7.7%)	9(23.1%)	20 (50.3%)	0.49
CLD n=33		3 (9.1%)	2 (6.1%)	7 (21.2%)	21 (63.6%)	0.63
Stroke n=20		6(30%)	3 (15%)	8 (40%)	3(15%)	0.001
MMSE		18.52±3.8	22.06±3.7	24.72±2.6	26.46±2.3	<0.001*
GDS		4.0±3.25	4.6±3.54	3.8±2.43	2.7±1.90	0.012*
TUG		32.66±6.8	20.53±8.05	29.45±12.63	18.46±11.78	<0.001*
HGS		5.76±5.04	12.66±5.53	7.50±3.55	17.06±7.2	<0.001*

Body mass index measurement showed limited difference between the groups. As the mean was 26.11±7.14 among group with cognitive frailty, while the mean was 27.34±6.42 among those with cognitive impairment without frailty. The mean was 29.12±9.75 among the frail group with intact cognition and was 30.77±11.36 among robust without cognitive impairment (P-Value 0.46) (Table 1).

The distribution of different chronic comorbid conditions among the studied groups was mentioned in (Table 1). Sixty three cases had DM, distributed as following 7 (11.1%) among group with cognitive frailty, 6 (9.5%) were among those with cognitive impairment without frailty, while 23 (36.5%) among the frail group with intact cognition, and 27(42.9%) robust without cognitive impairment. (P-Value 0.022).

Regarding congestive heart failure (CHF) there were 41 cases, distributed as following 2(4.9%) among group with cognitive frailty, 6(14.6%) were among those with cognitive impairment without frailty, while 7 (17.1%) among the frail group with intact cognition, and 26 (63.4%) robust without cognitive impairment. (P-Value 0.15). For COPD there were 44 individuals with 3 (6.8%) of them in group with cognitive frailty, 1(2.3%) were among those with cognitive impairment without frailty, while 4(9.1%) among the frail group with intact cognition, and 36 (81.8%) robust without cognitive impairment. (P-Value <0.001). Participants with CKD were totally 39 as 7 (17.9%) were among group with cognitive frailty, 3(7.7%) were among those with cognitive impairment without frailty, while 9(23.1%) among the frail group with intact cognition, and 20 (50.3%) robust without cognitive impairment. (P-Value 0.49).

Chronic liver disease in individuals participated in the study were 33 in total, as 3 (9.1%) were among group with cognitive frailty, 2 (6.1%) were among those with cognitive impairment without frailty, while 7 (21.2%) were among the frail group with intact cognition, and 21 (63.6%) were in the robust group without cognitive impairment. (P-Value 0.63). Stroke was also one of the studied comorbid conditions as 20 cases had stroke and they were distributed 6(30%) among group with cognitive frailty, 3 (15%) were among those with cognitive impairment without frailty, while 8 (40%) among the frail group with intact cognition, and 3(15%) were among robust without cognitive impairment. (P-Value 0.001).

Moreover, cognitive assessment by MMSE was illustrated in Table 1. MMSE mean was 18.52±3.8 for individuals with Cognitive frailty, the mean was 22.06±3.7 for those that had cognitive impairment without frailty. While the mean was 24.72±2.6 for frail but with intact cognition, and robust without cognitive impairment had mean 26.46±2.3. (P-Value <0.001). Assessment of depression using GDS showed that the mean was 4.0±3.25 for individuals with Cognitive frailty, those that had cognitive impairment without frailty had mean 4.6±3.54. While the mean was 3.8±2.43 for frail but with intact cognition, and robust without cognitive impairment had mean 2.7±1.90. (P-Value 0.012).

The group with least risk of fall as it had shorter duration of TUG was the robust group without cognitive impairment with mean 18.46±11.78, followed by those that had cognitive impairment without frailty with mean 20.53±8.05. While those that were frail but with intact cognition their mean was 29.45±12.63, and the longest duration was among group with cognitive frailty 32.66±6.8. (P-Value <0.001). Muscle strength assessed by HGS was weakest among cognitive frailty group with mean 5.76±5.04, then mean was 7.50±3.55 among frail but with intact cognition. However, those that had cognitive impairment without frailty had the mean 12.66±5.53, while strongest HGS was among robust without cognitive impairment with the mean 17.06±7.2. (P-Value <0.001).

Table 2 demonstrated effect of both cognitive impairment and physical frailty on occurrence of depression, malnutrition, and risk of fall. Depression was more prevalent among cognitively impaired group without frailty, however there was minimal difference between the other groups in prevalence of depression and this didn't reach level of significance (P-Value 0.205). Although risk of Malnutrition as well as malnutrition was higher in the cognitive frailty group, however it didn't reach level of significance as among cognitive frailty group malnutrition was 5 (29.4%), those at risk were 8 (47.1%),

***Table 2**: Depression, malnutrition, and fall risk assessment among different groups.*

		Cognitive frailty N=17	Cognitive impairment without frailty N=15	Frail with intact cognition N=36	Robust without cognitive impairment N= 81	P value
Depression	Yes	4(23.5%)	6 (40%)	8 (22.2%)	13 (16%)	0.205
N (%)	No	13(76.5%)	9 (60%)	28(77.8%)	68 (84%)	
Malnutrition	Yes	5(29.4%)	5 (33.3%)	5(13.9%)	16 (19.8%)	
N (%)	At risk	8 (47.1%)	4 (26.7%)	14 (38.9%)	17 (21%)	0.07
	No	4(23.5%)	6 (40%)	17 (47.2%)	48 (59.3%)	
Risk of fall a	At risk	3 (17.6%)	11(73.3%)	21(58.3%)	36(44.4%)	
N (%)	No	0	2 (13.3%)	3 (8.3%)	40(49.4%)	<0.001*
	immobile	14(82.4%)	2 (13.3%)	12 (33.3%)	5(6.2%)	

***Table 3:** Correlation between MMSE, GDS, TUG scores and HGS.*

		MMSE	GDS	TUG
HGS	r	0.448	-0.189	-0.375
	P value	<0.001*	0.021*	<0.001*

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while those with no risk 4 (23.5%). For the other groups risk of malnutrition was high among the frail with intact cognition14(38.9%). (P-Value 0.007).

Comparing risk of fall as well as immobility among the different groups revealed that level of immobility was the highest among cognitive frailty group as it involved 14(82.4%) immobile, and the remaining cases had risk of fall 3 (17.6%). However, those who are frail but with intact cognition had more than half of the cases with risk of fall 21(58.3%) case, then 12 (33.3%) were immobile while only 3(8.3%) had no risk. The group with cognitive impairment with no frailty had also high risk of fall 11(73.3%) case, but limited number were immobile cases 2 (13.3%). For robust individuals with no cognitive impairment nearly half had no risk of fall 40(49.4%). (P-Value <0.001).

Hand grip strength is part of physical frailty so Table 3 explained the correlation between scores of HGS among cases in the current study and scores of MMSE, GDS, and TUG. The results showed that there was significant negative correlation between HGS and depression, as well as risk of fall so the more increase in strength of HGS the better the mood (lower scores of GDS), also it is associated with lower risk of fall (lower duration of TUG) (P-Value 0.021), (P-Value <0.001) respectively. Moreover, the table also illustrated the relation of HGS with MMSE scores and showed there was a positive correlation this means that stronger HGS was associated with better MMSE score so better cognition. (P-Value <0.001).

Discussion

Physical frailty and cognitive impairment are conditions that occur among elderly population, both have impact on general health and have adverse outcome on health increasing risk of disability and mortality**.** So, the current study was investigating the association between cognitive impairment and physical frailty and their impact on mood, nutrition, and fall risk.

The participants were classified according to both frailty status and cognition to four groups. Cognitive frailty, cognitive impairment without frailty, frail but with intact cognition, and robust without cognitive impairment.

The oldest age was presented in the cognitive frailty group while the youngest age group was among robust without cognitive impairment**.** A s regard gender there was no difference between male and females as nearly each group had equal number of male and female except robust group were male number exceeded female number. BMI measurement showed limited difference between the groups.

Number of studies had similar results to current study as Sugimoto et al., Xie et al. & Kim et al, [15, 16] all illustrated that older age was associated with a higher prevalence of cognitive frailty. Regarding sex Sugimoto et al. & Ruan et al. demonstrated that women were more likely to be diagnosed with cognitive frailty unlike our study that found no difference between females and males which was like number of studies that also didn't show association of sex with cognitive frailty [16-19].

Different chronic comorbid conditions were investigated among cases this involved DM, CHF, COPD, CKD, CLD, and stroke. Regarding GDS scores the highest score was among individuals with Cognitive frailty, while the lowest scores was among robust without cognitive impairment**.** The least risk of fall as it had shorter duration of TUG was the robust group without cognitive impairment, followed by those that had cognitive impairment without frailty, while the longest duration and higher risk of fall was among group with cognitive frailty**.** Muscle strength assessed by HGS was weakest among cognitive frailty group, while strongest HGS was among robust without cognitive impairment**.**

The number of comorbidities rather than specific diseases was reported by Sugimoto et al. to be associated with cognitive frailty, also the previously mentioned study as well as other studies by Deng et al. & Tseng et al. reported that DM is associated with higher risk of cognitive frailty. The underlying mechanism linking cognitive frailty and diabetes remains unclear. However, possible suggested mechanisms could be associations with insulin resistance or metabolic syndrome. This is different from our study that showed Significant high numbers of DM and COPD among robust cases, but this is probably because large number of cases were in the robust group [20, 21].

While stroke in the current study was higher in the frail group without cognitive impairment followed by cognitive frailty group this was like other studies by Hanlon et al. that reported that Frailty is common after stroke, and those with frailty plus cognitive impairment are at greater risk of mortality than people with an equivalent level of frailty but no cognitive impairment. A study by Hassan et al. suggested possible mechanism involved in explaining association between stroke and post stroke frailty, cognitive decline, and even depression. One of it is the serum levels of post-stroke inflammatory markers including interferons 1, 2, 6, 8, 10, 12 and gamma, C-reactive protein, and tumor necrosis factor, as these markers are associated with muscle and bone volume decline and cognitive affection [22, 23].

Other comorbidities in the study didn't show difference among frail and non-frail group or cognitively impaired groups. Studies on CKD and relation with frailty and cognitive frailty showed variable results. However, study by Luo et al. showed that elderly patients with CKD are often at greater risk of cognitive frailty due to anemia, inflammatory vascular diseases and various metabolic disorders and the prevalence increases among hemodialysis patients. Studies on CLD association with frailty and cognitive frailty showed high prevalence of frailty in individuals with non-cirrhotic NAFLD [24, 25].

Depression was more prevalent among cognitively impaired group without frailty, however there was minimal difference between the other groups in prevalence of depression and this didn't reach level of significance**.** Regarding risk of Malnutrition as well as malnutrition both were higher in the cognitive frailty group, however it didn't reach level of

significance. For the other groups risk of malnutrition was high among the frail with intact cognition.

Depressive mood is reported to be associated with cognitive frailty. Sugimoto et al., Rivan *et al*., Malek et al., investigated the risk factors of cognitive frailty and showed that higher score on the Geriatric Depression Scale which reflect depression is associated with physical frailty and cognitive impairment. This association might be explained by fact that they have common underlying pathophysiological mechanisms [26, 27].

Sugimoto et al., Kwan et al. & Chye et al. demonstrated that Poor nutritional status based on the Mini-Nutritional Assessment, or the Nutrition Screening Initiative was associated with cognitive frailty, which is similar to the current study [28, 29].

Comparing risk of fall as well as immobility among the different groups revealed that level of immobility was the highest among cognitive frailty group, and the remaining cases had risk of fall. However, those that are frail but with intact cognition had more than half of the cases with risk of fall followed by immobile cases. The group with cognitive impairment with no frailty had also high risk of fall, but limited number were immobile. For robust individuals with no cognitive impairment nearly half had no risk of fall and it was significant**.**

The association of cognitive frailty with lower physical performance including a slower timed up and go test, weaker grip strength, slower dual task walking speed, as well as disability in activities of daily living was reported by various studies as Zhao H et al. & Kim et al., this is similar to results of our study that showed higher risk of immobility and fall among cognitive frailty group. Tsutsumimoto et al. & Zhao D et al., also reported significant association between cognitive frailty and falls as well as fall-related fractures [30-33].

The correlation between scores of HGS and scores of MMSE, GDS, and TUG among the current study showed that there was significant negative correlation between HGS and depression, as well as risk of fall so the more increase in strength of HGS the better the mood, also lower risk of fall. Moreover, there was positive correlation between HGS with MMSE, so the stronger HGS was associated with better cognition.

The current study had similar result to the study by Wiśniowska-Szurlej et al. that demonstrated negative correlation between Hand Grip Strength (HGS) and the Timed Up and Go (TUG) test. Moreover, results of the current study had similar outcome to the study Filardi et al. by as regard the positive correlation between HGS and MMSE, and Haagsma et al, found a bidirectional association between HGS and different cognitive functions. Depression is also associated with lower HGS in study by Fastame et al, [34-37].

Conclusion

Increasing age is a risk factor for cognitive frailty. Chronic comorbidity as stroke carries higher risk of physical frailty as well as cognitive frailty. Cognitive frailty that contains both element of cognitive impairment as well as physical impairment had more effect on depression, malnutrition, and risk of fall in comparison to those that were only frail or cognitively impaired only or those who had intact both cognition and physical function. However, the significance mainly was at risk of fall. So, early identification and proper assessment as well as proper intervention should be done to decrease the risk of fall and malnutrition in cognitively frail elderly and treatment of depression.

Ethical Considerations:

An informed consent was obtained from each participant and when needed their caregivers. Participants and their caregivers were oriented by the nature of the study and the data extracted from this study. Approval of the ethical committee of the faculty of medicine, Ain Shams University was taken before beginning of the study (approval FMASU R215/2023).

This study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

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Author Contributions

All authors assisted in the collection of samples and patients' data. NG assisted in manuscript drafting and revision. All authors contributed significantly to the study's conception, design.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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