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Association of cognitive impairment with frailty in elderly: a cross-sectional study on community-dwelling non demented elderly referred to an outpatient geriatric service in Egypt.

KEYWORDS: Frailty, cognitive impairment, non demented elderly

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ABSTRACT *Frailty is highly prevalent in elderly and is associated with adverse health events, but its association with cognitive function is poorly understood.*

Aim; The aim of this study was to examine the association between cognitive function and frailty in community-dwelling non demented elderly.

Methods; 115 non demented elderly, 60 years and older recruited from outpatient geriatric clinic at Al Mansoura General Hospital, Dakahlia, Egypt. Each participant underwent Comprehensive geriatric assessment, assessing frailty status by Edmonton frail scale (EFS) and assessing cognitive function using the mini-mental state examination (MMSE) and Montreal cognitive function test (MoCA).

Results; It was found that Frail older adults had significantly worse performance on the MMSE and the Montreal cognitive function test even after controlling for covariates. According to the MoCA, among the pre-frail 66.67% had cognitive impairment, among the mild frail 94.44% had cognitive impairment, among the moderate and sever frail 100% had cognitive impairment, while according to MMSE, among the mild frail 55.56% had impairment , the moderate frail 56.25% had impairment, while the sever frail 100% had cognitive impairment. It was found that frailty status significantly correlates with age, education, function, and depression and by Linear Correlation Coefficient a significant correlation between frailty and age, function, cognition and depression was found.

Conclusion; we concluded that being frail is associated with worse cognitive performance, as assessed by the MMSE and Montreal cognitive function test.

Recommendations; It is recommended that the assessment of frail older adults should include assessment of their cognitive status.

Background;

With the aging of the population, the prevalence of frailty is expected to increase markedly (Ahmed et al., 2007)

In the past 10 years, the concept of frailty has gained more precise definitions, and there is agreement that it can be considered an age-associated syndrome linked to diminished physiological reserves and lower resistance to environmental stressors. There is also consensus that being identified as frail increases the risk for negative health outcomes, such as immobility, hospitalization and death (Ensrud et al., 2009 and Song et al., 2010). However there is no consensus about the best definition and criteria to identify the syndrome (Abellan et al., 2010 and Walston et al., 2006), and whether cognitive impairment should be added to frailty criteria (Ávila-Funes, 2009 and Song, 2010) . It has been suggested that the current concept of frailty focusing on physical functioning needs to be expanded to include other aspects of health, such as cognitive function (Langloi et al., 2012)

Several studies have reported that frailty is associated with cognitive performance, cross sectional analyses have suggested that frailty and cognitive impairment are associated phenomena. (Fried et al., 2001). Recent longitudinal studies have reported that being identified as frail is a significant predictor of future cognitive decline (Samper-Ternent et al., 2008 and Auyeung et al., 2011) also a predictor to incident dementia and Alzheimer's disease (Buchman et al., 2007 and Buchman et al., 2008) as well as a risk to mild cognitive impairment (Boyle et al., 2010)

Frailty has been shown to better predict adverse outcomes, such as disability, mobility impairment, and hospitalization, once cognitive impairment has been taken into account (Ávila-Funes et al., 2009)

There is still controversy as to whether cognitive impairment is a symptom of frailty or a separate syndrome (Buchman et al., 2008)

So, the aim of this study was to evaluate the association between frailty and cognitive function among community dwelling non demented elderly.

Methods;

Study population were 115 non demented elderly patients 60years and above recruited from outpatient geriatric clinic at Al Mansoura General Hospital ,Egypt, both Males and females , With a consent to participate and able to answer questionnaire during the interview.

Participation was based on informed consent from all participants and approved by the scientific board of Geriatrics and Gerontology department, Faculty of Medicine, Ain Shams University

Each participant was assessed by an experienced clinician and underwent comprehensive geriatric assessment (CGA) in the form of;

a**) Detailed medical history**, and clinical examination.
b) Assessment of cognitive function using the

1) Mini Mental state Examination (MMSE) (Folstein et al., 1975)the MMSE is a brief 30-point questionnaire test that is used to screen for cognitive impairment. It is commonly

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used in medicine to screen for dementia. The MMSE examines orientation, immediate and short-term memory, attention and calculation, language and praxis. An Arabic version was used (El Okl et al., 2002)

Age, education, cultural and socioeconomic background can cause a considerable bias in the MMSE's scores (Crum et al., 1993)So results were correlated with the age and educational level of the participants.

2) Montreal cognitive function test :(MoCA)
The Montreal Cognitive Assessment (Nasreddine et al., 2005) was developed as a quick screening tool for mild cognitive impairment (MCI) and early Alzheimer's dementia. It assesses the domains of attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. The total possible score is 30 points with a score of 26 or more considered normal, for lower educated individuals, 1 point should be added to the total MoCA score for those with less than or equal 12 years of education. The MoCA detected MCI with 90%-96% range sensitivity and specificity of 87% with 95% confidence interval (Nasreddine et al., 2005) we used the Arabic version (Taha & Mohammed 2009) the Arabic MoCA showed 92.3% sensitivity and 85.7% specificity

c) Screening for depression by Geriatric depression scale 15 items (Sheikh & Yesavage 1986), using an Arabic version (Shehata et al., 1998)

d)Functional assessment
By Activities of daily living (ADL) (personal care, clothing, moving, going to the toilet, eating) were measured with the Katz scale (Katz et al., 1963), the total score ranges from 0 to 6 with higher scores means better function (Katz et al., 1963).The Lawton's assessment scale was used to assess abilities in instrumental activities of daily living (IADL), such as giving phone calls, shopping, driving and using money (Lawton & Brody 1969) The scores range from 0 to 8 with higher scores means better function (Lawton & Brody 1969)

e) Assessment of frailty by the Edmonton frail scale (EFS),

The EFS (Rolfson et al., 2006) samples 10 domains;. Two domains are tested using performance-based items: the Clock test (Brodaty & Moore 1997) for cognitive impairment and the 'Timed Get Up and Go' (Podsiadlo & Richardson 1991) for balance and mobility. The other domains are mood, functional independence, medication use, social support, nutrition, health attitudes, continence, burden of medical illness and quality of life (all standard historical items in geriatric assessment) the maximum score is 17 and represents the highest level of frailty, proposed a five-level categorization (robust= 0–4, apparently vulnerable(pre-frail) = 5–6, mildly frail= 7–8, moderately frail= 9–10, severely frail= 11–17 (Rolfson et al., 2006)

The EFS correlated significantly (r= 0.64, $p<0.001$) with the Geriatrician's clinical impression of frailty (based on a 1 hour CGA) and medication count (r= 0.34, $p<0.001$) (Rolfson et al., 2006)

A unique characteristic of the EFS as a clinical frailty instrument is its inclusion of the domain of social support, suggesting an endorsement of the dynamic model of frailty (Rockwood et al., 1994)

The following subjects were excluded from the study:
- Those with sever cognitive impairment as detected by MMSE ≤10 = severe impairment (Folstein et al., 2001)
- Those with either sever hearing, visual and functional impairments preventing them from completing the questionnaires.

All the questionnaires were done with face-to-face interview with each participant, as high illiteracy level was present between the participants and to avoid the problems associated with self-completion.

Statistical analysis;
Statistical presentation and analysis of the present study was conducted, using the chi-square for qualitative data and T- test and ANOVA for quantitative data and Linear Correlation Coefficient, also ANCOVA for analysis of co variants by SPSS V18

Results;
Among the 115 non demented participants, 74.78% (n=86) were 60 to 74 years old, 25.22% (n=29) were 74 to 85 years, mean age was 67.452 ± 5.382, 37.39% (n=43) were males and 62.61% (n=72) were females. The majority of the participants were illiterate 59.13% (n=68), 29.57% (n=34) can read and write and only 2.61(n=3) had 1ry education, 7.83% (n=9) had 2nd education and 0.87% (n=1) had high education.

According to MMSE, 26.96% (n=31) with mean 19.484± 1.313 had cognitive impairment, while according to MoCA 56.52% (n=65) with mean 22.559± 1.580 had cognitive impairment, according to EFS, robust represented 44.35%(n=51) ,pre frail were 20.87% (n=24), while mild frailty represented 15.65% (n=18), Moderate frailty were 13.91%(n= 16) and Severe frailty were 5.22% (n=6) of the studied sample, n=40 had frailty

Table 1 presents baseline characteristics of the participants stratified by frailty status:

It was found that frail participants had more prevalent cognitive impairment by both MMSE and MoCA, and the degree of frailty had an inverse relation to cognition, as according to MMSE, robust participants with mean 24.510±2.436 (n=51) 3.92% had cognitive impairment, among the pre-frail with mean 22.958±2.368 (n=24) 16.67 % had cognitive impairment, and mild frail with mean 20.778± 1.353 (n=18) 55.56% had impairment , the moderate frail with mean 20.188±2.562 (n=16) 56.25% had impairment, while the sever frail with mean 19.500±0.837 (n=6) 100% had cognitive impairment, and this was of statistical significance, as shown in (table1). Also according to the Montreal cognitive test, robust participants with mean 25.490± 1.736 (n=51) 19.61% had cognitive impairment, among the pre-frail with mean 23.542±2.587 (n=24) 66.67% had cognitive impairment, and mild frail with mean 21.444±1.653 (n=18) 94.44% had impairment, the moderate frail with mean 21.063±2.048 (n=16) 100% had impairment, while the sever frail with mean 19.667±1.211 (n=6) 100% had cognitive impairment, and this was of statistical significance, as shown in (table1)

Regarding demographic data and past medical history, it was found that the frail group were older, had greater prevalence of stroke, widow and had lower education than the non frail group.

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Regarding geriatric assessment tools, ADL, IADL, GDS, it was found that those who were frail were more functionally dependent in ADL and IADL and had more depressive symptoms by GDS, and the degree of frailty had an inverse relation to function and education, and a positive relation with age and depression, and this was of statistical significance, as shown in table1.

In order to determine the true correlation between frailty and cognition, we performed multiple regression analyses by analysis of co-variants (ANCOVA) controlling for confounders (age, ADL, IADL, GDS, and education) and we found that there is a significant correlation between frailty assessed by EFS and cognition assessed by both MMSE and MoCA F=11.420, P=0.000.

By Linear Correlation Coefficient, there was a negative significant correlation between EFS scores and MMSE, MoCA, ADL, and IADL while there was a positive significant correlation between EFS scores and age and GDS (table 2).

Comparing the EFS scores of 34 elderly with impaired MoCA and normal MMSE (impaired MoCA 65 elderly minus 31elderly impaired MMSE=34 elderly) with subjects with normal MoCA (n=50) showed significant difference between the 2 groups, as the mean EFS of the cognitively impaired elderly (n=34) was 6.147±2.176, which indicates mild frailty status by EFS, and the mean EFS of the cognitively intact elderly by MoCA (n=50) was 3.106±1.283, robust by EFS (Table 3).

Discussion

In this cross-sectional study of the correlation between frailty status and cognition in a sample of community-dwelling non demented elderly, those who were frail showed a higher percentage of cognitive impairment, as 62.5% of the frail group (mild, moderate and sever) had cognitive impairment by MMSE, also by Montreal cognitive assessment test 97.5% of the frail group had cognitive impairment. Frailty status significantly correlates to cognition as assessed by MMSE and MoCA, even after adjusting for covariates, age, education, ADL, IADL and GDS

The pattern of increased cognitive impairment among the frail elderly was found in previous studies (Ávila-Funes et al, 2009 and Samper-Ternent et al., 2008)

In a sample of 384 elderly in brazil, 38.7% of frail older adults had impaired cognitive impairment by MMSE (Macuco et al., 2012) In another sample of older adults, 85 years and older in Jerusalem, 53% of frail seniors had cognitive impairment by MMSE (Jacobs et al., 2011)

In our study it was found that the degree of frailty had a significant direct negative correlation with cognition as assessed by both MMSE and MoCA. According to the Montreal cognitive test, among the pre-frail 66.67% had cognitive impairment, among mild frail 94.44% had impairment, among the moderate and sever frail 100% had cognitive impairment, also according to MMSE, among the mild frail 55.56% had impairment , the moderate frail 56.25% had impairment, while the sever frail 100% had cognitive impairment, also it was found that the mean of both MMSE and MoCA gradually decreases as the degree of frailty increases, this was also found by Linear Correlation Coffient as there was a negative significant correlation between EFS scores and both MMSE and MoCA scores. This to our knowledge, was not discussed in previous studies, as most studies divide elderly according to the frailty scales they used to non-frail, pre-frail and frail (Macuco et al., 2012, Han et al., 2014 and vila-Funes et al., 2011)while in our study we used the EFS, it has five-level categorization of the frailty status (Rolfson et al., 2006) , and this categorization is not found in most frailty scales used in previous studies, further studies with larger sample size are needed to support our findings.

These findings suggest that both cognitive impairment and frailty status may share similar etiology and pathogenesis.

Cognitive impairment has been reported to occur concurrently with frailty as well as to precede frailty and vice versa (Auyeung et al., 2011)

Weight loss, diminished gait speed, loss of muscle mass and weakness are all key components of frailty and independently associated with AD, the presence of weight loss is predictive of the clinical evolution of AD (Soto et al., 2011)and associated with a subsequent rapid cognitive decline (Billota et al., 2010)

Authors have hypothesized that frailty and impaired cognition may share underlying biological causal explanatory factors, as changes in inflammatory markers, such as the increase in interleukin-6 and in the Tumor

Necrosis Factor alpha (TNF-alpha), and changes in hormones, such as the decrease in Dehydroepiandrosterone (DHEA) and increase in cortisol levels, might be involved in both phenomena Buchman et al., 2007, Auyeung et al., 2011 and Jacobs et al., 2011)

It was found that 31 elderly had cognitive impairment by MMSE and 65 had cognitive impairment by MoCA , so we wanted to know the elderly with impaired MoCA and not impaired by MMSE (65-31=34) and see their frailty status by EFS compared with cognitively intact elderly by MoCA (n=50), we found that their frailty status ,as assessed by the EFS, was significantly worse than those cognitively intact elderly, as the mean EFS of the cognitively impaired elderly was 6.147±2.176, which indicates mild frailty status by EFS, and the mean EFS of the cognitively intact elderly by MoCA was 3.106±1.283, robust by EFS. The MoCA detected 90% of mild cognitive impairment (MCI) subjects, in the mild AD group, the MMSE had a sensitivity of 78%, whereas the MoCA detected 100% (Nasreddine et al., 2005), so from this we can say that the 34 elderly mentioned above had MCI, not even detected by MMSE, and that MCI elderly had mild frailty status. Most studies assessing the relation between cognition and frailty used the MMSE to assess cognitive function (Macuco et al., 2012 and Han et al., 2014) this needs further studies with larger sample size to support this relation. Epidemiological studies have suggested that frailty may indeed be a precocious marker of mild cognitive impairment (Boyle et al., 2010)

Prevalence of frailty status among studied group as assessed by Edmonton frail scale was about 34.8% (mild, moderate and sever frailty).

This high prevalence agree with a cross-sectional study by Billota et al., 2010 according to the Study of Osteoporotic Fractures (SOF) (33%) were "frail". While in another study by Fried et al., 2001, prevalence of frailty was 7% in men and women aged 65 years and older.

This high prevalence in frailty status found in our study can be explained by that our participants are outpatients, it

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was found that frail subjects make large use of health and community services than subjects who are not frail (Rochat et al., 2010) also the low socioeconomic status of the participants, as there is a high prevalence of illiteracy, and this has been associated with frailty (Blaum et al., 2005 and Newman et al., 2001)

It was found that those who were frail were older, with lower education, had more prevalence of stroke, more functionally dependent in ADL and IADL and had more depressive symptoms by GDS, and the degree of frailty had an inverse relation to function, and a positive relation with age and depression. This was also found by Linear Correlation Coefficient that showed a significant negative correlation between the EFS scores and ADL and IADL, and a positive correlation between EFS scores and age and GDS scores.

In our study, A high proportion of the participants had lower education, illiteracy was found in 59.13% and 29.57% can read and write, this might be an explanation for the high cognitive impairment by MoCA, as 56.52% had impaired MoCA, it has been found that older age and less education are independent risk factors for MCI among apparently healthy elderly subjects (Taha & Mohammed 2009)

Study limitations included the small sample, only out patients as well as the cross-sectional approach of our analyses, which is mainly due to lack of cooperation of elderly as the concept of doing scientific research is still not widespread in our community

Study strengths, this study included a broad spectrum of measurements of cognition instead of using just one instrument as the MMSE, we also used the MoCA which is more sensitive than the MMSE in detecting cognitive impairment and assess more cognitive domains (Nasreddine et al., 2005) and both tests were adapted according to educational level which is important in our study due to the high level of illiteracy, also measurement of possible confounding factors as age, depression and functional dependence were taken into account, making it possible to find the true correlation between cognition and frailty.

In conclusion, this study showed that there is a close link between frailty and cognitive function in community dwelling elderly and that as the frailty status worsens cognitive function declines.

Recommendations; Geriatricians need to be aware that frailty and cognitive impairment may be present simultaneously, so it is recommended that the assessment of frail older adults should include assessment of their cognitive status, and intervention protocols need to consider both forms of vulnerability.

DISCLOSURE

There are no conflicts of interest of any kind, no potential conflicts of interest were disclosed, as the research was funded totally by our saving. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors".

1) Characteristics of participants according to Edmonton frail scale (EFS)

			EFS				Chi-Square	
			Normal	Pre	Mid	Moderate	Severe	P-value
SEX	**Male**	N	24	7	7	5	0	0.072
		%	47.06	29.17	38.89	31.25	0.00	
	Female	N	27	17	11	11	6	
		%	52.94	70.83	61.11	68.75	100.00	
		N	31	11	7	3	0	
marital	**married**	%	60.78	45.83	38.89	18.75	0.00	0.005*
	single	N	4	5	1	2	0	0.005*
		%	7.84	20.83	5.56	12.50	0.00	
	widow	N	14	8	10	11	6	
		%	27.45	33.33	55.56	68.75	100.00	
	divorced	N	2	0	0	0	0	
		%	3.92	0.00	0.00	0.00	0.00	
	alone	N	2	1	1	0	0	0.005*
		%	3.92	4.17	5.56	0.00	0.00	
	with family	N	47	22	17	12	6	
		%	92.16	91.67	94.44	75.00	100.00	
	with care giver	N	2	1	0	4	0	
		%	3.92	4.17	0.00	25.00	0.00	
Education	**illiterate**	N	16	17	15	14	6	<0.001*
		%	31.37	70.83	83.33	87.50	100.00	
	can read and write	N	25	5	3	1	0	
		%	49.02	20.83	16.67	6.25	0.00	
	1ry education	N	0	2	0	1	0	
		%	0.00	8.33	0.00	6.25	0.00	
	2ry education	N	9	0	0	0	0	
		%	17.65	0.00	0.00	0.00	0.00	
	high education	N	1	0	0	0	0	
		%	1.96	0.00	0.00	0.00	0.00	

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smoking	**smoker**	N	12	2	3	2	0	0.249
		%	23.53	8.33	16.67	12.50	0.00	
	non smoker	N	39	22	15	14	6	
		%	76.47	91.67	83.33	87.50	100.00	
HTN		N	41	18	13	13	6	0.459
		%	80.39	75.00	72.22	81.25	100.00	
DM		N	10	8	8	5	3	0.224
		%	19.61	33.33	44.44	31.25	50.00	
LCF		N	0	2	2	1	0	0.120
		%	0.00	8.33	11.11	6.25	0.00	
chronic renal impairment		N	1	3	1	1	0	0.408
		%	1.96	12.50	5.56	6.25	0.00	
OA		N	18	13	7	8	1	0.331
		%	35.29	54.17	38.89	50.00	16.67	
COPD		N	3	1	0	2	0	0.416
		%	5.88	4.17	0.00	12.50	0.00	
Cardiac diseases(heart failure- IHD)		N	7	5	5	5	0	0.218
		%	13.73	20.83	27.78	31.25	0.00	
stroke		N	2	3	4	1	3	0.023*
Living arrangement		%	3.92	12.50	22.22	6.25	50.00	
cataract		N	3	4	4	3	0	0.183
		%	5.88	16.67	22.22	18.75	0.00	
MMSE	**Not impaired**	N	49	20	8	7	0	<0.001*
		%	96.08	83.33	44.44	43.75	0.00	
	Impaired	N	2	4	10	9	6	
		%	3.92	16.67	55.56	56.25	100.00	
MoCA	**Not**	N	41	8	1	0	0	<0.001*
	impaired	%	80.39	33.33	5.56	0.00	0.00	
	Impaired	N	10	16	17	16	6	
		%	19.61	66.67	94.44	100.00	100.00	
MMSE		Mean	24.510	22.958	20.778	20.188	19.500	<0.001*
		SD	2.436	2.368	1.353	2.562	0.837	
Montreal		Mean	25.490	23.542	21.444	21.063	19.667	<0.001*
		SD	1.736	2.587	1.653	2.048	1.211	
age		Mean	65.137	66.917	69.278	72.563	70.167	<0.001*
		SD	4.191	6.413	4.522	3.829	4.665	
ADL		Mean	6.000	5.833	5.278	4.438	2.167	<0.001*
		SD	0.000	0.381	0.752	1.094	2.483	
IADL		Mean	7.980	7.458	6.500	5.250	3.000	<0.001*
		SD	0.140	0.658	1.043	1.183	1.265	
GDS		Mean	3.000	3.667	4.056	4.500	5.333	<0.001*
		SD	0.872	1.007	0.938	0.966	1.033	

MoCA= Montreal cognitive assessment test, MMSE= mini mental state examination, HTN= hypertension, DM= diabetes mellitus, LCF= liver cell failure, OA= osteoarthritis, COPD= chronic obstructive pulmonary disease ,ADL= activities of daily living, IADL= instrumental activities of daily living, GDS=geriatric depression scale

Table 2) Linear correlation coefficient between EFS scores and different variables

	Edmonton frail scale	
	r	P-value
MMSE	-0.622	<0.001*
MoCA	-0.687	<0.001*
Age	0.438	<0.001*
ADL	-0.677	<0.001*
IADL	-0.815	<0.001*
GDS	0.615	<0.001*

MMSE= mini mental state examination, ADL= activities of daily living, IADL= instrumental activities of daily living, GDS= geriatric depression state., MoCA= Montreal cognitive assessment test

Table 3) comparison between the subjects with impaired Montreal cognitive test and normal MMSE (n=34) and the subjects with normal MoCA (n=50) as regards EFS scores

	Impaired MoCA and normal MMSE n=34		**Normal cognition by MoCA n=50**			
	Mean	**SD**	**Mean**	**SD**	**t**	**P-value**
EFS	6.147	2.176	3.160	1.283	-7.905	0.000

MoCA= Montreal cognitive assessment test, MMSE= mini mental state examination, EFS= Edmonton frail scale.

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REFERENCE

Abellan, v. K. G., Rolland, Y., Houles, M. et al (2010). The assessment of frailty in older adults. Clinics in Geriatric Medicine, 26, 275. | Ahmed, N., Mandel, R. & Fain, M. J. (2007). Frailty: an emerging geriatric syndrome. American Journal of Medicine, 120, 748–753 | Auyeung T W, Lee J S, Kwok T. and Woo J. (2011). Physical frailty predicts future cognitive decline – a four-year prospective study in 2737 cognitively normal older adults. Journal of Nutrition, Health and Aging, 15, 690–694. | Ávila-Funes, J. A. et al. (2009). Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: the Three-City Study. Journal of the American Geriatrics Society, 57, 453–461. | Ávila-Funes J A, Pina-Escudero S D, Aguilar-Navarro S .et al (2011) Cognitive impairment and low physical activity are the components of frailty more strongly associated with disability. the Journal of Nutrition, Health & Aging ,volume 15, Number 8 | Billota C, Bowling A, Case A ., et al(2010): Dimensions and correlates of quality of life according to frailty status: a cross-sectional study on community-dwelling older adults referred to an outpatient geriatric service in Italy. Health and Quality of Life Outcomes 8:56 | Blaum CS, Xue QL, Michelon E, et al. (2005)The association between obesity and the frailty syndrome in older women: The Women's Health and Aging Studies. J Am Geriatr Soc;53(6):927-934. | Boyle P A, Buchman A S, Wilso R S, Leurgans S E and Bennett D A (2010). Physical frailty is associated with incident mild cognitive impairment in community-based older persons. Journal of the American Geriatrics Society, 58, 248–255. | Buchman A. S, Boyle P. A., Wilson R. S., Tang Y. and Bennett, D. A. (2007). Frailty is associated with incident Alzheimer's disease and cognitive decline in the elderly. Psychosomatic Medicine, 69, 483–489. | Buchman A S, Schneider J A, Leurgans S and Bennett DA (2008). Physical frailty in older persons is associated with Alzheimer disease pathology. Neurology, 71, | 499–504. | Brodaty H and Moore CM.(1997) The clock drawing test for dementia of the Alzheimer's type: a comparison of three scoring methods in a memory disorders clinic. Int J Geriatr Psychiatry ; 12: 619–27. | Crum RM, Anthony JC, Bassett SS, Folstein M.F.(1993) Population-based norms for the Mini-Mental State Examination by age and educational level. JAMA. 12,269(18):2386-91 | Cronin-Stubbs D, Beckett LA, Scherr PA, et al (1997) Weight loss in people with Alzheimer's disease: a prospective population based analysis. BMJ 314 : 178-9 | El Okl MA et al. (2002),Prevalence of Alzheimer dementia and other causes of dementia in Egyptian elderly. MD thesis, Faculty of Medicine, Ain Shams University | Ensrud KE, Ewing SK, Cawthon PM et al (2009) Osteoporotic Fractures in Men Research Group. A comparison of frailty indexes for the prediction of falls, disability, fractures, and mortality in older men. Journal of the American Geriatrics | Society 57: 492-498. | Folstein MF, Folstein SE, McHugh PR., (1975), ""Mini-mental state". A practical method for grading the cognitive state of patients for the clinician". Journal of psychiatric research,12 (3), 189–98. | Folstein M F, Folstein S E, McHugh P R, & Fanjiang, G. (2001). Mini-Mental State Examination User's guide. Odessa, FL: Psychological Assessment Resources. | Fried LP, Tangen C, Walston J et al (2001) for the Cardiovascular Health Study Collaborative Research Group Frailty in older adults: Evidence for a phenotype. The Journals of Gerontology, 56A:M146-156. | Han ES, Lee Y and Kim J (2014) Association of cognitive impairment with frailty in community-dwelling older adults. InternationaL Psychogeriatrics , 26:1, 155–163 | Jacobs J M, Cohen A, Ein-Mor E et al (2011). Frailty, cognitive impairment and mortality among the oldest old. Journal of Nutrition Health and Aging, 15, 678–682. | Katz S, Ford AB, Moskowitz RW et al (1963): Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. JAMA; 21(9): 185:914-919. | Langlois F, Vu T T M, Kergoat M et al (2012). The multiple dimensions of frailty: physical capacity, cognition, and quality of life. International Psychogeriatrics, 24, 1429. | Lawton MP and Brody EM (1969): Assessment of older people: Self-maintaining and instrumental activities of daily living. The Gerontologist; 9(3): 179-86. | Macuco CRM, Batistoni SST, Lopes A, et al. (2012) Mini-Mental State Examination performance in frail, pre-frail, and non-frail community dwelling older adults in Ermelino Matarazzo, São Paulo, Brazil. International Psychogeriatrics, 24(11): p. 1725–1731 | Nasreddine ZS, Phillips NA, Bédirian V et al (2005)The Montrealcognitive assessment: a brief screening tool for mild cognitive impairment. JAGS; 53: 1–5. | Newman AB, Gottdiener JS, Mcburnie MA, et al (2001)Cardiovascular Health Study Research Group. Associations of subclinical cardiovascular disease with frailty. J Gerontol A Biol Sci Med Sci ;56(3):M158-M166 | Podsiadlo D and Richardson S.(1991) The timed 'Up and Go': a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc ; 39: 142–8. | Rochat S, Cumming RG, Blyth F, Creasey H, Handelsman D, Le Couteur DG, et al (2010) Frailty and use of health and community services by community-dwelling older men: the Concord Health and Ageing in Men Project. Age Ageing , 39:228-233. | Rolfson DB, Majumdar SR, Tsuyuki RT et al.(2006) Validity and reliability of the Edmonton Frail Scale. Age Ageing ;35:526–569. | Rockwood K, Fox RA, Stolee P et al (1994) Frailty in elderly people: an evolving concept. Can Med Assoc J ; 150: 489–95. | Samper-Ternent R., Al Snih S, Raji, M. A., Markides, K. S. and Ottenbacher, K. J. (2008). Relationship between frailty and cognitive decline in older Mexican Americans. Journal of the American Geriatrics Society, 56, 1845–1852 | Shehata AS, El-Banouby MH, Mortagy AK (1998), Prevalence of depression among Egyptian geriatric community. Master thesis, Faculty of Medicine, Ain Shams University | Sheikh JI and Yesavage JA (1986), Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. Clinical Gerontology. A Guide to Assessment and Intervention, 165-173, NY: The Hawarth Press. | Song X, Mitnitski A, Rockwood K (2010). Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. Journal of the American Geriatrics Society 58:681-687 | Soto ME, Secher M, Gillette-Guyonnet S, et al (2011) Weight Loss and Rapid Cognitive Decline in Community-Dwelling Patients with Alzheimer's Disease. J. Alzheimers Dis [Epub ahead of print] | Song X, Mitnitski A and Rockwood K. (2010). Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. Journal of the American | Geriatrics Society, 58, 681–687. | Taha T A , Mohammed M E (2009) Montreal Cognitive Assessment Arabic version: Reliability and validity prevalence of mild cognitive impairment among elderly attending geriatric clubs in Cairo. Geriatr Gerontol Int 9: 54–61 | Walston, J. et al. (2006). Research agenda for frailty in older | adults: toward a better understanding of physiology and etiology. Summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. Journal of the American Geriatrics | Society, 54, 991–1001 | Yassuda M, Lopes A, Cachioni M, et al. (2012) Frailty criteria and cognitive performance are related: Data from the Fibra study in Ermelino Matarazzo, Sao Paulo, Brazil. The journal of nutrition, health & aging, 16(1): p. 55–61. |