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Relationship Between Coronary Risk Factors, Bone Mineral Density and Carotid Circulation Among frail elderly

KEYWORDS: Coronary risk factors, frailty, osteoporosis, carotid intima–media thickness.

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ABSTRACT *Background& aim of the work: To study the relation between bone mineral density, coronary risk factors and frailty in elderly and also the changes in carotid intima–media thickness(CIMT) and their relation to other comorbidities in frail elderly. Methods:104 elderly patients, who were assigned to: Group A (52 frail participants) and Group B (52 non-frail participants) diagnosed by Fried's criteria as applied by Avila-Funes et al., 2008. Assessment of all participants included: History, examination, comprehensive geriatric assessment, measurement of BMD by DEXA scan, measurement of CIMT by carotid ultrasound and laboratory investigations including; low density lipoprotein (LDL), high-density lipoprotein(HDL), total cholesterol, and triglycerides.Results: The frail group had significantly lower levels of HDL, CIMT was significantly higher ,BMD was lower when compared with the control group. Frail cases also had higher ADL & IADL assistance, were more depressed with increasing cognitive impairment and mean number of associated comorbidities. CIMT was positively correlated to age and number of chronic diseases.*

Conclusion: Frailty is associated with changes in markers like HDL which may suggest its use in identification of frailty. CIMT was positively correlated to age & the number of comorbidities. These findings may support the hypothesis that frailty is associated and overlaps with disability.

Introduction:

Frailty is closely linked to advanced age and disease-related processes. It is increasingly used as a marker of vulnerability, identifying individuals with a diminished capacity to effectively compensate for external stressors(1,2).

Central to its definition has been the concept that multiple systems must be involved. Dysregulation of neuromuscular, endocrine, and immune systems with aging were suggested . Low-level inflammation, sarcopenia, osteopenia, and nutritional changes are diagnosed, and often the presence of contributing factors of chronic and acute illness, and environmental stresses could be found(3).

Frailty and cardiovascular disease (CVD) share a common biological pathway, CVD may accelerate its development and frailty is identified in up to half of patients with CVD (4).Newman et al. suggested that the relationship between frailty and CVD may be explained by finding that pathological processes can lead to subclinical end organ damage, decreasing total physiologic reserve. Other possibility is that atherosclerosis, a state of chronic inflammation, may result in a catabolic state contributing to frailty, and this study found that CIMT was higher among frail elderly (5).

Osteoporosis appears to be a good marker of frailty and is a sign of vulnerability. Frail subjects seem to be particularly exposed to hip fracture , the major complication confronting elderly subjects (6).

CIMT is a well-established surrogate of atherosclerosis and has been associated with both prevalent and incident CVD.(7-8) Furthermore, CIMT has also been used as a surrogate endpoint to monitor the efficacy of therapy against atherosclerosis in clinical trials.(9-11)

Atherosclerosis of a single coronary artery in patients ≥ 65 years was associated with a CIMT of approx 0.9 mm, 2-vessel disease with a CIMT of 1.2 mm, and 3-vessel disease with a CIMT of 1.3 mm. (12)

Aim of the study:

To study the relation between coronary risk factors, carotid circulation, and bone mineral density and frailty, also the changes in carotid intima –media thickness and their relation to other comorbidities in frail elderly.

Patients and methods:

1-Study Design and Setting

The study is a Case-control study, including 104 Elderly male and female participants aged ≥ 60 years old. They were recruited from Ain Shams University hospital, Geriat-

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ric inpatient wards and outpatient clinics during the period between January 2011 and December 2012. They were divided into two groups:

Cases Group:
52 frail elderly ≥60 years diagnosed by modified Fried's criteria(13), applied by Avila-Funes et al (14). They were considered to be "frail" if they had ≥ 3 components among the five diagnostic criteria for frailty .

Controls Group:
52 elderly ≥60 years. They are not frail or have ≤ 2 of frailty diagnostic criteria .

2- Collection of data:
An informed consent has been obtained from all participants. Any patient who refused to participate in the study, was taking anti- inflammatory drugs like steroids, aspirin and statins or patients who suffered from acute infection, were excluded from this study.

Each patient then underwent comprehensive geriatric assessment in the form of detailed history and physical examination, cognitive function assessment by Minimental status examination (MMSE) (15), Arabic version (16) , Geriatric depression scale 15 items (GDS-15) (17)was used to screen for depression with the Arabic version (18), functional assessment using Activities of daily living (ADL) (19) , Arabic version (20) , and Instrumental activities of daily living (IADL) (21), Arabic version (22).

Frailty was defined according to Fried et al. construct in the Cardiovascular Health Study (13). All five components from the original phenotype were retained; however, the method used to characterize the frailty criteria was defined by Avila-Funes et al (14) which was slightly different (23,24).

3-Laboratory Investigations:
Lipid profile was done in the central laboratory in Ain Shams University hospital.

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.

5-Carotid ultrasound:
To quantify the degree of thickening of the carotid artery walls, bilateral measures of intimal–medial thickening (IMT) of the common carotid artery, using B-Mode Ultrasound.

Measurements were made in a 1 cm segment in the distal CCA, 1 cm of the carotid artery bifurcation, and 1 cm in the proximal ICA of both right and left sides using a Biosound 2000IISA system (8 MHz transducer, axial resolution_0.10 mm, and an effective lateral resolution in the focal plane slightly better than 1.0 mm). Maximum CIMT measures were obtained at 1 mm increments. In addition, information about the presence or absence of plaque was also recorded. The presence of plaque was judged by trained readers using the presence or absence of two of the following three criteria: abnormal wall thickness (defined as CIMT 0.8 mm *Kalva & Mueller 2008),* abnormal shape (protrusion into the lumen and loss of alignment with adjacent arterial wall boundary), and abnormal wall texture (brighter echoes than adjacent boundaries).(25-26) For the purpose of this analysis, both the mean far-wall IMT of the right and left carotid arteries and information about the presence or absence of plaque in each subject were used. The reproducibility of CIMT and plaque measurements has been published previously. (25,27,28). Overall, of all the segments, the CCA measurements had the best coefficient of variation, although not the best reliability coefficient.

Data Management:
Analysis of data was performed by using the 12th version of Statistical Package for Social Science (SPSS).Description of all data in the form of mean (M) and standard deviation (SD) for all quantitative variables was done. Frequency and percentage was done for all qualitative variables. Comparison between quantitative variables was done using t-test to compare two groups and ANOVA to compare more than two groups. Comparison of qualitative variables was done using the Chi-square test.Correlation coefficient also was used to find linear relation between different variables using r-test or Sperman correlation co-efficient.Significant level measured according to P value, P>0.05 is insignificant, P<0.05 is significant and p<0.01 is highly significant.

Results:
The mean age of cases was 69 whereas it was 66.8 for controls. There was no statistically significant differences between cases and controls regading: age , gender & smoking habits , cases were significantly more illiterate(P<0.01).

Frail cases had higher mean number of associated chronic disease than controls. Cases were more assisted & dependent in ADL & IADL than controls which is highly significant(P<0.01). Also there was higher prevalence of depression & cognitive impairment among cases and the differences are highly significant (P<0.01).

There was a significantly higher percentage of spinal and femoral neck osteoporosis among cases compared to controls (P<0.01). Frail cases had higher CIMT and lower HDL levels than controls and these differences were statistically significant

Table(1):Characteristics of study participants as regards studied parameters.

Mean		Cases		Control		P
		SD	Mean	SD		
Cholesterol		162.2	36.6	159.0	41.9	0.6
Triglycerides		127.1	56.2	122.4	40.0	0.6
LDL		100.9	33.1	111.4	32.1	0.1
HDL		38.3	14.0	44.8	16.2	0.03*
CIMT		1.29	0.3	0.7	0.2	0.000**
Lumber DEXA	Normal	No.	%	No.	%	P
		14	26.9	36	69.2	0.000**
	Low BMD	38	73.1	16	30.8	
Femoral DEXA	Normal	8	15.4	40	76.9	0.000**
	Low BMD	44	84.6	12	23.1	

***P<0.05 significant **P<0.01 highly significant**

Table(2):Correlation betweenCIMT & studied parameters

	CIMT
Age	R=0.420 P=0.002**
MMSE	R=0.723 P=0.50
GDS	R=0.556 P=0.084
T.cholesterol	R=0.153 P=0.27

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Triglycerides	R=0.041 P=0.77
LDL	R=0.139 P=0.32
HDL	R=0.887 P=0.02
Number of chronic diseases	R=0.389 P=0.004**
Dexa (femur)	R=0.460 P=0.001**
Dexa (spine)	R=0.291 P=0.036
ADL	R=0.199 P=0.1
IADL	R=0.060 P=0.6

P<0.05 significant P<0.01 highly significantDiscussion:
Frailty has been recognized as a common clinical syndrome with decrease physiologic reserve and is associated with a higher morbidity and mortality (29).

Applying routine comprehensive geriatric assessments showed that frail patients had higher levels of ADL and IADL dependence in addition to higher grades of depression and cognitive impairment and also a higher mean number of associated chronic diseases which was consistent with *Espinoza et al* who stated that frailty is associated with multiple impairment and comorbidities (30).

Our study showed that frail elderly had higher prevalence of carotid artery stenosis (as a reflection of atherosclerosis burden) & higher CIMT than non-frail controls, this agrees with the work of *Newman et al* where Carotid wall thicknesses were strongly related to frailty level(5).

Regarding lipid profile, current study showed that frail participants had significantly lower mean HDL levels , higher mean cholesterol & triglycerides (but it wasn't significant statistically), which agrees with Landi et al 2008 who stated that low level of HDL is associated with frailty & that HDL level can be used as a marker of frailty & poor prognosis among the oldest elderly.Our study also found that frail patients had higher prevalence of lumbar spine & femoral neck osteopenia & osteoporosis, these results perfectly matches those of *Frisoli et al* (31).

Finally our study showed significant positive correlation between CIMT and age of patients which was also proved by *Youn YJ et al* (32). It has been also positively correlated to the number of associated chronic diseases, which goes with many studies, like that done by *O'Leary et al* finding positive linear correlation between CIMT and vascular events and that an increased CIMT (>1 mm) at baseline was related to a 2.2-fold increased risk of myocardial infarction(33).

Conclusion:
This study found that frailty was significantly associated with low BMD, lower HDL. CIMT was also positively correlated to age & to the number of comorbidities. These findings may support the hypothesis that frailty is associated and overlaps with disability. The results of this study also reflect the role atherosclerosis has to play in the pathogenesis of frailty.

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All authors contributed to the work and agreed to the work content.

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