The Journal of Nutrition, Health & Aging©
Volume 16, Number 8, 2012

FRAILTY IS ASSOCIATED WITH LONGER HOSPITAL STAY AND INCREASED MORTALITY IN HOSPITALIZED OLDER PATIENTS

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Abstract: *Introduction:* With the onset of frailty, there is often a rapid, progressive, and self- perpetuating downward spiral towards death. Frailty has enormous impact on acute hospital care and has been shown to be a more effective predictor of mortality than conventional clinical measures. *Methods:* Hospitalized older patients admitted in medical wards at a teaching public hospital were studied to determine the prevalence of frailty; its association with anemia, congestive heart failure, clinically active tuberculosis and cognitive impairment; as well as its impact upon short-term outcome. *Results:* A total of 250 older hospitalized patients were included, and their frailty status was assessed using Fried's criteria. Of these, 83 (33.2%) patients were frail, with frailty found to be significantly associated with increasing age. A lower mean level of haemoglobin (p, 0.002), higher chance of congestive heart failure (p, <0.001), lower mean MMSE score (p, <0.001), was found in frail older patients. Frail subjects had a higher median hospital stay. There were total of 5 deaths, all among the frail group. *Conclusion:* Our study showed that almost a third of hospitalized older patients are frail, and have anemia, higher frequency of CHF, cognitive impairment, longer hospital stay and higher mortality.

Key words: Frailty, elderly, in-hospital mortality.

Introduction

First used by Brocklehurst (1), the term frailty, analogous to "failure to thrive" in young children (2) has been accepted as an important geriatric syndrome, supported by an operational definition, validation of a set of criteria, and evidence for its syndromic nature. It identifies older persons at increased risk of morbidity, mortality, compromised autonomy and is identified by decreased reserves in multiple organ systems, and may be initiated by disease, lack of activity, inadequate nutritional intake, stress, and/or the physiologic changes of aging (3). Often developing insidiously with increments of decline precipitated by acute events it progresses gradually, leading to increased comorbidity and disability over time.

Evolving definitions improved understanding of molecular and physiological declines in frail older adults has encouraged investigators from many disciplines to contribute to this emerging field of research. In 2003, the Institute of Medicine identified frailty as 1 of 20 priority areas, selected from several hundred potential candidates, in need for improvement in health care quality (4).

Once the community dwelling older person becomes frail, there is often a rapid, progressive, and self-perpetuating downward spiral toward failure to thrive and death. The term primary frailty is used when the state is not associated directly with a specific disease; secondary frailty when the syndrome is associated with a known comorbidity (5). It has been shown that 3-7% of older people are frail in developed countries (6) and have 1.2 to 2.5-fold increase in their risk for falls, decreased mobility, worsening activities of daily living (ADL), institutionalization, and death (7). Frailty has enormous impact on acute hospital care in older patients. Not only have measures of frailty been found more effective predictors of outcome (principally mortality) than conventional clinical measures such as diagnosis, specific disease severity or age (8), but also newer parameters to define it in acute care settings have emerged in recent years (9, 10).

According to the last census, India is home to more than 100 million older people. Though this figure is expected to grow to 170 million in 2025 and with increase in life expectancy from the current 66 to 72 years, yet information on health status and medical needs for this group is limited. Not only are older persons riddled with several comorbid conditions that are often neglected but also 10% of them get hospitalized each year and several more seek health care (11, 12). Approximately half of the beds in acute hospital care are presently occupied by older patients. Among these, majority are frail inpatients at high risk of adverse clinical outcomes (13). Yet, standards for institutional and outpatient care for older persons remain poorly established.

Limited data indicates prevalence of frailty to be higher in hospitalized older patients as compared to the community dwelling population (14). Measures of frailty in some populations have been shown to be more effective predictors of mortality than other conventional clinical measures (8, 15). Those showing signs of frailty are at particular risk of adverse outcomes in need of specific and effective intervention. The concept of the inpatient unit for frail older people has developed to include stroke and hip units, nurse-led units, geriatric assessment and acute care for elders (ACE) units (16).

The present study was designed to assess the prevalence of frailty among hospitalized older patients, and attempts to understand its dynamics and its association with short term mortality in acute care settings. The current study also attempts to determine the association of frailty with some predefined diseases, including tuberculosis, hypertension, diabetes and

Received August 1, 2011
Accepted for publication November 9, 2011

congestive heart failure.

Methods

The current prospective study was done on older patients hospitalized in medical wards at a public teaching hospital. A total of 250 serial patients more than 60 years of age admitted to medical wards were included in the study. Those who were seriously ill including those on mechanical ventilation, life support systems or comatose were excluded from the study. Patients with obvious neurological deficit such as stroke or Parkinson's disease were also excluded from the study since these could not be assessed for frailty.

After obtaining clearance from the Institutional Ethics Committee 250 subjects were included in the study after they gave a written informed consent. Besides a detailed history and physical examination, the study subjects were assessed using Fried's frailty diagnostic criteria7. This includes assessment for unintentional weight loss of greater than 4.5kg in the last year or body mass index (BMI) less than 18.5; walking speed; average grip strength measured in the dominant hand using a hand held dynamometer, set at level 2; self reported exhaustion based on two questions from the Center for Epidemiological Studies – Depression Scale (CES-D) and low physical activity based on the modified Minnesota leisure time physical activity questionnaire and involved self-report regarding whether a person has performed these specific activities in the prior week along with the frequency and duration of these activities (17). The study subjects also underwent cognitive status assessment using Folstein's Mini Mental Status Examination. The patients were also assessed for presence of tuberculosis, congestive heart failure (CHF), diabetes and hypertension.

Anemia was diagnosed as per WHO criteria (18). Anemia was considered, when haemoglobin was less than 13 g/dL for males and 12 g/dL for females. Diagnosis of CHF was made clinically using Framingham criteria for CHF (19). Clinically active tuberculosis was diagnosed considering compatible clinical features, radiological features, microbiological or histological features including AFB smear positive from appropriate specimen, or culture / PCR positive from appropriate specimen, or Granuloma / AFB stain positivity demonstrated in FNAC / biopsy from appropriate tissue. Response to ATT during hospital course and biochemical markers like ADA was also considered in appropriate setting. All patients underwent cognitive status assessment by using Folstein's Mini Mental Status Examination (20). Patients having score less than lower limit of normal as per their educational level were considered to have cognitive impairment (21). Short-term outcome of hospitalized frail elderly patients was classified as discharge, death or length of hospital stay.

The data analysis was done by the SPSS software for windows version 11.5. Quantitative variables were reported as mean ± standard deviation or median with range as appropriate and were compared by Student t-test or Mann-Whitney test respectively. Qualitative variables were reported as percentages, and were compared by chi-square test, or by Fischer's exact test, as appropriate. A p value less than 0.05 was considered statistically significant.

Results

Two hundred and fifty acutely ill subjects older than 60 years of age, hospitalized in medical wards who consented to participate in the study were included. The mean age of the subjects was 66.43 + 6.27 years. 154 (61.6%) were males and 96 (38.4%) patients were females. In our study, 83 (33.2%) were found to be frail as indicated by the criteria of Fried et al. Of 154 males, 56(36.4%) were frail, while among 96 females, 27(28.1%) were frail.

The baseline characteristics of the study subjects have been shown in table 1.

Table 1
Baseline characteristics of study participants

Characteristics	Male (n=154)	Female (n=96)	Total (n=250)
Age, mean± SD	67.13 ± 6.01	65.31 ± 6.53	66.43 ± 6.27
Current or past smokers, n (%)	109 (70.8%)	13 (13.5%)	122 (48.8%)
Diabetes mellitus, n (%)	29 (18.83%)	22 (22.9%)	51 (20.4%)
Hypertension, n (%)	50 (32.47%)	46 (47.92%)	96 (38.4%)
Hb, mean± SD	11.25 ± 2.37	10.99 ±1.82	11.15 ± 2.17
Anemia, n (%)	118 (76.6%)	72 (75%)	190 (76%)
MMSE Score, mean± SD	26.86 ± 3.54	24.08 ± 4.22	25.79 ± 4.04
Years of Schooling (median with range)	8 (0-20)	0 (0-18)	5 (0-20)

Data is shown in mean (= Standard deviation) or in number (percentage) wherever applicable. Hb = hemoglobin; HT = hypertension; MMSE = Mini Mental Status Examination.

The most common primary indication for hospitalization among older individuals was acute febrile illness including lower respiratory tract infection (LRTI), urinary tract infection (UTI), and other short febrile illnesses like enteric fever, viral fevers, malaria etc. The number of individuals positive for each specific criterion of frailty has been shown in table 2.

Table 2
Number of subjects with individual parameters for frailty (n = 250)

Criteria	No of patients positive	% of patients positive
Weight loss	58	23.2 %
Walking speed	99	39.6 %
Grip strength	233	93.2 %
Exhaustion	91	36.4 %
Low physical activity	42	16.8 %

Frailty was significantly correlated to advancing age and there was a linear increase in the subset of frail patients in older age groups (correlation coefficient r, 0.128; p, 0.44). While 34 (28.8%) subjects in the age group between 60-64 years were

identified to be frail, as many as 16 (41%) of those over 75 years were found to be frail.

Table 3 shows the comparison between frail and non-frail participants. There was no significant difference between frail and non-frail group among baseline characteristics. However, a significantly longer hospital stay was noted in the frail group besides a higher incidence of cognitive impairment (p, <0.001), congestive heart failure (p, <0.001), lower mean MMSE score and level of haemoglobin. No death was noted in the non-frail group. History of past or current smoking and current active tuberculosis were also seen to be more in the frail older individuals but the difference did not reach significant levels (p, 0.06).

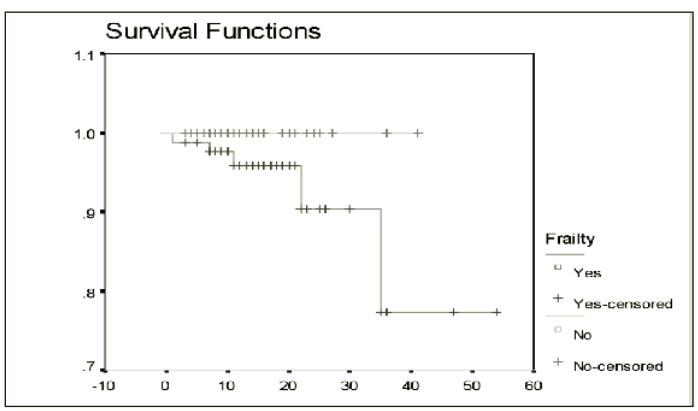
Table 3
Comparison of frail subjects with non-frail individuals (n = 250)

Characteristics	Frail (n = 83)	Non-frail (n =167)	Significance (p)
Age, mean± SD	67.57± 7.29	65.87± 5.64	0.06
Current or past smokers, n (%)	48(57.8%)	74(44.3%)	0.06
Males, n (%)	56(67.5%)	98(58.7%)	0.21
Diabetes mellitus, n (%)	18 (21.7%)	33 (19.8%)	0.74
Hypertension, n (%)	29 (34.9%)	67 (40.1%)	0.49
Years of Schooling (median with range)	5(0-18)	5(0-20)	0.65
Hb*, mean ± SD	10.54± 2.48	11.45± 1.94	0.002
Anemia, n (%)	69(83.1%)	121(72.5%)	0.08
MMSE Score*, mean± SD	24.22± 4.73	26.57± 3.41	<0.001
Cognitive impairment*, n (%)	16(19.3%)	4(2.4%)	<0.001
Active TB, n (%)	6(7.2%)	3(1.8%)	0.06
CHF*, n (%)	23(27.7%)	7(4.2%)	<0.001
Duration of hospital stay* (median with range)	14(1-54)	8(3-41)	<0.001
Number of deaths*, n (%)	5(6%)	0	0.004

The data is represented as mean + standard deviation or as number (percentage) or as median (range) wherever applicable. Hb = hemoglobin, MMSE = mini mental status examination; TB = tuberculosis; CHF = congestive heart failure. Data has been presented as number (percentage) or mean (+ standard deviation). * Indicates significant differences with p value < 0.05

The Kaplan Meier survival curves for the study participants are shown in figure 1.

Figure 1
Kaplan-Meier Survival curves for the study participants (n = 250)



Discussion

In the current study, 250 older patients (154 males and 96 females) with a mean age of 66.43 + 6.27 years, from medical wards, hospitalized for acute problems, were assessed for their frailty status by Fried's criteria.7 Of these, 83 (33.2%) patients were frail, with a rising trend of frailty with increasing age.

Incidence of frailty

The incidence of frailty has been found to be between 6.9 and 32% in different studies depending on the population studied and the criteria used (7, 22-24). Purser et al, studied hospitalized older patients with minimum two vessel-CAD, and found prevalence of frailty was 27% using Fried's criteria (24). Other authors also have found prevalence of frailty between 15% and in excess of 50% in older inpatients using other surrogate markers like cognitive dysfunction for measuring frailty (14). Prevalence of frailty in our patients was not very different, as compared to these studies.

Frailty and comorbid illness

Anemia is often regarded as a common occurrence with advancing age and the need of medical intervention in a pale, anemic older adult is often belittled (25). Anemia may contribute to a functional decline by reducing oxygen supply to the muscle, brain or heart and herald the frailty syndrome. Leng et al compared eleven frail with 19 non-frail community dwelling older persons and found significantly lower hematocrit and haemoglobin levels in those frail along with a higher level of interleukin 6 indicating a higher level of inflammation (26). Similarly, we report a higher incidence of normochromic normocytic anemia in hospitalized frail older individuals. Cognitive impairment has been found to co-exist with frailty and improve the reliability of the frailty model for predicting a poor outcome in frail community dwelling older patients (27, 28). Our data also indicate a close association of cognitive impairment as determined by mini-mental status examination among the frail hospitalized patients. Congestive heart failure has been the most extensively studied co-morbid illness with frailty and has lead to the promotion of specific disease management programs (29). Not only does the presence of frailty portend a poor short as well as a long-term outcome in subjects with heart failure but also negatively affects health related quality of life (30-32). In our study 27% of those frail were found to have symptomatic heart failure as compared to only 4% in the non-frail group indicating a strong association foretelling poorer prognosis.

Frailty and outcome

The current study indicates a significant association between frailty and poor outcome in hospitalized patients. Presence of frailty not only increases mortality but also prolongs hospital stay, which is likely to be associated with increased cost of treatment. Mitnitski et al studied 36,424 people aged 65 and

older in seven population-based and four clinical/institutional surveys in four developed countries and showed that increasing frailty index, measured in terms of increasing deficit accumulation is associated with increasing mortality (33). However, they measured frailty in terms of an index based on deficit accumulation in a retrospective manner, and a formal validated classification criterion to measure frailty was not used.

The current study is first of its kind, showing direct association of frailty, defined using formal validated criteria in hospitalized patients and increasing short term mortality during period of hospitalization as well as prolonged hospital stay.

In our study, the admitted patients had heterogenous diagnoses, which were not taken in to consideration while analysing outcomes and the primary disease could be a confounding factor in the demonstrated association of frailty with poor outcome. For the purpose of simplicity, frailty was treated as a binary outcome. It is possible that use of measures that depict frailty as a continuum might provide more insight in to association of frailty with individual diseases and outcome. Also, relationship between anemia and frailty by the specific type of anemia was not assessed in this study. Since patients were included only from medical wards from a tertiary care referral centre; generalization of results to other clinical settings could be difficult. In addition, presence of frailty, anaemia, dementia, CHF was assessed only at admission, while all these entities are dynamic during hospital course.

Conclusion

As the impact of advancing age is increasingly appreciated throughout individual families, economic and social systems, provision of accessible, effective and economic inpatient care for frail older people will become a key issue. This is now evident in view of almost one third of hospitalized older patients being frail, and their poor outcome not only in terms of mortality but also a prolonged hospital stay which will translate in to an increased cost of treatment. Screening of frailty in older inpatients might help frame dedicated patient care with better understanding of the medical complexity, prognosis, and risk of adverse outcomes in frail patients. Recognizing the frail or vulnerable elders with anemia, heart failure, cognitive impairment or tuberculosis at admission is crucial to help frame patient care and discussions with a better understanding of the medical complexity, prognosis, and risk of adverse outcomes.

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