CHAPTER – 1
FRAILTY

Introduction:

Though life expectancy has markedly increased due to improved health-care facilities, a global burden of aging population is also on the rise. Frailty is an inexorablepath of old age that ultimately escorts an individual to death. Aristotle described this phase as a period when the heatdispels from the body resulting in loss of coordination, balance and energy; illness,diminished strength, and ultimately the human capitulate to death (1). Frailty is an age-linked syndrome that is exemplified by increased vulnerabilityand reduced capability to perform physical activity (2). But it has to be remembered that ageing is allied with a ploddingdecline in the physical functioning, but there is difference in the rate of deterioration. Therefore, ageing cannot be essentially coupled with the process of frailty. Co-habitation of many chronic diseases and comorbidities that can negatively influence the normal functioning is generic midst older individuals. Nonetheless,it must be differentiated from the concept of frailty as the treatment approaches, outcome, and prognosisare different for both the cases.

The observations on frailty reinforce the prerequisite of improved understandingregarding the disparity in the capacity to perform tasks, resilience, and adverse outcomeamongst individuals of the same chronological age.An individual with this syndrome hasmoderated strength, enduranceand physiologic function. Furthermore, the condition isexacerbated by various stressors and leads to an increasing dependency oncaregivers to perform daily activities (3). The key features of frailty are cognitive impairment and physical unsteadiness, with

impreciselimitations between social and medical demands. This leads to falls,hospitalization, institutionalization, dependency andeventually death (4).

Background:

The Almagest, an ancient Mathematical Systematic Treatise, describes the humans at the end stage of life as "dispirited,weak, easily offended, and hard to please."Eli Metchnikoff, fondly called as the "father of gerontology", in 1908 had a question on how to transform in to old age under normal physiological condition without any pathological conditions (5). This question lead to various researches onaging and longevity; however, even almost a century later geriatriciansstruggle to define frailty.

Contradicting acommon belief that all elderly are weak,frailty syndrome is more often an age-related pathologic transformation (6).The rimsto differentiate age and frailty seem to be imprecise that it is commonlypresumed that at a particular age, everyone becomes frail. Physicians have frequently related the term frailty to label the feeblest andmost vulnerable subgroup of older adults. Conversely,'frail' is not an alternative term to describe the oldest of old adults nor any disability or comorbidity.Contemporaryresearches have attempted to describe the clinicaland physiological traits of frailty and to focus on the etiology for vulnerability of the frail, older adults.

In 1990s, the prevalence was 9.2% which is expected to surge up to 21.3% amongst the people of the global population, aged 60 years or older (7). The incidence of frailty increases with age,reaching more than 32% in those aged more than 90 years (8). Besides,if an individual is pre-frail, it indicates the downward spiral of the condition and they tend to become moreliable to develop frailty syndrome.

Definition:

Frailty can beequated to reduced functional reserves of multiple organ systems. This could be attributed to various factors such as any systemic disease, physicalinactivity, insufficient nutrient supplementation or stress.Precisely, frailty is an outcome of"excess demand imposed upon reduced capacity" (9).Frailty, once initiated, causes a rapid and progressive decline in physical and mental health,ultimately leading towards failure tothrive and death.

The WHO defined frailty as "a clinically recognizable state in which the ability of older people tocope with everyday or acute stressors is compromised by anincreased vulnerability brought by age-associated declinesin physiological reserve and function across multiple organsystems" (10).

Clinically, Fried et al defined frailty as "meetingthree out of five phenotypic criteria indicating compromised energetics (table 1): low grip strength,low energy, slowed waking speed, low physical activity, and/or unintentional weight loss" (11). He also proposed certain criteria to define this condition that encompassed the following factors:

- Walk time, as delineated by a 15-foot walk test.
- Grip strength, estimated by a dynamometer.
- Physical activity, measured by the MinnesotaLeisure Time Activity (MTLA) Questionnaire
- Exhaustion, measured by the Center for EpidemiologicStudies Depression Scale (CES-D Scale).
- Weight loss up to 10 pounds or 5% of total weight in the past1 year.

These criteria tactfully compute the manifestations of frailty, vitally the signs of sarcopenia, malnutrition by assessing the grip strength, and weight lossrespectively.

An individual must possess at least 3 among the 5 criteria to be diagnosed as frail.

Table 1: Criteria Used to Define Frailty

Criteria	Male		Female	
Weight Loss	Greater than 10 lbs or 5% of weight loss in the last year		Greater than 10 lbs or 5% of weight loss in the last year	
15-Foot Walk Time	Height ≤173 cm Height >173 cm	≥7 seconds ≥6 seconds	Height ≤159 cm Height >159 cm	≥7 seconds ≥6 seconds
Grip Strength	BMI ≤24 BMI 24.1-26 BMI 26.1-28 BMI >28	≤29 ≤30 ≤30 ≤32	BMI≤ 23 BMI 23.1-26 BMI 26.1-29 BMI >29	1≤7 ≤17.3 ≤18 ≤21
Physical Activity (MLTA)	<383 kcal/wk		<270 kcal/wk	
Exhaustion	A score of 2 or 3 on either question on the CES-D*			

*How often in the last week did you feel this way?

(a) I felt that everything I did was an effort.

(b) I could not get going.

0 =1 day; 1 =1-2 days; 2 =3-4 days; 3 =more than 4 days.BMI= body mass index

Adopted from: Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. JGerontolA BiolSciMedSci 2001;56(3):M146–M156

Natural history:

The idea of frailty is continuouslyadvancing, and there is an increasing deliberation regarding the etiology and progression of the disease.For over two decades, four importantfactors remained consistent while attempting to define the concept of frailty (12).

1. Frailty is multidimensional, with physical and psychosocial factors playing a vital role in its

pathogenesis.

2. Frailty is an extreme consequence of the normal ageing process and its prevalence increases with increase in age. However, the notion is not purely age-related, signifying on the negative and conventional opinion regarding the ageing process.
3. It is important to consider a frail individual's context, and therefore incorporate subjective perceptions. A frail individual can fluctuate between different states of severity of the condition.
4. The concept must credit the influence of both individual and environmental factors.

Interpreting theideas on thecommencement of frailty is essential to detect the individuals at high risk and to enable early intervention of those affected, at a stage where turning-around the condition is still feasible. Preclinical identification ofinitial manifestations of the frailty syndromenecessitates awareness and clear understanding regarding the natural history of frailty development and progression.

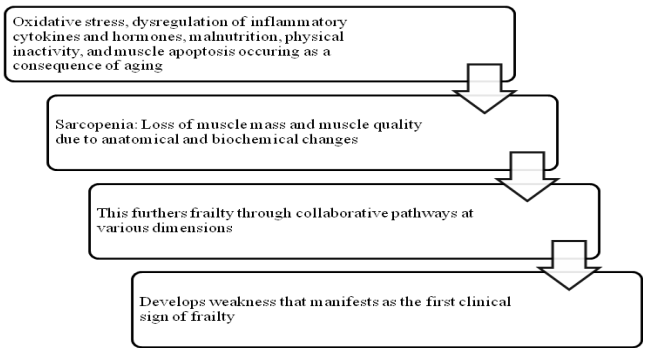
Xue QL in 2011 suggested two hypotheses to elaborate the natural history of frailty syndrome. The hypotheses are as follows (13):

1. The process of frailty might be instigatedby means of any of the clinical manifestations that can possiblyhasten a "vicious cycle" terminating in an amassed syndrome; and
2. Distinctearly manifestations couldpilot to varied rates of disease progression.

A 7.5-year longitudinal study comprising 420 WHAS II participants who were classified as non-frail at baseline based on Fried's phenotype suggested that weakness occupied the topmost position on the hierarchy of symptoms (Figure 1).Incidence of weakness, sluggishness,

andreduced activity headedtiredness and weight loss in 76% of the women who were non-frail at baseline (14).

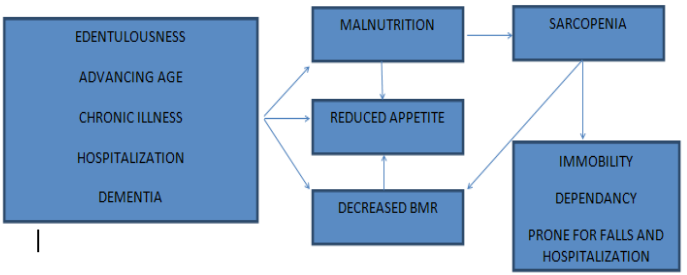
Figure 1: Explanation for weakness experienced by a frail individual



Factors influencing frailty:

Since it has already been established that frailty is multifactorial in etiology, many hypotheses emerged to find the various factorsassociated with the disease. Early researches revealed that the individuals lacked strength and balance, and this was considered to be the forecasters offrailty. But, during old age, many factorssuch asidleness, lessened appetite, malnutrition, and long-standing illness can lead to frailty. This preceded the development of the "frailty cycle" concept. This concept includes a systematic link between chronic malnutrituion, reduced apetitie, sarcopenia, and thus overall reduction in basal metabolic rate (BMR). All the above-mentioned factors are inter-related to each other and the end result will be a frail individual (Figure 2).

Figure 2: The frailty cycle



Association between frailty, disability and comorbidities:

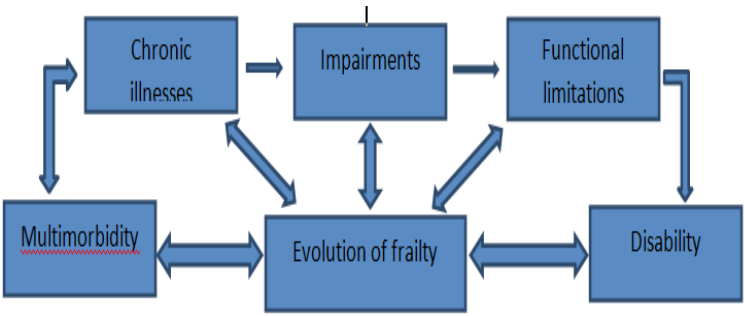
Most of the developed countries face a challenge of increasingolder adult population. It is considered as a challenge because older individuals fall prey to chronic illnesses, co-morbidities, various disabilities, and frailty. All these terminologies are very different from each other and yet possess certain similarities; therefore, these terms are often employed interchangeably.

The term multimorbidity can broadly be described as the "co-existence of two or more chronic conditions, where one is not necessarily more dominant than the other chronic conditions" (15). Comorbidity is defined as the "co-existence of certain medical conditions occurring in one individual in which an index disease occurs first" (16).Disabilitydenotes inconvenience and complexity whilecarrying out day-to-day activities that are obligatory to uphold an individual's life, such as eating, bathing, and toileting.

Nagi in the year 1991 developed the Disablement Process Model (DPM) that highlighted the similarities, differences and inter-relationship between the four above-mentioned terminologies. It encompasses a disease-disability pathway that includes four successive stages from 1) disease to

2) impairment to 3) functional limitation to 4) disability, all of which can contribute towards developing frailty in an individual (Figure 3). This framework implies that a disease process will cause impairments and this in turn leads to functional limitations. The limited functional movements of an individual will be succeeded by varying degree of disability. All of these factors, individually as well as sequentially will lead to evolution of frailty.

Figure 3: Association between multimorbidity, disability, and frailty



Epidemiology, prevalence and incidence:

Currently, frailty is thought to inhabit millions of older individuals globally, but the worldwide prevalence of this disease is not known up till now. This paradox can partially be contributed to the lack of research incorporating the population all over the world and the use of diversefunctional definitions of frailty in the various studies. Collard RM et al in 2012 estimated the prevalence of frailty to range anywhere between 4% and 59%. This vast range could mainly be due lack of standardisation of concepts or measures. The prevalence of frailty was computed to be 53% among long-term care residents, 5% to 29% among individuals with HIV infection, and 37% in patients with end-stage renal disease(18, 19, 20). Likewise, patients suffering from certain haematological malignancies

showed a prevalence rate of 42% (21).Furthermore, frailty was seen to be more prevalent in people of lower socio-economic groups, certain ethnic minorities such as African-American race and females (22, 23).

Predictors of frailty:

Old age, chronic illnesses, excessive alcohol consumption, allostatic load, sedentary lifestyle with reduced physical activity,obesity, excessive stress and depression, cognitive impairment, and lack ofsocial support are the predictors of developing frailty in future.Thechronic diseasesrelated tofrailty are cardiovascular diseases (CVD), pulmonary diseases, rheumatoid arthritis, and uncontrolled diabetes.

Except age, all the other predictors are modifiable and can be converted into signs of vitality if detected and treated at the initial stage. Early diagnosis and intervention of these predictors can reduce the risk of developing the disease.

Frailty scores/index:

Frailty index was given by Rockwood and Mitnitski in the year 2007 (24). The index scores were constructed on a comprehensive geriatric assessment by including the number of deficits accrued. The deficits were basically the predictors of frailty, and common geriatric syndromes other than frailty. The index comprises oftotalling the various signs, symptoms, disabilities, anddiseases to arrive at a score. The index scoring pattern is described below (24).

- Frailty index (deficit accumulation)
- Counts health deficits (at least 30), such as:
    - Signs
    - Symptoms
    - Diseases
    - Disabilities
    - Abnormal test results (example: laboratory, imaging, electrocardiogram)

Health deficits should meet these criteria:

- Represent multiple domains of functioning or multiple organ systems
- The prevalence must increase with age
- Not be too common before the age of 65 (early saturation)
- The prevalence should not be lower than 1%

Frailty score=sum of health deficits present divided by total number of deficits measured.

The scoring is rated between 0 and 1, where in higher scores indicate higher degree of frailty.

Prevention:

The measures to prevent frailty can be categorized into primary, secondary, and tertiary prevention.

- **Primary prevention:**

Identifying a pre-frail older individual with modifiable predictors of frailtysuch as sedentary lifestyle, malnutrition, and uncontrolled diabetes mellituscan essentially aid in preventing the disease at an early stage. Recognition of an older individual's gradualwaning of physical function and sarcopenic conditioncan aid aphysician to highlight on the necessity to change the lifestyle by practising regular exercise, and consuming healthy foods that have high nutritional value.

- **Secondary prevention:**

Identification of factors leading to frailty in an individual before developing severe problems such as unstable angina due to CVD canhelp a clinician to investigate about the aforesaid deficits. This will improve thepatient's compliance towards the medical treatments and health maintenance visits. When a clinician contemplates regarding the treatment options for various diseases or conditions,frailty plays a key role in predicting if the

patient will benefit from the treatment, and withstand the iatrogenic stress caused bythe procedures.

- **Tertiary prevention:**

Recognition of frailty in advance will aid the clinician to conscript the help of a comprehensive geriatric assessment team to amplify the possibility of functional recovery after any surgical procedure in an individual susceptible to frailty.

Summary:

Frailty is vastly prevalent and is related toaugmented health-care expenses. The worldwideinfluence of frailty is predicted to upsurge due to progressive increase in ageing population. Therefore, frailty should be focussed as a publichealth problem that needs immediate attention. Substantial development has been made in understanding the etiology, risk factors and methods of prevention of frailty in the pastdecades. Nevertheless, the conversion of these concepts from researchto clinical practice remains a challenge.Introduction more assessment tools and improvement in facilities to early diagnosis and primary prevention of the disease is mandated.

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