Correlates of Frailty in Old Age:

Falls, Underweight and Sarcopenia

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Dedications

To my geriatrics patients, their families, and their caregivers.

And to all the future geriatricians-to-be.

Also to my father who lived to the ripe old age of 85.

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Abstract

This thesis is focused on frailty in old age. The frailty syndrome is the newest geriatric syndrome and can be aptly called the ultimate geriatric syndrome due to the complexity of its causes and the wide range of adverse outcomes it may lead to in older persons. Several of the important correlates of frailty, namely falls, underweight and sarcopenia, are discussed in the context of their relationship with frailty. These entities are geriatric syndromes in their own rights, sharing many common risk factors and arriving at adverse health outcomes either directly or via the pathway of frailty. In the publications that arose from this work, the risk factors of falls, in particular the relationship between medications and chronic diseases in causing falls; risk factors and outcomes of sarcopenia, in particular its relation to diabetes mellitus and other chronic diseases; and how underweight poses survival risks in both community-living and institutionalized older people, are discussed. The final publication of this series of studies demonstrated the reversibility of the frailty syndrome, showing that not all who were in the pre-frailty stage will decline. Risk factors associated with improvement or decline in the pre-frail stage were identified in the local population, and a period of relative stability opened for possible interventions was observed. This thesis thus examines the complex interplay of these syndromes in old age. It is hoped that these publications will enable further research into the underlying mechanisms of frailty and to elucidate modifiable risk factors, hence enabling older people, in particular those in the pre-frail stage, to live healthier and longer lives.

List of abbreviations

ABI	Ankle-brachial index
ACEI	Angiotensin converting enzyme inhibitors,
ADL	Activities of daily living
ANCOVA	Analysis of covariance
ALM	Appendicular lean mass
ASM	Appendicular skeletal muscle mass
ASM/Ht^2	Height-adjusted appendicular skeletal muscle mass (ASM/Ht^2)
AWGS	Asia Working Group for Sarcopenia
BIA	Bioelectrical Impedance Analysis
BMI	Body mass index
CCB	Calcium channel blocker
CES–D scale	Center for Epidemiologic Studies Depression scale
CFS	Clinical Frailty Scale
CHS	Cardiovascular Health Study
CI	Confidence interval
COPD	Chronic obstructive pulmonary diseases
CSHA	Canadian Study of Health and Aging
CSI-D	Community Screening Instrument of Dementia
CT	Computerized Axial Tomography
DM	Diabetes mellitus
DXA	Dual X-Ray Absorptiometry

EWGSOP	European Working Group on Sarcopenia in Older People
GDS	Geriatric Depression Scale
GS	Gait speed
HOMA-IR	Homeostatis Model Assessment of Insulin Resistance
HR	Hazard ratios
HS	Handgrip strength
ICD	International Classification of Disease
IL-6	Interleukin-6
IWGS	International Working Group on Sarcopenia
LBP	Low back pain
MDS	Minimum Data Set
MDS/RAI	Minimum Data Set/Resident Assessment Instrument
MI	Myocardial infarction
MMSE	Mini-Mental State Examination
NS	Not significant
NSAIDs	Non-steroidal anti-inflammatory drugs
OR	Odds ratio
PASE	Physical Activity Scale of the Elderly
RAF	Relative abdominal fat
SAS	Statistical Analysis System
SD	Standard deviation
SES	Socio-economic status

SF-12	Short form 12 Quality of Life Score
SMI	Skeletal muscle index
SOF	Study of Osteoporotic Fracture
SPPB	Short Physical Performance Battery
SPSS	Statistical package for the social sciences
TNFα	Tumour necrosis factor α
UK	United Kingdom
US	United States
WHO	World Health Organization
WHR	Waist-hip ratio

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Chapter 1

Introduction

1.1 What are Geriatric Syndromes?

Geriatric syndromes are clinical presentations commonly seen in older people that are associated with adverse health outcomes or poor quality of living in late life. They are often not explicitly linked to any single disease but are the results of reduced reserve in multiple systems. (Tinetti et al., 1995) As a result, they may appear ill-defined, yet pose diagnostic challenges to clinicians because the presenting problem (e.g. delirium or a fall) may be related to a distant infection (e.g. urinary tract infection), rather than a primary problem in the brain. This is the basis of the so-called "atypical presentation" of illnesses in older patients. In addition, these syndromes often share similar sets of causes, which make their relationships to each other complicated.

1.2 Outcomes of Geriatric Syndromes

There are ample evidence that geriatric syndromes can predict mortality (Afilalo et al., 2009), institutionalization, prolonged hospitalization (Anpalahan & Gibson, 2008; Alarcón et al.,1999), and poor hospitalization, surgical or cancer treatment outcomes (Alarcón et al., 1999; Liu & Leung, 2000; Makary et al., 2010; Lee et al., 2010;

Extermann et al., 2005; Koroukian et al., 2010) in older people. (Kane et al., 2011; Inouye et al., 2007) The outcome of several geriatric syndromes will be specifically discussed in the following chapters.

1.3 Geriatric Syndromes as a Disease Model

If we try to classify geriatric syndromes according to models of diseases as described by Inouye et al. (Inouye et al., 2007), it would be obvious that they constitute the most complex model in which multiple intrinsic and extrinsic risk factors interact with each other, causing the older individual to present with one particular clinical phenotype, or presentation. It is therefore obvious that interventions at multiple levels have to be employed in order to prevent further decline, or revert the defect. One of the difficulties in geriatric medicine is that many of the risk factors are not reversible, such as old age and pre-existing organ degenerations, and that makes the study and management of geriatric syndromes much more complex than general adult medicine.

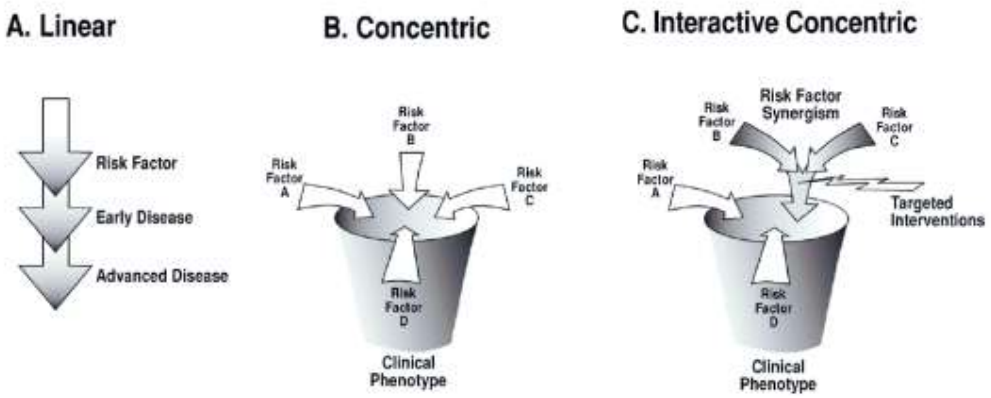

Figure 1.1 Different conceptual models of diseases or syndromes: adopted from: Inouye et al., 2007

1.4 Traditional and new geriatric syndromes

Geriatrics syndromes are not new concepts. Sir Bernard Isaac (1924-1995), a forerunner in British geriatric medicine, has coined the term “geriatric giants” or the Geriatric “I”s: immobility, instability (falls), incontinence and impaired intellect/memory. These, together with “iatrogenicity”, are the traditional geriatric syndromes.

However, in the recent one or two decades, new “giants” have emerged. Multiple morbidities, under-nutrition, sarcopenia, frailty, impaired homeostasis, chronic inflammation, pressure ulcer and functional decline are some of the more recently proposed geriatric giants. (Kane et al., 2011; Inouye et al., 2007) They too shared common risk factors which will be discussed below.

1.5 Underlying risk factors

Intrinsic factors

Ageing

Ageing as a natural process causes degeneration in biological systems, resulting in decline in vision, cognition, changes in body composition thus loss of body mass, decline in physical performance, and increase pain in degenerative joints. These degenerative processes will take place even in someone who suffers from no disease, and therefore is

free from any pathological processes. One example is the occurrence of cataracts, which, without intervention, will lead to diminished visual acuity, and put an older person at risk of falls. By the same token, degeneration of knee joints and age-related loss of muscle (sarcopenia) will predispose the person to limitations of mobility, loss of independent functioning in instrumental or basic daily care, falls, fractures, and even hospitalization secondary to injuries thus sustained.

Medical Illnesses

Pathological processes that a person has acquired as a result of genetic predisposition, unhealthy lifestyle, or injuries during the life course will aggravate the damages done to the individual during the natural ageing processes. An example is diabetes mellitus developed due to genetic tendency, unhealthy eating and the lack of exercise in the decades preceding old age. This will aggravate or accelerate cataract develop and lead to earlier risk of falls due to decline in vision. Its associated obesity will also accelerate the toll of knee osteoarthritis, leading to earlier physical limitations.

Extrinsic factors

Environment and drugs

Younger adults are able to compensate for environmental perturbations or risks by

adaptation. Older adults were less able to compensate due to marginal reserves in multiple systems, thus are more prone to adverse effects of extrinsic risk factors such as extremes of temperatures, insufficient lighting or obstacles during locomotion. They are also more prone to the adverse effects of medications due to reduced body water, thus reduced volume of distribution for water-soluble drugs; increased in body fat proportion, thus delayed clearance of drugs; and reduced liver and renal metabolism due to ageing or other diseases.

Social changes

Older adults are also more subjected to adverse social conditions such as social isolation, depression, poverty and limitation in food choices. Unhealthy lifestyle such as smoking would have been present for decades and damages to organs well-established. Regular physical exercise is often not possible due to musculoskeletal degeneration or cardio-pulmonary function decline. Maintaining exercise is difficult especially for older women who frequently did not acquire the habit in younger days.

In the following chapters, four geriatric syndromes and their complex inter-play in old age will be discussed.

Chapter 2

Falls

2.1 Introduction

Millions of people fall each day all over the world, and most of them would be toddlers. A fall can be part of the learning process for these very young children, or it can be a result of trying out new techniques, such as falls sustained while learning to ride the bicycle or skating. However, falls are very serious events in old age. Falls are one of the traditional geriatric syndromes, frequently also termed “instability”. Instability can result in falls, injuries, fractures, hospitalization, and occasionally death due to injuries or their complications. Instability can also be attributed to dizziness or syncope, which is another geriatric giant on its own.

2.2 Definition

A fall is defined as any unexpected loss of balance resulting in coming to rest on the ground or floor. Recurrent fallers were defined as those subjects with 2 or more falls in the past year.

2.3 Falls as a geriatric syndrome

Falls or instability is one of the traditional geriatric syndromes. It satisfies all the criteria of being one with a high prevalence rate in the older population, has multiple interacting risk factors, and results in many adverse outcomes in old age.

Prevalence

Approximately 18 to 60% of older community dwellers all over the world fall each year. (Ho et al., 1996; Hanlon et al., 2002; Cesari et al., 2002; Rubernstein & Josephson, 2002; Chu et al., 2005). Institutionalized elderly had an even higher prevalence of falls up to 45 – 70% per year. (Gryfe et al., 1977; Tinetti et al., 1987) Among the latter, fall rate differs between those with different mobility levels, with the bedridden having the lowest fall rate (4.1 per 100 person-years), increasing to 17.0 per 100 person-years in those who could ambulate by themselves. More mobile residents tended to have more serious fall-related injuries. (Thapa et al., 1996)

Outcomes

Not all falls in old age will result in serious injuries, but approximately 20% leads to soft tissue injury, 5% results in fractures, and 1% will sustain a hip fracture. (Tinetti et al., 1988; Chu et al., 2007; Kannus et al., 2005) Apart from the pain, subsequent surgical risk,