THE PREVALENCE, RISK FACTORS AND OUTCOMES OF FRAILTY IN ELDERLY CRITICALLY ILL PATIENTS

BY

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A dissertation submitted in fulfillment of the requirement for the degree of Master of in Medicine (Anaesthesiology)

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ABSTRACT

Frailty is a multidimensional syndrome of loss of physiologic and cognitive reserves resulting in increased vulnerability to adverse outcomes. This research sought to determine the prevalence, risk factors, outcomes of frailty and the association between frailty and outcomes of critically ill elderly patients in two ICUs. This study's purpose is to assess the applicability of the CFS and MFI as screening tools in guiding ICU admission of elderly patients. This is a two centre, prospective observational study of elderly critically ill patients. Inclusion criteria were ICU patients 60 years old and older, patients or family members were able to consent and patients admitted > 24 hours in ICU. The demographic variables were assessed as risk factors and clinical characteristics were analysed as outcomes. Correlation between CFS and MFI was investigated as well. Our results showed that 30 out of 58 (51.7%) of our patients were frail. MFI was significantly higher in frail patients. No significant risk factors and outcomes of frailty were detected. Mechanical ventilation and nosocomial infection were significantly associated with frailty as mechanically ventilated patients were 7.735 times more likely to be frail and patients with nosocomial infection were 6.685 times more likely to be frail compared to patients who were not inflicted with the corresponding outcomes. Conclusion: Around half of the elderly critically ill patients were frail and significant correlation between the CFS and MFI was established. Mechanical ventilation and nosocomial infection were significantly associated with frailty. Age, sex, ethnicity, marital status, level of education and living arrangement were not determined as risk factors of frailty. ICU LOS, hospital LOS, SAPS II, source of transfer to ICU, vasoactive therapy, mechanical ventilation, RRT, blood transfusion, tracheostomy, surgery, CPR limitation of therapy, self-extubation, reintubation, nosocomial infection and mortality were not recognized as outcomes of frailty.

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Medicine (Anaesthesiology).

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DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

Nur Khairunnisa Binti Abdul Aziz

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LIST OF ABBREVIATIONS

ACE-III	Addenbrooke's Cognitive Examination
ADL	Activity of Daily Living
AKI	Acute Kidney Injury
APACHE II	Acute Physiology and Chronic Health Evaluation Second Version
APACHE III	Acute Physiology and Chronic Health Evaluation Third Version
ARDS	Acute Respiratory Distress Syndrome
BMI	Body Mass Index
CFS	Clinical Frailty Scale
CNS	Central Nervous System
COVID-19	Coronavirus Disease 2019
CRBSI	Catheter Related Bloodstream Infection
CSHA	Canadian Study of Health and Aging
CSHA-FI	Canadian Study of Health and Aging Frailty Index
CVA	Cerebrovascular Accident
DSM-III-R	The Revised Third Edition of The Diagnostic and Statistical Manual of Mental Disorders
DVT	Deep Venous Thrombosis
ECMO	Extracorporeal Membrane Oxygenation
ED	Emergency Department
EFS	Edmonton Frailty Scale
FI	Frailty Index
FI-LABS	Laboratory Frailty Index
FP	Frailty Phenotype
GFI	Groningen Frailty Indicator
HAP	Hospital Acquired Pneumonia
HRPB	Hospital Raja Permaisuri Bainun
ICU	Intensive Care Unit
LOS	Length of Stay
MCI	Mild Cognitive Impairment
MCO	Movement Control Order
MFI	Modified Frailty Index
MI	Myocardial Infarction
MMSE	Mini Mental State Examination
MODS	Multiple Organ Dysfunction Score
MOH	Ministry of Health
NSQIP	American College of Surgeons National Surgical Quality Improvement Program
OT	Operation Theatre
PE	Pulmonary Embolism
PSQI	Pittsburgh Sleep Quality Index
RRT	Renal Replacement Therapy
SAPS II	Simplified Acute Physiology Score Second Version
SAPS III	Simplified Acute Physiology Score Third Version

SASMEC @ IIUM	Sultan Ahmad Shah Medical Centre
SD	Standard Deviation
SOFA	Sequential Organ Failure Assessment
SSI	Surgical Site Infection
UN	United Nations
UTI	Urinary Tract Infection
QOL	Quality of Life
VIP	Very Old Intensive Care Patient (≥ 80 Years)
VIP1 study	The Impact of Frailty on ICU and 30-Day Mortality and The Level of Care in Very Elderly Patients (≥ 80 Years) By Flaatten Et Al (Flaatten et al., 2017)
VIP2 study	The Contribution of Frailty, Cognition, Activity of Daily Life and Comorbidities on Outcome in Acutely Admitted Patients Over 80 Years in European ICUs By Guidet Et Al (Guidet et al., 2020)
VO_2 max	Maximum Oxygen Consumption

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Frailty is a term widely used to describe a multidimensional syndrome of loss of physiologic and cognitive reserves which give rise to increased risk of vulnerability to adverse outcomes (Rockwood, 2005). These outcomes include susceptibility to acute illness, incident falls, disability, unplanned hospital admissions, perioperative complications, need for institutional care, and death (Dasgupta, Rolfson, Stolee, Borrie, & Speechley, 2009; Kristjansson et al., 2010; D. H. Lee, Buth, Martin, Yip, & Hirsch, 2010; J. S. Lee et al., 2011; Makary et al., 2010; Rockwood et al., 2005; Rockwood, Song, & Mitnitski, 2011; Sundermann et al., 2011).

Although there are no definite consensus for the definition of frailty syndrome (Fried et al., 2001; Xue, 2011), the frailty phenotype (FP) is widely used as a measure of frailty which includes the presence at least three of the following features: unintentional weight loss of more than 4.5kg over the past one year, self-reported exhaustion, low physical activity, slow walking speed, and decreased grip strength (Fried et al., 2001):

There are numerous scoring systems developed as an effort to recognise frailty. A systematic literature review has identified a few identifying factors used to define and screen for frailty, which includes assessment on physical function, gait speed or mobility, cognition, weight loss or body mass index (BMI), physical activity, activities of daily living (ADLs), health problems, instrumental ADLs, nutrition, level of energy, self-rated health issues, urinary incontinence, age, and use of health services (Sternberg, Wershof Schwartz, Karunananthan, Bergman, & Mark Clarfield, 2011). One of the

assessment tools used to evaluate frailty is the Canadian Study of Health and Aging Frailty Index (CSHA-FI) which consist of 70 items. The CSHA-FI was developed from the first stage investigation of the Canadian Study of Health and Aging (CSHA-1) (Rockwood et al., 2005). This particular study was initiated in 1991 and recruited a total of 10,263 people who were 65 years and older (Rockwood et al., 2005) with the aim of determining the important health issues and epidemiology of cognitive impairment in elderly Canadians (Canadian Medical Association, 1994).

Another assessment tool used to define frailty is the Clinical Frailty Scale (CFS) which was developed by the authors of CSHA-FI. The CFS is a 9-point validated tool (Figure 1.1) developed to stratify the general level of fitness or frailty in the elderly using simple clinical descriptors following evaluation by health care professionals (Dalhousie University, 2007-2009; Rockwood et al., 2005). The CFS was initially developed in 2005 as a 7-point frailty scale which was derived from the second stage of the Canadian Study of Health and Aging (CSHA-2) from the assessment of the same cohort of CSHA-1 (Rockwood et al., 2005), and was expanded into a 9-point scale in 2007 (Dalhousie University, 2007-2009; Geriatric Medicine Research, 2007-2007). The authors of the CFS have stated that a score of more than 4 represents frailty which ranges from mild, moderate, severe or very severe by comparing scores from CFS with other validated tools which measure function and comorbidity to indicate level of frailty (Rockwood et al., 2005). The CFS is commonly used due to its relative simplicity ("Canadian Study on Health & Aging, Revised 2008.," ; Rockwood et al., 2005) and has been validated to be used in a variety of community health care and hospital settings (Faller et al., 2019). The CFS has been shown to be a reliable frailty assessment tool in critically ill patients as well (Pugh, Thorpe, & Subbe, 2017; Shears et al., 2018).

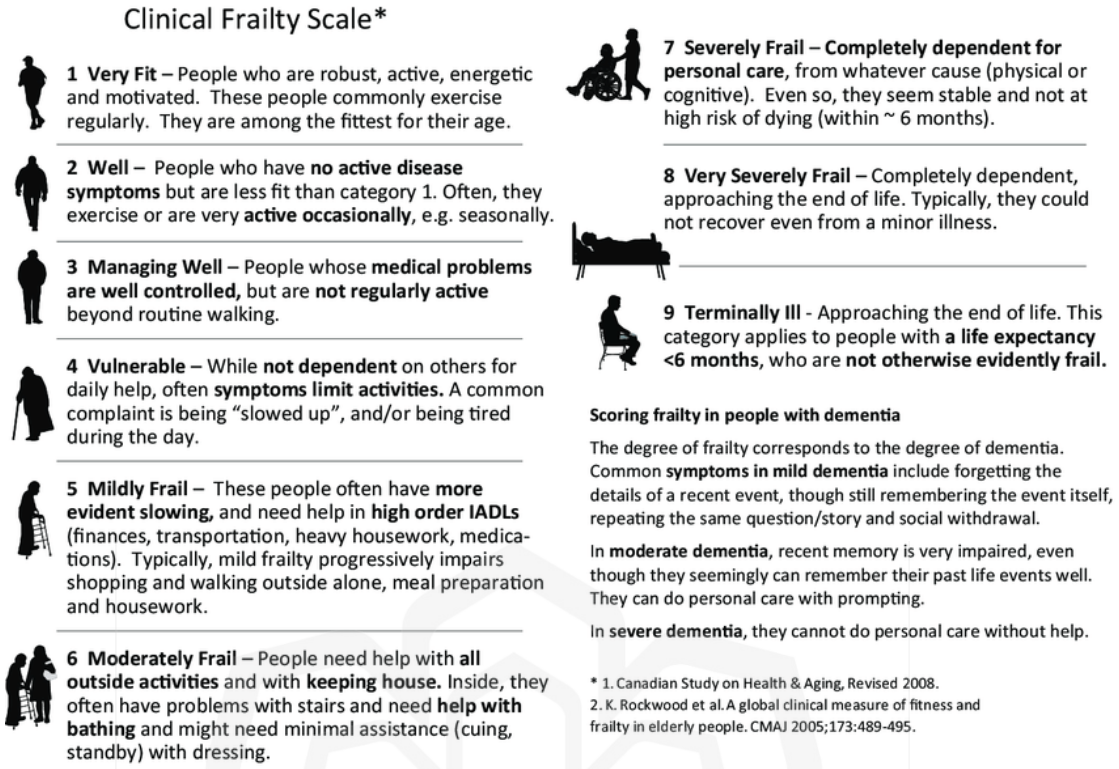

Figure 1.1 The Clinical Frailty Scale (CFS) (Geriatric Medicine Research, 2007-2007)

Another frailty index (FI) available is the Modified Frailty Index (MFI) which was developed to predict postoperative complications in elderly patients (older than 60 years) who underwent general emergency surgery. The MFI was created by comparing the 70 items in the CSHA-FI with variables measured in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) dataset from 2005 to 2009 and evaluated data from 35,344 patients who were older than 60 years. The purpose of its development was to reduce the time required to assess for frailty in the acute care setting. The MFI consists of 11 variables (Table 2.2) and the presence of each variable is scored as 1 point. The MFI score is obtained by tabulating the total points scored and the MFI for each patient is then determined by dividing the number of scores with 11 (total number of MFI variables). The lowest score, 0 (MFI 0) signifies absence

of frailty and the highest positive score, 11 (MFI 1) specifies maximum frailty. The authors described the values of the MFI as a scale and did not specify a cut-off value which would determine the presence of frailty (Farhat et al., 2012). The MFI has also been validated for all surgical specialties (Adams et al., 2013; Karam, Tsiouris, Shepard, Velanovich, & Rubinfeld, 2013; Tsiouris et al., 2013; Velanovich, Antoine, Swartz, Peters, & Rubinfeld, 2013).

The prevalence of frailty increases with increasing age (Fried et al., 2001; Rockwood et al., 2011) and the number of elderly patients admitted to intensive care units (ICUs) had been increasing with improvements in the medical and surgical fields and with increased life expectancy (Blot et al., 2009; Ihra et al., 2012; Kvale & Flaatten, 2002). This would result in an increase of ICU patients with pre-existing frailty (Bagshaw et al., 2009). The presence of reduced physiologic reserves in frail elderly individuals leads to diminished ability to adapt and respond to external stressors, such as in the case of a critical illness, and this would further lead to adverse clinical events and outcomes (Bagshaw & McDermid, 2013). This particular event of accumulation of functional deficits causing deterioration in an individual's condition has been described as an 'avalanche-like destruction of the organism' (Mitnitski, Mogilner, MacKnight, & Rockwood, 2002). Several studies have shown that intermediate survival and functional recovery is significantly affected by premorbid functional status (Goldstein, Campion, Thibault, Mulley, & Skinner, 1986; Orwelius et al., 2010; Roch et al., 2011; Sligl, Eurich, Marrie, & Majumdar, 2011). This indicates the importance of physiologic reserve, and recovery from critical illness may either be significantly prolonged or impossible when reserve is depleted (Bagshaw & McDermid, 2013).

As per the United Nations' (UN) criteria, the elderly population are people 60 years old and older (United Nations). By that definition, the elderly population in

Malaysia is expected to increase to 3.3 million by the year 2020 (Mafauzy, 2000). With the majority of elderly Malaysian population diagnosed with chronic illnesses (Sherina, Rampal, & Mustaqim, 2004), it can be predicted that Malaysia will have an increase in frail elderly patients as well.

The number of ICU beds in Ministry of Health (MOH) hospitals are highly limited, as there are only 668 beds in the whole country, with some centres even having as low as two ICU beds (Tai, Lim, Nor, Ismail, & Ismail, 2017). From these numbers, there is an estimate of 2.1 functional ICU beds per 100,000 of the Malaysian population (Malaysia, 2017). In view of these limited resources, there is an unavoidable necessity to select patients for ICU admission.

1.2 STATEMENT OF THE PROBLEM

A recent systematic review and meta-analysis on the impact of frailty on intensive care unit outcomes have concluded that frail patients have increased risk of mortality and adverse outcomes, including longer hospital length of stay (LOS), less likely to be discharged home and reduced quality of life (QOL). Interestingly, the article found no significant difference in regards to duration of ICU stay, requirement of mechanical ventilation and requirement of vasopressors (Muscedere et al., 2017). According to the latest Malaysian Registry on Intensive Care Report, the average age for all ICU patients was 46.0 years (median 47.9 years) and the average age at admission was 49.6 years (median 51.0 years) for adults (≥ 18 years old) with 18.6% of in-ICU and 26.2% of in-hospital mortality rates (Tai et al., 2017). However, no published data is available on the percentage of elderly patients (≥ 60 years old) in our Malaysian ICU or their mortality rates compared to the general ICU population.

1.3 PURPOSE OF THE STUDY

Currently, there are no published Malaysian data on the prevalence, risk factors and outcomes of frailty in elderly critically ill patients. The purpose of this study is to investigate these topics which have not been researched on previously with the main purpose of assessing the applicability of the CFS and MFI as screening tools to guide decisions for ICU admissions, especially in elderly patients. The selection of both screening tools was based on their ease of use, applicability in the acute and critical care setting and their reliability (Ali, Schwalb, Nerenz, Antoine, & Rubinfeld, 2016; "Canadian Study on Health & Aging, Revised 2008.," ; Faller et al., 2019; Hodari, Hammoud, Borgi, Tsiouris, & Rubinfeld, 2013; Pugh et al., 2017; Shears et al., 2018). Additionally, both screening tools were specifically created for the elderly population (Farhat et al., 2012; Rockwood et al., 2005) and have been validated in numerous studies (Ali et al., 2016; Darvall, Greentree, Braat, Story, & Lim, 2019; Faller et al., 2019; Guidet et al., 2020; Hamidi et al., 2019; Hodari et al., 2013; Montgomery et al., 2019). Moreover, both can be assessed from interviews with the primary carers and from medical notes in situations where direct assessment from the patients are not feasible. Other frailty assessment tools such as the CSHA-FI (Rockwood et al., 2005) and FP (Fried et al., 2001) requires self-reporting by the participants which is not always applicable in the critical care setting.

1.4 RESEARCH OBJECTIVES

This research aimed to achieve the following objectives:

1. To determine the prevalence of frailty in elderly critically ill patients.
2. To determine if age, sex, ethnicity, marital status, level of education, pre-admission residence and living arrangement are risk factors for frailty in elderly critically ill patients.
3. To determine if ICU LOS, hospital LOS, Simplified Acute Physiology Score second version (SAPS II), MFI, source of transfer to ICU, vasoactive therapy, mechanical ventilation, renal replacement therapy (RRT), blood transfusion, tracheostomy, surgery, cardiopulmonary resuscitation (CPR), limitation of therapy, self-extubation, reintubation, nosocomial infection and mortality are outcomes of frailty in elderly critically ill patients.
4. To determine the association between frailty and outcomes of elderly critically ill patients.

1.5 RESEARCH QUESTIONS

This research was conducted to answer the following questions:

1. What is the prevalence of frailty in elderly critically ill patients?
2. What are the risk factors of frailty in elderly critically ill patients?
3. What are the outcomes of frailty in elderly critically ill patients?
4. What is the association between frailty and outcomes of elderly critically ill patients?

1.6 THEORETICAL FRAMEWORK

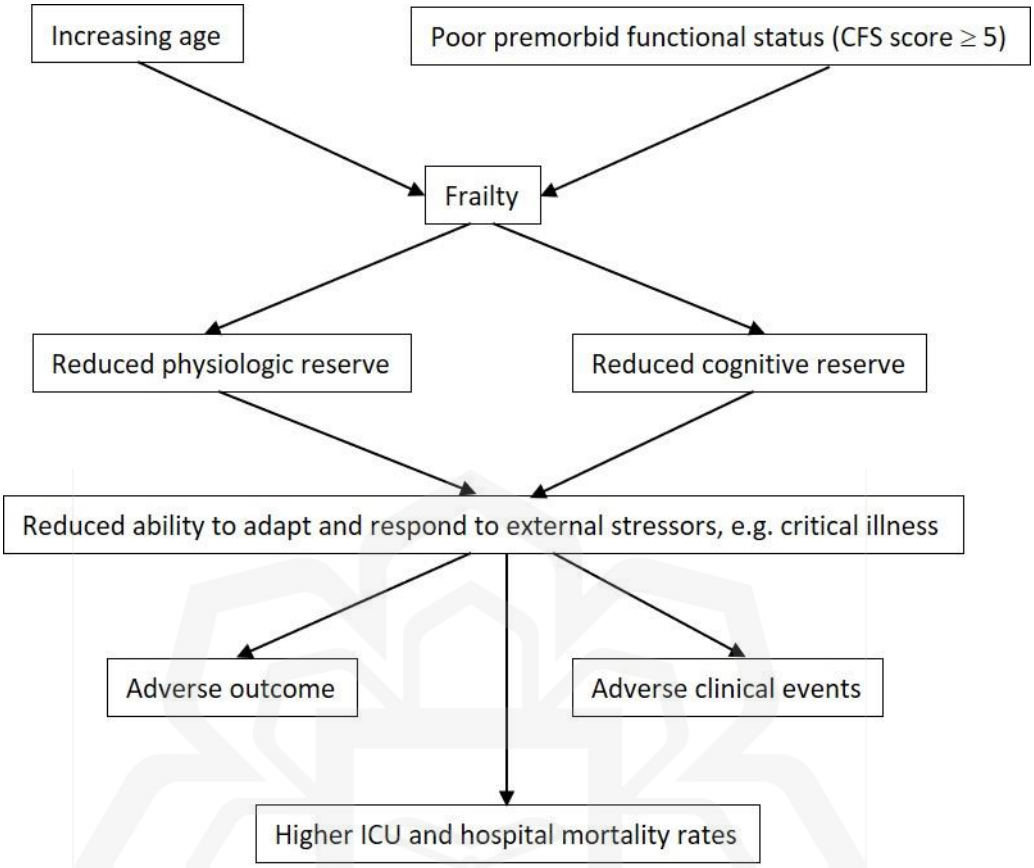

Figure 1.2 Theoretical Framework

1.7 RESEARCH HYPOTHESES

It is hypothesized that the prevalence of frailty in elderly critically ill patients is around 20-30%. It is also hypothesized that the risk factors for frailty in elderly critically ill patients are older age, male, Malay ethnicity, never married, no formal education received, living at assisted living residence, and living alone prior to hospital admission. Additionally, it is hypothesized that frail elderly critically ill patients have worse outcomes that their non-frail counterparts.

1.8 SIGNIFICANCE OF THE STUDY

The aim of this study is to determine the prevalence, risk factors and outcomes of frailty in elderly critically ill patients, and additionally to determine the association of frailty with outcomes in this particular patient group, as this topic have not been previously investigated in our Malaysian population.

The findings of this study will help guide our patient selection in regards to which patient will benefit most from ICU admissions for the purpose of better resource allocations, especially in the case of limited ICU beds.

1.9 DEFINITIONS OF TERMS

Elderly

People who are 60 years old and older (United Nations).

Critically ill patients

Patients who require admission to the ICU.

Frailty

Frailty is defined as a decrease reserve in multiple physiologic systems, resulting in reduced resistance to withstand stressors (Fried et al., 2001). In this study, it is defined with a CFS score ≥ 5 (Geriatric Medicine Research, 2007-2007; Rockwood et al., 2005).

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1.10 CHAPTER SUMMARY

This chapter introduces the concept of frailty and its association with age. It also includes the theoretical framework to correlate between frailty and the issues addressed by this study. Explanation on the study's significance is included in this chapter as well. This chapter also outlines the study objectives, research questions and hypotheses.

CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION

This study aimed to determine the prevalence, risk factors and outcomes of frailty in elderly critically ill patients which have not been previously investigated in our Malaysian population. Therefore, the literature review includes the concept and definition of frailty, association between frailty and critical illness and studies which studied the validity and reliability of the CFS and the MFI as frailty assessment tools. The review also includes frailty associated studies conducted in the Malaysian population.

2.2 THE CONCEPT OF A COMPLEX BIOLOGICAL SYSTEM AND PHYSIOLOGIC RESERVE

The human physiologic framework consists of a complex biologic system that is able to tolerate and adjust to various external insults (Varela, Ruiz-Esteban, & Mestre de Juan, 2010). However, events such as injury, disease and aging affect the ability of the system to sense changes to its baseline state and restricts the system's capability to adapt those changes. As a result, the system becomes less complex, less adaptive and less resilient, leading to increased susceptibility to insults such as injury or acute illness. This condition has been inferred to as diminished or loss of 'physiologic reserve' (Bagshaw & McDermid, 2013).